

Conformational equilibria of (E)-6-bromo-7-hydroxy-3,7-dimethyl-2-octene

Citation for published version (APA):

van Dommelen, M. E., Ven, van de, L. J. M., Buck, H. M., & Haan, de, J. W. (1981). Conformational equilibria of (E)-6-bromo-7-hydroxy-3,7-dimethyl-2-octene. *Recueil des Travaux Chimiques des Pays-Bas*, 100(5), 180-184. <https://doi.org/10.1002/recl.19811000504>

DOI:

[10.1002/recl.19811000504](https://doi.org/10.1002/recl.19811000504)

Document status and date:

Published: 01/01/1981

Document Version:

Publisher's PDF, also known as Version of Record (includes final page, issue and volume numbers)

Please check the document version of this publication:

- A submitted manuscript is the version of the article upon submission and before peer-review. There can be important differences between the submitted version and the official published version of record. People interested in the research are advised to contact the author for the final version of the publication, or visit the DOI to the publisher's website.
- The final author version and the galley proof are versions of the publication after peer review.
- The final published version features the final layout of the paper including the volume, issue and page numbers.

[Link to publication](#)

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal.

If the publication is distributed under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license above, please follow below link for the End User Agreement:

www.tue.nl/taverne

Take down policy

If you believe that this document breaches copyright please contact us at:

openaccess@tue.nl

providing details and we will investigate your claim.

The copper atom is coordinated by one oxygen and one nitrogen atom of the bidentate **ap** and four chlorine at positions: x_1, y_1, z_1 ; x_2, y_2, z_2 ; $x_1, y_1, -1 + z_1$, and $-x_2, \frac{1}{2} + y_2, \frac{1}{2} - z_2$.

Table IV Intermolecular hydrogen bond lengths (Å) and bond angles (°)^a.

	bond length	bond angle
O(A)—Cl(1)	3.20(1)	166(1)
O'(A)—Cl'(1)	3.20(1)	166(1)
O(B)—Cl(1)	3.18(2)	
O(C)—Cl'(1)	3.04(1)	
N(A)—Cl(2)	3.25(1)	157(1)
N'(A)—Cl'(2)	3.25(1)	157(1)
N(A)—Cl'(2)	3.54(1)	137(1)
N'(A)—Cl(2)	3.54(1)	137(1)
N(B)—Cl(2)	3.21(1)	
N(B)—Cl'(1)	3.52(1)	
N(C)—Cl(1)	3.05(1)	
N(C)—Cl'(2)	3.45(1)	

^a The atoms of the inverted form of A are called X'(A).

Inspection of Figs. 2 and 3 shows that the copper coordination corresponds to distorted octahedra of chlorine atoms and bidentate ligands A, B and C. The atoms O, N, Cl(1) and Cl(2) constitute a distorted square-planar coordination about the copper atom. The average deviations from the least-squares planes through Cu, O, N, Cl(1) and Cl(2) for the cases A, B and C are 0.12, 0.08 and 0.26 Å, respectively. In all cases the coordination about Cu is completed by the atoms Cl'(1) and Cl'(2), which are relatively well removed, *viz.* 2.993(1) and 3.181(1) Å, respectively from the Cu centre.

Moreover, these bonds are not colinear (deviation 10°) and the total coordination of Cu can be seen as a *Jahn-Teller* distorted octahedron.

In the $P2_1/c$ part, both enantiomorphic forms of **ap** are present in the structure. Notwithstanding the use of a racemic mixture of R- and S-**ap** in the preparation of the coordination compound, only D- or L-isomers of **ap** occur within the $P2_1$ part of the B and C forms (see torsion angles in Table III).

All chlorine atoms are shared between different coordination octahedra, which form slabs parallel to (100). The octahedra in a slab alternately share edges and corners. The chlorine atom Cl(2) involved in the (single) corner coupling has Cu—Cl distances of 2.247(1) Å in its "own" octahedron and a long Cu—Cl distance of 3.181(1) Å in the neighbouring octahedron. The chlorine atom Cl(1) involved in the edge coupling has distances of 2.273(1) Å in its "own" octahedron and a distance of 2.993(1) Å in the neighbouring octahedron. The packing in the slab is fortified by O—H.....Cl and N—H.....Cl hydrogen bridges with distances varying between 3.04 and 3.54 Å (see Table IV and Fig. 3). Table IV reveals that the hydrogen bridges in the alternative structures of the minor forms B and C are shorter, *e.g.* O(A)—Cl(1) = 3.20 Å, while O(B)—Cl(1) = 3.18 Å and O(C)—Cl(1) = 3.04 Å. An intramolecular hydrogen bond between the hydroxyl group and the amine group is not present. The network has a herring-bone pattern.

Acknowledgement

The authors wish to thank Dr. G. C. Verschoor for his advice during this investigation.

Conformational equilibria of (*E*)-6-bromo-7-hydroxy-3,7-dimethyl-2-octene*

M. E. van Dommelen, L. J. M. van de Ven, H. M. Buck and J. W. de Haan

Laboratories of Organic Chemistry and of Instrumental Analysis, Eindhoven University of Technology, The Netherlands

(Received April 2nd, 1980)

Abstract. The ¹H NMR spectral parameters of the title compound have been determined in cyclohexane-*d*₁₂ and *p*-dioxane-*d*₈ solutions by means of high-frequency NMR. The results are interpreted in terms of conformational equilibria.

Linear Electric Field (LEF) effects may play a major role in explaining the differences between the ¹³C NMR chemical shifts of the title compound and those of the model (*E*)-2,6-dimethyl-2,6-octadiene. Some preliminary calculations of the LEF-induced shifts are presented, as well as the problems involved in the recognition of the LEF contributions to the experimental shift differences.

Introduction

In a previous paper¹ we described the tentative conformational analysis of 3-bromo-2-hydroxy-2,3-dihydrosqualene (1) and of the corresponding derivative (2) of 2,6-dimethyl-2,6-octadiene (3) by means of ¹³C NMR. Special attention was given to the sizeable changes in ¹³C NMR chemical shifts at the positions C(6') and C(7') upon substitution at C(2') and C(3') of squalene and of 2,6-dimethyl-2,6-octadiene. (See Fig. 1). A number of possible explanations were offered. In this study we describe the continued conformational analysis of 2 in cyclohexane-*d*₁₂ and *p*-dioxane-*d*₈ by means of high-frequency ¹H NMR.

Experimental

The syntheses and ¹³C-spectral assignments of compounds 1 and 2 are described in ref. 1.

The ¹H NMR spectra were measured at 360 MHz in 5 mol% solutions in cyclohexane-*d*₁₂ and in *p*-dioxane-*d*₈.

* Part III of "A ¹³C NMR Study of Squalene". Preceding part M. E. van Dommelen, L. J. M. van de Ven, H. M. Buck and J. W. de Haan; Rec. Trav. Chim. Pays-Bas 96, 295 (1977).

¹ M. E. v. Dommelen, L. J. M. v. d. Ven, H. M. Buck and J. W. de Haan, Recl. Trav. Chim. Pays-Bas 96, 295 (1977).

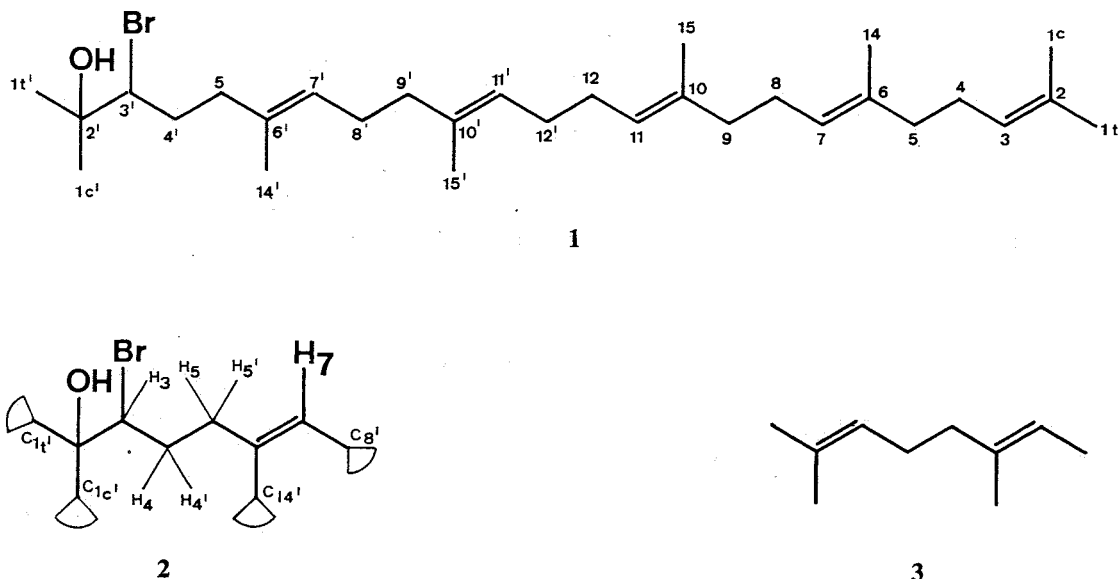


Fig. 1. Structural formula of 1, 2 and 3.

Spectral assignments

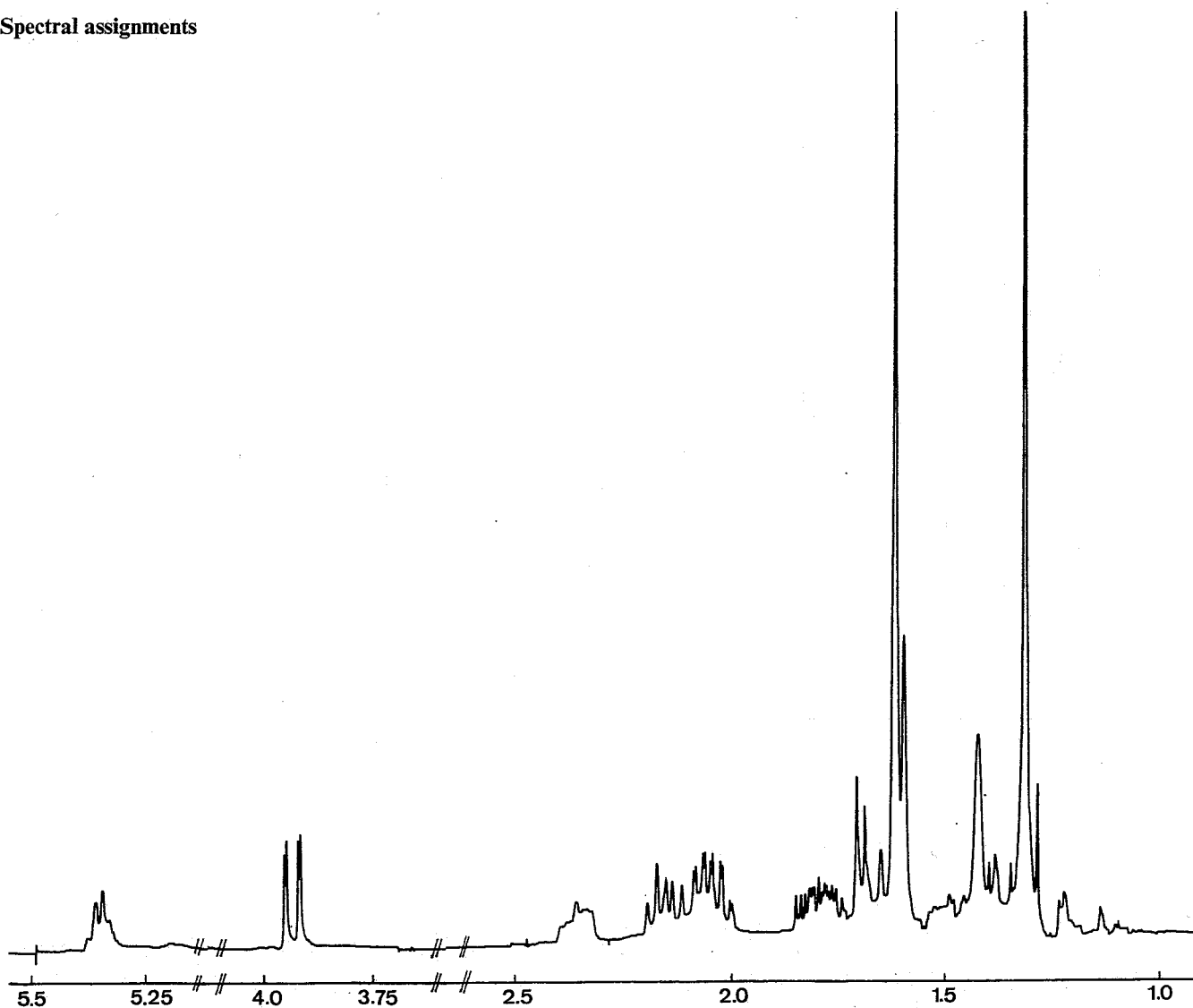


Fig. 2. 360 MHz ^1H NMR spectrum of 2 in cyclohexane- d_{12} .

The spectrum, depicted in Fig. 2, consists of an olefinic signal at 5.34 ppm with a broadened quadruplet structure, H(7), a doublet of doublets at 3.93 ppm assigned to H(3), four multiplets, each comprising the signal of one proton, found

between 2.5 and 1.7 ppm and finally, four methyl signals, two near 1.6 ppm (one doublet and a broadened singlet) and two near 1.32 ppm (broadened singlets). The latter signals can be ascribed to the C(1 t') and C(1 c') methyl groups. The

doublet near 1.6 ppm belongs to methyl group C(8') and the singlet to methyl group C(14'). The multiplets between 2.5 and 1.7 ppm were assigned by means of a combination of decoupling experiments. The doublet of doublets of H(3) shows splittings of *ca.* 1.8 Hz and *ca.* 11.5 Hz. Irradiation of the signal of H(3) removes a coupling of 1.8 Hz from the signal at δ 2.05 ppm and a coupling of 11.5 Hz from the multiplet at δ 1.81 ppm. The signals at δ 2.05 and at δ 1.81 were, therefore, assigned to the protons at carbon C(4') and the remaining signals at δ 2.16 and at δ 2.37 to the protons at C(5').

A number of decoupling experiments were carried out by irradiating the signals of H(4), H(4'), H(5) or H(5') while observing those of the other three. Irradiation of the allylic methyl signals near 1.6 ppm results in a remarkable sharpening of the multiplet at δ 2.37 ppm. This points to homo-allylic spin-spin coupling between the protons of the methyl group C(8') and one of the allylic protons at C(5'); the other signal at δ 2.16 ppm is not affected within the resolving power of the instrument. Rough values of all coupling constants of the set of protons H(3), H(4), H(4'), H(5) and H(5') were taken from the spectra (fully coupled). The spectra were subsequently simulated by means of the TWOSUM² program after which the final values were obtained after assignment and iterations. Results are given in Tab. I.

Table I ¹H NMR data of compounds 2 and 3

	Chemical shifts (δ)			Coupling constants (Hz)			
	2 ^a	2 ^b	3 ^a		2 ^a	2 ^b	3 ^a
H(1t)	1.32		1.66	J_{34}	+11.48	+11.26	6.9
H(1c)	1.32		1.58	$J_{34'}$	+ 1.80	+ 1.60	6.9
H(3)	3.93	3.98	5.13	J_{45}	+ 4.64	+ 4.25	6.5 \pm 0.5
H(4)	1.81	1.89	2.08	$J_{4'5'}$	+ 7.97	+ 7.66 ⁵	6.5 \pm 0.5
H(4')	2.05	2.28	2.08	$J_{4'5}$	+ 8.15	+ 8.45	9 \pm 0.5
H(5)	2.37	2.46	1.98	$J_{45'}$	+ 8.27	+ 8.34	9 \pm 0.5
H(5')	2.16	2.25	1.98	$J_{78'}$	\approx 6		6.6
H(7)	5.34		5.22	$J_{58'}$	1.5 \pm 0.5		—
H(8')	1.61		1.55	$J_{5'8'}$	\approx 0		—
H(14')	1.62		1.58	$J_{44'}$	-14.47	-14.41	—
				$J_{55'}$	-13.92	-13.97	—

^a In cyclohexane-*d*₁₂. ^b In *p*-dioxane-*d*₈.

The spectrum of 2 in *p*-dioxane solution was analysed in the same way (see Tab. I), except that, by chance, the solvent effects on the protons H(4') and H(5') were such that their chemical-shift difference amounts to only 0.03 ppm. This renders the spectrum quite complex, even at 360 MHz, so no values of the coupling constants of H(4), H(4'), H(5) and H(5') could be taken directly from the spectra. Instead, simulations were initiated, taking coupling constants of the cyclohexane solution as starting values.

Decoupling of the allylic methyl group yielded no conclusive results. The signals belonging to H(3), H(4) and H(4') have a width of *ca.* 1.4 \pm 0.2 Hz (in cyclohexane and in *p*-dioxane) while those belonging to H(5) and H(5') have widths of *ca.* 2.7 \pm 0.3 Hz (the spectra show widths of 4.4 Hz \pm 0.3 of which *ca.* 1.7 Hz is due to non-coincidental single lines). We have, as yet, no explanation for this, and can only point out that it is not due to coupling with either H(7) or H(3).

Discussion

Part A

The possible conformations around the successive bonds C(2')-C(3'), C(3')-C(4') and C(4')-C(5') are shown in Figs. 3, 4 and 5 respectively.

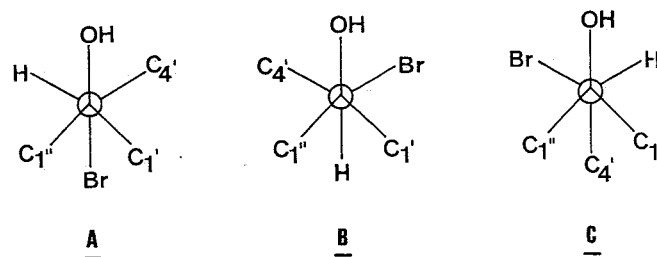


Fig. 3. Conformations around C(2')-C(3') in 2.

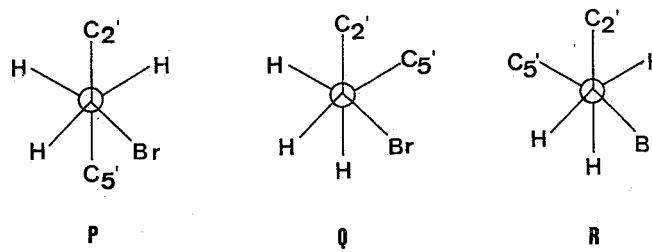


Fig. 4. Conformations around C(3')-C(4') in 2.

Conformations A, B and C (Fig. 3) cannot be distinguished by ¹H NMR. Arguments based on steric energy considerations point to the presence of A and B¹. Similarly, a single conformation around C(3')-C(4') was previously selected¹, i.e. P (see Fig. 4) with C(2') and C(5') *anti*. The coupling constants $J_{34} + 11.48$ Hz and $J_{34'} + 1.80$ Hz are in accordance with this latter assumption. Assuming that the ring geometry of equatorial bromocyclohexane does not deviate too much from that of cyclohexane, the following Karplus-type relation can be derived³ for vicinal couplings between H(3) and H(4), H(4'):³ $J(\text{HH}) = 12.83 (\cos^2 \psi + 0.04 \cos \psi)$. $J_{34'}$ and J_{34} then correspond to dihedral angles of 69° and 165°, respectively. Calculation of the *gauche* dihedral angle between H(3) and H(4'), by means of the method of Forrest⁴ and that of Altona⁵, which both take into account substituent electronegativities, yield 68° and 71°, respectively. The latter method⁵ is developed especially for H-C-C-H fragments bearing three non-hydrogen substituents in nucleosides and nucleotides.

The values of the four vicinal spin-spin couplings among the protons H(4), H(4'), H(5) and H(5') yield four equations (1)-(4) and eight unknowns, i.e. the concentrations of the conformers X, Y, Z and Z'Y'Z', respectively *x*, *y*, *z*, *x'*, *y'* and *z'* and the values of vicinal spin-spin couplings in *anti* and *gauche* conformations, J^a and J^b (see Fig. 5). It may be

* The equations expressing the contributions to J_{45} , $J_{4'5'}$, $J_{45'}$ and $J_{4'5}$ were set up with the concentrations of conformers Y and Z' set to zero *a priori* (see above). For the cyclohexane solution, subtraction of the equation for $J_{45'}$ and $J_{4'5}$ yields $z = 0.12/(J_a - J_b)$. For the *p*-dioxane solution one obtains $z = -0.11/(J_a - J_b)$. Leaving aside the assumption of zero concentrations for Y' and Z' yields the following result by subtracting the equations for $J_{45'}$ and $J_{4'5}$: $z - y = 0.12/(J_a - J_b)$ (cyclohexane) and $z - y = -0.11/(J_a - J_b)$ (*p*-dioxane). An alternative result from our calculations would involve small concentrations of Z and Y with Z prevailing in cyclohexane and Y in *p*-dioxane.

² G. R. Demare, A. J. Quirt, J. S. Martin and F. W. Birss, Dept. of Chem., Univ. of Alberta, Edmonton, Canada, private communication, 1968.

³ D. Höfner, S. A. Lesko and G. Binsch, Org. Magn. Reson. 11, 179 (1978).

⁴ T. P. Forrest, J. Am. Chem. Soc. 97, 2628 (1975).

⁵ C. A. G. Haasnoot, F. A. A. M. de Leeuw, H. P. M. de Leeuw and C. Altona, Recl. Trav. Chim. Pays-Bas 98, 576 (1979).

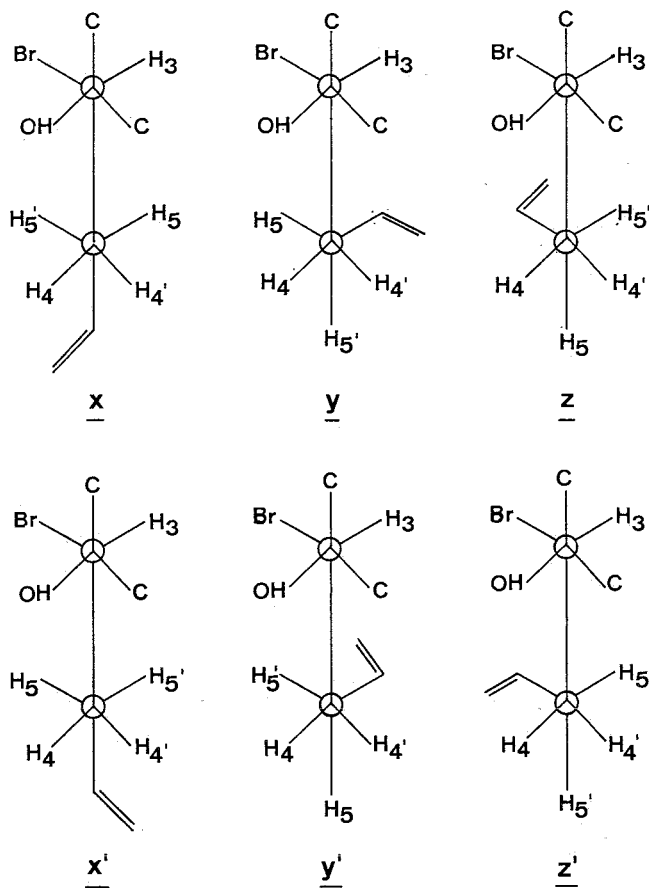


Fig. 5. Conformations around $C(4')-C(5')$ in **2**.

assumed, however, that contributions of conformations Y and Z' will be very small, based on the proximity of bulky substituents leading to rather severe steric interactions¹.

$$J_{4,5} = (z + x' + y')J^B + xJ^A = 4.64 \quad (1)$$

$$J_{4,5'} = (z + x')J^B + (x + y')J^A = 7.97 \quad (2)$$

$$J_{4,5''} = (x + y')J^B + (z + x')J^A = 8.27 \quad (3)$$

$$J_{4,5'''} = (x + z + y')J^B + x'J^A = 8.15 \quad (4)$$

Further, taking the difference between *anti* and *gauche* vicinal couplings as 10.0 Hz⁶ and taking into account the requirement $x + z + x' + y' = 100\%$ results in the following: 15.2% X, 1.2% Z, 50.3% X' and 33.3% Y'.

The coupling between H(4), H(4'), H(5) and H(5') in *p*-dioxane solution differ only slightly from those in the cyclohexane solution, see Tab.I. Some of the small differences observed between the two solutions could be due to the fact that the polar part of **2**, C(1')-C(3'), is subjected to media of different polarities. The orientations around C(2')-C(3') may change¹ and this could cause the electronegative bromine substituent to exert different influences on the vicinal spin-spin couplings. The different media might also influence the C(3')-Br bond directly. Neglecting solvent-induced changes of coupling constants (*i.e.* independent of conformational changes) and solving the same equations as for the cyclohexane solution leads to the following result*: 12.5% X, 0% Z, 53.4% X' and 34.1% Y'.

Irradiation of the methyl protons at C(8') for the cyclohexane solution of **2** yields considerable changes in the signal of H(5) but not in the signal of H(5'). This indicates that one of the allylic protons [H(5')] shows no measurable homoallylic coupling with the methyl protons at C(8'). This is in agreement with the result that ca. 85% of **2** resides either in the conformation X' or in Y', *i.e.* with the same proton (H(5')) in the plane of the double bond C(6')=C(7').

The following free energy differences can be calculated from the relative concentration in cyclohexane (values in *p*-dioxane in parentheses): $\Delta G(Y') - \Delta G(X') = 246$ cal/mol (267

cal/mol) and $\Delta G(X) - \Delta G(X') = 713$ cal/mol (866 cal/mol). At present, we have no explanation for the change in the latter free-energy difference unless one assumes coupling between rotation around C(5')-C(6') ($X \leftrightarrow X'$) and around C(2')-C(3') ($A \leftrightarrow B$).

Part B

The resulting conformational equilibrium of **2** is of particular interest with regard to the rather large ¹³C NMR chemical shift differences of the unsaturated carbon atoms compared to those in **3**¹, see Fig. 6.

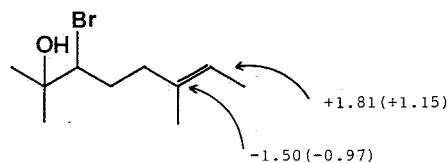


Fig. 6. ¹³C NMR chemical shift differences of C(6') and C(7') of compound **2** compared with **3**, measured in *n*-hexane. Values measured in glyme are given in parentheses.

Similar differences occur in the 2-hydroxy-3-bromo derivative of squalene itself with respect to squalene¹. Originally, these differences were rationalised by us in terms of steric interactions between the bromine atom and the C(6')=C(7') bond in conformation ZP¹. This conformation is now ruled out by the ¹H NMR results. In conformation X'P the distances from the Br atom to C(6') and C(7'), as deduced from Dreiding models, are ca. 5 Å and ca. 6 Å, compared to ca. 4.5 Å and 5 Å in XP. In Y'P both distances amount to ca. 4 Å. Considering the *Van-der-Waals* radii, the above mentioned distances suggest that steric interaction, as a cause of the observed shift differences, is rather unlikely, at least for conformers XP and X'P.

Recently we noticed quite large halogen-induced Csp²-shift differences in compounds where steric interactions, or hindrance of the kind invoked earlier¹, are extremely unlikely, namely in geranyl chloride and bromide and in equatorial 4-bromomethylcyclohexane and the corresponding chloroderivative⁷.

The induced shifts can be rationalised mainly in terms of LEF (Linear Electric Field) effects. An important factor to take into account in comparing chemical shift differences between **2** and **3**, for example, is the LEF effect caused by the C-Br dipole or, more appropriately, by the total C(3')-OH-C(2')-Br group. A contribution from a square electric field effect will probably be small, due to the rather large dipole double bond distances⁸. There are a few other factors which should be considered prior to correlating observed shift differences at C(6')=C(7') in **2** and **3** with calculated LEF effects in different conformations. Firstly, there are the mutual effects of two double bonds in a hydrocarbon chain, discovered by Bus⁹. This effect is quite general, its magnitude depending upon the number of intervening saturated bonds and also upon the substitution patterns of the unsaturated bonds. The nature of these differences is still largely unknown, although changing conformational equilibria are probably important. When comparing the ¹³C NMR shifts of **2** and **3**, corrections should be made for the loss of the above-mentioned double bond interactions

⁶ E. W. Garbisch and M. G. Griffith, *J. Am. Chem. Soc.* **90**, 6543 (1968).

⁷ M. E. v. Dommelen, J. W. de Haan and H. M. Buck, *Org. Magn. Reson.*, **13**, 447 (1980).

⁸ H.-J. Schneider and W. Freitag, *J. Am. Chem. Soc.* **99**, 8363 (1977).

⁹ J. Bus, I. Sies, M. S. F. Lie Ken Jie, *Chem. Phys. Lipids* **18**, 130 (1977).

in **2** with respect to **3**. Since the magnitude of the correction can only be estimated by comparison with Bus' results, the "isolation" of the LEF contributions from the experimental ^{13}C NMR chemical shift differences for $\text{C}(6')=\text{C}(7')$ is also an approximation. Finally, considering small contributions of the magnetic anisotropy of the $\text{C}(3')-\text{Br}$ bond on $\text{C}(6')=\text{C}(7')$ (+0.2 ppm on both C atoms) and keeping in mind the above-mentioned approximations, one arrives at a "nett experimental LEF effect" of the Br and OH substitution at $\text{C}(3')$ and $\text{C}(2')$ of ca. -2.5 ppm for $\text{C}(6')$ and ca. +2.0 ppm for $\text{C}(7')$, respectively.

The LEF effect can be calculated by means of the formula of $\Delta\delta = A \cdot E_a$ where A is a sensitivity factor and E_a is the component of the electric field strength along the $\text{C}(6')=\text{C}(7')$ bond. We performed, in a separate study, calculations on 5-chloro-1-pentene¹⁰, which can be seen as a model for **2**. Using the results of that study¹⁰ and inserting the bond dipole of C-Br instead of that of C-Cl leads to the results shown in Fig. 7.

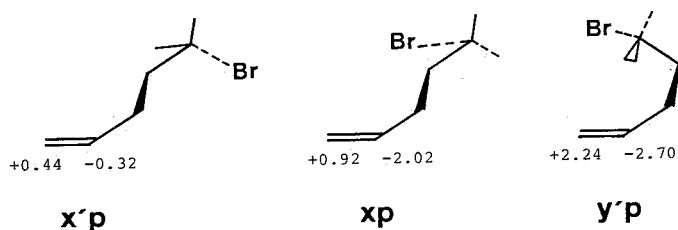


Fig. 7. Calculated bromine induced LEF effects (in ppm) on $\text{C}(1)$ and $\text{C}(2)$ of 5-bromo-1-pentene (from ref. 10 using the bond dipole of C-Br instead of C-Cl).

¹⁰ M. E. v. Dommelen, J. W. de Haan and H. M. Buck, *Org. Magn. Reson.*, **14**, 497 (1980).

In the case of the conformational equilibrium calculated from the ^1H NMR spectrum in cyclohexane, one obtains -1.40 ppm for $\text{C}(6')$ and +1.13 ppm for $\text{C}(7')$, which in its order of magnitude is correct. Seven out of nine conformations of the model 5-halo-1-pentene yield similar results using these calculations. This makes the ^{13}C NMR results rather inconclusive, although they are in agreement with the results obtained by ^1H NMR. More refined calculations of the LEF contributions to the shift differences at $\text{C}(6)$ and $\text{C}(7)$ between **2** and **3** are presently unwarranted in view of the existing uncertainties within the LEF concept itself^{7,10} and the additional difficulty of isolating the experimental LEF effect. Moreover, the unknown influence of the solvents on the individual di- (or tri-) poles of $\text{C}(3')-\text{Br}$ and $\text{C}(2')-\text{OH}$, both intrinsic and via conformational changes around $\text{C}(2')-\text{C}(3')$, cannot be properly assessed. On the other hand, we now know that the rather large changes in the ^{13}C NMR chemical shifts of $\text{C}(6')$ and $\text{C}(7')$ of **2** and of the corresponding squalene derivative, found between solutions in an apolar and a polar solvent, (see Fig. 6) are not due to large conformational changes around $\text{C}(4')-\text{C}(5')$ ¹. However, definite statements regarding the background of these changes, which also occur on $\text{C}(10')$ and $\text{C}(11')$ (to a lesser extent) have to await the results of studies on model compounds where, for instance, the molecular conformations are not solvent dependent.

Acknowledgements

The authors wish to thank Mrs. Anne J. W. van den Berg for the preparation of 6-bromo-7-hydroxy-3,7-dimethyl-2-octene. This investigation has been supported by The Netherlands Foundation for Chemical Research (SON) with financial aid from The Netherlands Organization for the Advancement of Pure Research (ZWO).

The chemistry of small ring compounds. Part 43. Synthesis of 1-substituted cyclopropyl sulfides

R. Jorritsma, H. Steinberg and Th. J. de Boer*

Laboratory for Organic Chemistry, University of Amsterdam, Nieuwe Achtergracht 129,
1018 WS Amsterdam, The Netherlands
(Received August 25th, 1980)

Abstract. 1-Hydroxy- and 1-halocyclopropyl sulfides can be conveniently prepared starting from cyclopropanone. Cyclopropyl sulfides with halogen or a dimethylsulfonium group in the α -position can be transformed into 1-substituted cyclopropyl sulfides with a variety of nucleophiles. This means that the usual difficulties encountered with nucleophilic substitution at three-membered rings - i.e. low rates and ring opening - are largely removed by the presence of an alkylthio group at the same ring carbon atom as the leaving group.

Introduction

Cyclopropyl sulfides can be prepared in various ways. One method involves ring closure by 1,3-elimination of hydrogen halide from γ -halosulfides (1), and represents a general synthesis for cyclopropyl phenyl sulfides¹ and cyclopropanone dithioacetals²⁻⁴. Ring closure has also been induced by the action of a Grignard reagent on a β -keto thioketone⁵

³ T. Cohen and W. M. Daniewski, *Tetrahedron Lett.* 2991 (1978); J. P. O'Brien, A. I. Rachlin and S. Teitel, *J. Med. Chem.* **12**, 112 (1969);

C. C. Price and J. S. Vittimberga, *J. Org. Chem.* **27**, 3736 (1962); C. Feugeas and J. P. Galy, *C.R. Acad. Sci. Ser. C* **270**, 2157 (1970).

⁴ M. Braun and D. Seebach, *Chem. Ber.* **109**, 669 (1976). Cf. also G. Köbrich, *Tetrahedron* **24**, 4327 (1968).

⁵ J. Masson, P. Metzner and J. Vialle, *Tetrahedron* **33**, 3089 (1977).

A. Couture, M. Hoshino and P. de Mayo, *J. Chem. Soc., Chem. Commun.* 131 (1976).

K. Kondo and I. Ojima, *Chem. Lett.* 119 (1972).

¹ W. Truce, K. R. Hollister, L. B. Lindy and J. E. Parr, *J. Org. Chem.* **33**, 43 (1968).

² L. Brandsma, *Recl. Trav. Chim. Pays-Bas* **89**, 593 (1970).