

ON THE CONFORMATION OF THUJANOLS

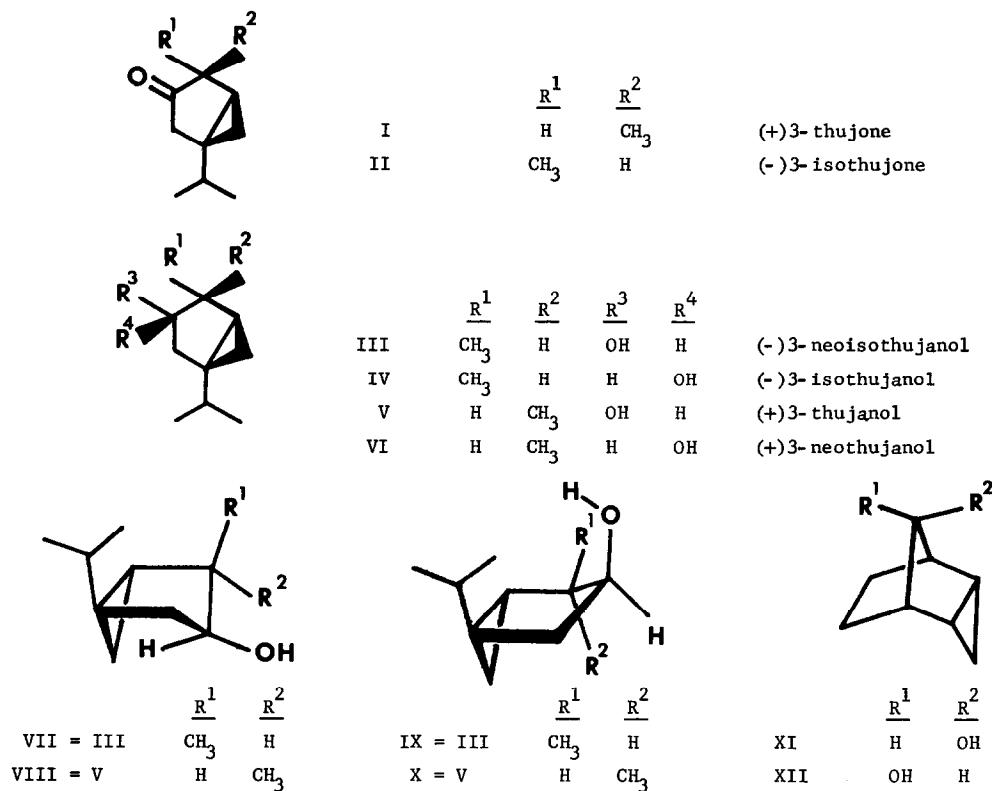
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In recent years the conformations of (+)3-thujone I, (-)3-isothujone II, and the corresponding thujanols (III-VI) (1) and thujylamines have been the subject of studies by Tori (2 a), Norin et al. (2 b) and Smith et al. (2 c). Mostly on the basis of evidence obtained by nmr spectroscopy, a boat-like conformation of the bicyclohexane skeleton in these compounds has been proposed and discussed (1,3). However, Tori (2 a) and others (4) consider the interpretation of nmr spectra of bicyclo (n,1,0) compounds and thujane derivatives ambiguous. Chemical evidence is not always in accord with the boat-like conformation. When evaluating results obtained from reductions of these two ketones, Banthorpe (3) had to assume a chair-like conformation for (-)3-isothujone II and a boat-like conformation for (+)3-thujone I.

We now wish to report evidence against the boat-like conformation of the thujanols in solution, particularly (+)3-thujanol V and (-)3-neoisothujanol III. This evidence is based on the hydrogen bond formation between the hydroxy group and the cyclopropane ring.

Various authors have indicated the possibility of hydrogen bond formation between a cyclopropane ring and an OH group. However, only recently did Schleyer et al. (5) unambiguously confirm its existence. Although the cyclopropane ring is only a weak H^+ acceptor, ir spectroscopy has proven to be a sensitive and specific method for the detection of this bond. The presence of a H-bond is known to document itself by the appearance of a second (bonded) OH peak at lower frequency. The frequency difference ($\Delta\nu$) between the two OH bands is then an approximate measure of the strength (6) and length (7) of the bond. Schleyer also concluded that the site for the proton interaction is the "edge" of the cyclopropane ring (5). This observation can provide invaluable assistance in stereochemical interpretations and assignments (11).



In our work on the isomeric thujones and thujanols, we have repeatedly been confronted with the question of the bicyclohexane ring conformation. We believed the hydrogen bond method of Schleyer could contribute to the solution of this problem, and we presumed that thujanols III and V could not form a H-bond if they were in a boat-like conformation (VII and VIII). However, if the overall conformation of the system were chair-like (IX and X), then an intramolecular H-bond should be possible in this pair of alcohols and very unlikely in alcohols IV and VI. Furthermore, due to the probable sterical interference in III between the neighboring CH_3 and OH groups, we anticipated that $\Delta\nu$ for (III = IX) would be lower than for (V = X). This sterical interference would not allow the -OH group to acquire a "symmetrical" position with regard to the edge of the cyclopropane ring - a relevant feature pointed out by Schleyer.

The following table summarizes the results of our infrared studies (Perkin-Elmer 521) on the four thujanols (8) with the technique used by Schleyer et al (5), i.e., high sample

dilution in CCl_4 . Whereas Schleyer measured only one concentration (1 mg/ml) we applied in our studies the usual dilution technique in order to distinguish unambiguously intramolecular H-bonding. Over a concentration range from 2 mg/ml (0.0013 M) to 0.2 mg/ml (0.00013 M) the relative intensities of the free and bonded absorption bands remained constant thus indicating the presence of an intramolecular H-bond.

<u>Thujanol</u>	<u>Free OH cm^{-1}</u>	<u>Bonded OH cm^{-1}</u>	<u>$\Delta\nu$ cm^{-1}</u>
III = IX	3,633	3,620	13
IV	3,625	-	-
V = X	3,632	3,609	23
VI	3,630	-	-

All values are precise to $\pm 2\text{cm}^{-1}$.

These results indeed indicate an intramolecular H-bond in (-)3-neoisothujanol (III = IX) and (+)3-thujanol (V = X), as well as the anticipated difference in $\Delta\nu$. Inspection of Dreiding models constructed with a flat, five membered ring (overall L-shape conformation) indicates a distance of 3.3 Å between H in -OH and the edge of the cyclopropane ring. In the boat-like conformation (VII or VIII) this distance is still greater. Hydrogen bonds of this length have not been observed (7, 9, 10).

A case of specific interest to us is the pair of sterically rigid tricyclooctanols (XI and XII) studied by Schleyer. The octanol XI shows two (free and H-bonded) OH maxima at $3,631\text{ cm}^{-1}$ and $3,596\text{ cm}^{-1}$ ($\Delta\nu 35\text{ cm}^{-1}$), whereas XII shows only a single peak at $3,632\text{ cm}^{-1}$. Dreiding models of XI indicate a distance of 2.4 Å between H in -OH and the cyclopropane edge. From Kuhn's (7) equation relating the H-bond length to $\Delta\nu$ in dihydroxy compounds, it follows that $\Delta\nu$ of 35 cm^{-1} corresponds to a bond length of 2.3 Å. In the present situation this fact is only of an indicative nature. However, by making liberal use of this equation and by comparing the observed $\Delta\nu$ values and Å values (from Dreiding models) for tricyclooctanol XI and for (+)3-thujanol (V = X), we may project in the latter a H-bond length of 2.7 - 2.9 Å. This then would necessitate an overall chair-like conformation, X, of the bicyclohexane system - the five membered ring acquiring an envelope-like conformation with a flap angle of 20-30°. The $\Delta\nu$ value of 13 cm^{-1} in (-)3-neoisothujanol (III = IX) indicates either the mentioned steric interference of the neighboring methyl and OH groups, or a less pronounced chair-like conformation.

Although a direct observation regarding (+)3-neothujanol VI and (-)3-isothujanol IV by ir is not possible, by analogy we would expect a similar conformation. However, the intriguing possibility that in a dilute solution the conformation of IX and X is actually determined by the presence of a H-bond cannot be ruled out. Our work in this area continues.

References

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8. The four thujanols (III - VI) were obtained in milligram quantities by preparative glc (column 30' x 3/8", 15% carbowax 20M on acid washed Celite 545), then purified by preparative tlc (silica gel, CHCl₃) and finally their purity confirmed by glc (column 15' x 1/4", 15% carbowax on acid washed Celite 545). Subsequently we developed efficient methods to obtain three of the four alcohols in any desirable amount. Expanding on the work of Banthorpe et al (3), III was obtained by a stereospecific reduction of (-)3-isothujone (II). Details of this study will be published later. The stereospecificity of (+)3-thujone (I) reductions is low. However, pure (+)3-thujanol (V) and (+)3-neothujanol (VI) were easily obtained as follows. A mixture (1 g) containing 46% of VI and 54% of V was chromatographed on an Al₂O₃ (Fisher A-540) column 7/8" x 11", using cyclohexane and cyclohexane-benzene (8:2, 4:6 and 2:8) as eluents. Pure VI (99% + by glc) was eluted with cyclohexane: benzene (4:6) and subsequently pure V with cyclohexane:benzene (2:8). This procedure can conveniently be scaled up to separate a 10 g mixture of the two isomers.
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