THE BOAT FORM IN SIX-MEMBERED RINGS

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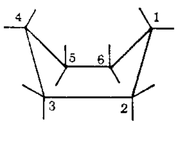
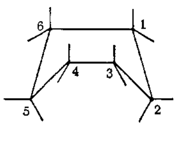
I. INTRODUCTION

Sachse (74) and Mohr (66) postulated that cyclohexane can exist in two forms, the boat and the chair, which would be free from angle strain. Now it is well known (13, 14, 30, 57, 70) that cyclohexane and its derivatives exist predominantly in the symmetrical chair conformation which is thermodynamically more stable than the boat conformation. The boat form is destabilized by the presence of two eclipsed ethane type interactions, whereas in the chair form all bonds are staggered. The non-bonded interaction between the two "flagpole" hydrogen atoms at the stern and bow of the boat will also make this form less stable. Apart from the chair and the boat form of cyclohexane, a third conformation has been proposed by recent workers (2, 46, 51, 58). This has been variously called as flexible (2, 58), stretched (46), skewed (73), or twisted (51). Such a form (II) is obtained during the conversion of one boat (Ia) into another boat (Ib) by twisting the C–C bonds. The energy barrier between these forms is so low that facile interconversion between them is possible; hence, II will be called the flexible form in this review. This form would be more stable than a regular boat form because the flagpole hydrogen atoms have moved away from each other, and the eclipsed ethane type interactions also are relieved partially.



Ia



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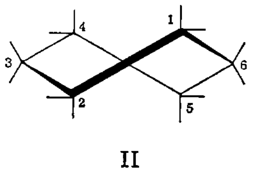
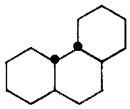


II

The boat form occurs necessarily in bridged cyclohexanes like camphor and other bicyclo[2.2.1]heptanes. In pinanes (bicyclo[3.1.1]heptanes), one of the six-membered rings should exist in the chair and the other in the boat conformation. The geometry of some fused polycyclic systems, such as *trans-syn-trans*-perhydrophenanthrene (III) and *trans-anti-trans*-perhydroanthracene (IV) also requires a boat conformation for the central ring (49, 50). Indeed, compounds of this type have been reported recently. Compound IV itself was obtained by Clarke (21). Two isomeric tricyclic lactones (V and VI) have been synthesized (51). Of these, the isomer VI with the central ring in a boat conformation is related to IV configurationally. Shoppee (76) has already discussed such geometrically anchored boat forms. Intrinsically more interesting compounds would be those in which a six-membered ring assumes a boat conformation, even though a chair conformation is not precluded. Examples of this type, which have been reported mostly during the last five years, are discussed in this review. The assignment of the boat conformation to a six-membered ring will not necessarily exclude the flexible form but will only exclude the chair conformation. Most probably the compound would prefer the more stable flexible form rather than the severe boat form. However, an unequivocal choice between these conformations is not possible because of the high mobility of such forms.



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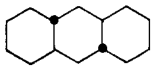

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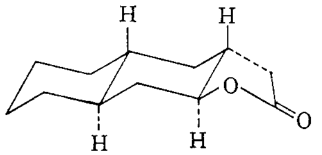

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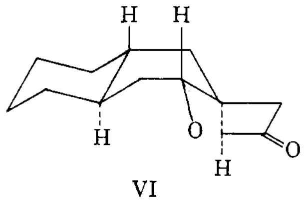
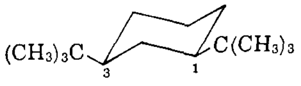


VI

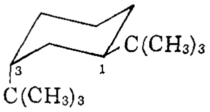
II. ENERGY CONSIDERATIONS

The energy difference between the chair and boat forms of cyclohexane has been evaluated by different workers (12, 16, 81). The approximations and assumptions involved in these calculations have led to values of 1.31 (12), 5.6 (16), and 10.6 (81) kcal./mole. Nevertheless, the value of 5.6 kcal./mole is widely accepted (13, 30, 70). In calculating this value (16), the eclipsed ethane type interactions present in the boat form were taken into account, but the non-bonded interaction between the 1,4-hydrogen atoms was neglected. Since the flexible form is free from this type of interaction, the value of 5.6 kcal./mole might be considered as giving approximately the energy difference between the flexible form and the chair form (58). Evaluation of the energy difference between the chair and the flexible form has led to values of 4.0 (47), 4.75 (46), and 5.1 (2) kcal./mole. Experimental verifications of these values have been carried out recently by the actual isolation of pairs of stereoisomers with one of them in each pair occurring in a flexible form.

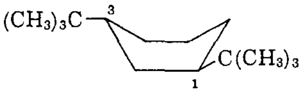
Heat of combustion and heat of vaporization data (51) on the tricyclic lactones, V and VI, were utilized in estimating the enthalpy difference between the chair and the flexible conformation of cyclohexane. The value so obtained, 5.5 kcal./mole, is in reasonable agreement with the predicted values. Significantly, there is close agreement with the value of 5.6 kcal./mole evaluated (16) on the basis of eclipsed ethane interactions, neglecting the interaction between the flagpole hydrogen atoms. Determination of the equilibrium constant between *cis*- and *trans*-1,3-di-*tert*-butylcyclohexane afforded (5) the enthalpy and entropy changes accompanying chair–boat isomerization. Again there is good agreement between this value of ΔH, 5.9 ± 0.6 kcal./mole, and the predicted values. In arriving at these results, it has been assumed that the *trans* isomer is forced into a boat conformation (IX) in order to avoid the axial orientation of the bulky *tert*-butyl group in the chair conformation (VIII). It is fairly well established (19, 20, 36, 37, 38, 85) that the *tert*-butyl group always avoids an axial orientation. On the other hand, the *cis* isomer can exist conveniently in the chair conformation (VII) with both the bulky groups in equatorial positions.



VII



VIII



IX

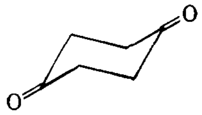
The inadequacy of utilizing stereoisomeric 1,3-di-*tert*-butyl-cyclohexanes in the evaluation of the energy difference between the chair and the boat cyclohexane has been pointed out (51). In the boat conformation (IX) the *tert*-butyl group at C-1 is eclipsed by the equatorial hydrogen at C-2. The chair form (VII) is free from such an interaction. Therefore, the enthalpy difference between VII and IX probably would be higher than that between chair and boat cyclohexanes. However, there is sufficient ground to assume that the value of 5.6 kcal./mole, postulated as the energy difference between the chair and the regular boat conformation of cyclohexane, might be considered as representing the energy difference between the chair and the flexible forms.

III. BOAT FORM IN ALICYCLIC COMPOUNDS

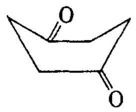
A. SIMPLE CYCLOHEXANE DERIVATIVES

In general, a boat conformation would be preferred if severe steric interactions that are present in the chair could be relieved in the boat. Electrostatic interactions might also play a significant part in either increasing the energy of the chair form or lowering the energy of the boat form. Further, the presence of a carbonyl group in the ring might also shift the equilibrium toward the boat. One or more of these effects could be recognized easily in every example of a six-membered ring which has been demonstrated to exist in a boat conformation.

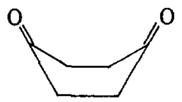
As early as 1935, Le Fèvre and Le Fèvre (59) noted that 1,4-cyclohexanedione showed a definite dipole moment of 1.2 *D*. Since the chair form of the diketone should have a zero dipole moment, and the presence of any enolic form having been excluded experimentally, the observed dipole moment could be accounted for only if the diketone existed as an equilibrium mixture of chair and boat forms. This observation was further supported (60) by the determination of the Kerr constant of 1,4-cyclohexanedione. The equilibrium mixture was considered (60) to consist of 80% of the chair (X) and 20% of the boat (XI).



X



XI



XII

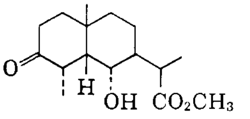
According to Kumler and Huitric (58), six-membered ring compounds most likely to have boat conformations are: (1) those with two or more atoms in the ring that do not have sp^3 binding, *e.g.*, a bivalent atom or a carbonyl carbon, and (2) those with one atom in the ring not having sp^3 binding and a strong dipole on an adjacent atom. Condition (1) is illustrated by 1,4-cyclohexanedione. The presence of two carbonyl groups in XI completely eliminates the two eclipsed ethane interactions that are present in the boat cyclohexane. Consequently, the difference in energy between X and XI would be considerably less than that between the chair and the boat form of cyclohexane. A value as low as 0.2 kcal./mole has been evaluated (2) for this difference. The suggestion (57) that the alternative boat form (XII) might contribute to the equilibrium mixture can be ruled out. The eclipsed 1,2-interactions, which mainly destabilize the boat form of cyclohexane, are present in XII, whereas they are absent in XI. It also has been suggested (2) that the equilibrium mixture probably is composed of the chair and flexible forms with neither of the extreme boat forms (XI or XII) being present.

On the basis of dipole moment studies (58), α-chloro- and α-bromocyclohexanone were reported to occur in the flexible form to an appreciable extent. These results were at variance with those obtained by Corey (25) on α-bromocyclohexanone from infrared spectral data. The apparently contradictory spectral and dipole moment data were re-examined (1, 3), and it was concluded that α-bromo- and α-chlorocyclohexanone exist almost entirely as an equilibrium mixture of the two interconvertible chair forms.

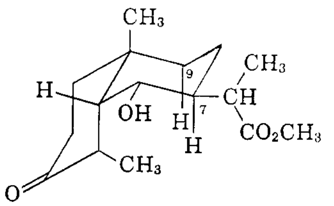
The preparation of *trans*-1,3-di-*tert*-butylcyclohexane with a preferred boat conformation for the ring has been mentioned earlier. *trans*-2,4-Di-*tert*-butylcyclohexanone also was expected to exist in a boat conformation (4). *cis*-1,4-Di-*tert*-butylcyclohexane might also be expected to exist in a boat conformation. In 1,2-di-*tert*-butylcyclohexanes, the proximity of the two large groups probably would result in severe distortion of the tetrahedral valence angles of both *cis* and *trans* isomers.

B. BICYCLIC COMPOUNDS

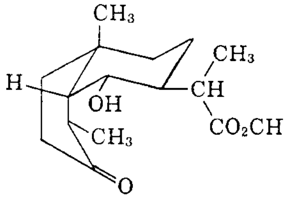
As far as the writer is aware, only one example of this type is known. Methyl tetrahydrosantoninate (XIII) was shown (11) to have an α-orientation of the methyl group at position 4. If a chair form (XIIIa) is assumed for the ring containing the carbonyl group, the methyl group will be in an axial orientation. However, the stability of the compound to isomerization indicated a stable equatorial conformation for the methyl. This is compatible only with a boat conformation (XIIIb) for the ring. Severe 1,3-interaction of the methyl group with the two axial hydrogen atoms at C-7 and C-9 in XIIIa is considered to be responsible in forcing the conformation XIIIb.



XIII



XIIIa

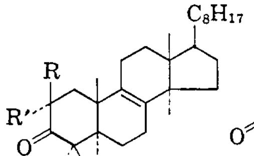


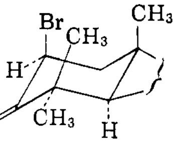
XIIIb

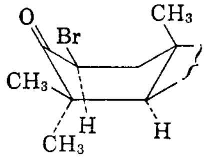
C. STEROIDS AND TRITERPENOIDS

Although ring flip to give an alternative chair form is not possible in interlocked polycyclic systems such as steroids, ring A in 5α-steroids and rings A and B in 5β-steroids are free to take up a boat conformation. Examples of ring A preferring the boat have come to light recently. The earliest observation was made by Nace and Turner (67), who found that the dipole moment of 5β-androstane-3,17-dione could be interpreted best by assuming an equilibrium composition of about 16% of the compound existing with ring A as the boat. A small contribution of the boat form in 5α-androstane-3,17-dione was, however, not excluded by them.

Barton, Lewis and McGhie (15) provided the first example of ring A in a steroid existing exclusively in the boat conformation. Two monobromo derivatives of lanost-8-en-3-one were obtained. The structure and configuration of these have been established unequivocally by chemical means as 2α-bromolanost-8-en-3-one (XIV) and 2β-bromolanost-8-en-3-one (XV). Both the bromoketones have infrared (55) and ultraviolet (23, 24) absorption spectra indicative of equatorial bromine. Since it is impossible to have a pair of isomeric 2-bromolanost-8-en-3-ones each having an equatorial bromine in a chair conformation, it was concluded that ring A in the 2β-bromoketone should have preferred the boat conformation (XVb). There are powerful 1,3-diaxial interactions between the bromine atom and the two methyl groups at C-4 and C-10 in the chair conformation (XVa) of the 2β-bromoketone. These repulsive interactions are avoided in the boat form (XVb).





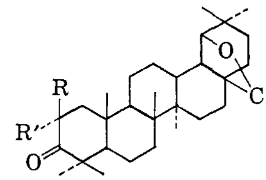


XIV, R = H, R′ = Br

XVa XVb

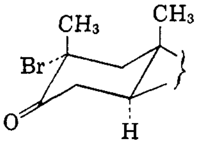
XV, R = Br, R′ = H

Exactly similar behavior was observed (15) with the corresponding saturated analogs, 2α- and 2β-bromolanostan-3-one, the latter having ring A in a boat conformation with bromine in the equatorial position. Recent studies (56) on 2β-bromo-allobetulone (XVI) showed that this should also have ring A in a boat conformation. Both XVI and XVII gave shifts in the infrared carbonyl frequency requiring equatorial orientation of bromine. Further, the α-bromoketone (XVII) gave an additional weak band corresponding to the frequency of the bromine-free ketone. This was taken as indicating a small contribution of the boat form in XVII also.

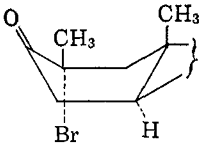


XVI, R = Br, R' = H   XVII, R = H, R' = Br

The application of optical rotatory dispersion studies (31) was chiefly instrumental in providing further examples of boat forms in steroids. Bromination of 2α-methylcholestan-3-one gave a monobromoketone (65) and the chemical evidence placed the bromine at position 2. The spectral properties of this compound required an axial bromine and, accordingly, the configuration was assigned (65) as 2β-bromo-2α-methylcholestan-3-one (XIX). The optical rotatory dispersion curve (32, 33) of this compound was characterized by a negative Cotton effect, whereas the axial haloketone rule (34, 35) would predict a curve with a strongly positive Cotton effect for a steroidal 2β-bromo-2α-methyl-3-ketone of the 5α-series. However, the rotatory dispersion data confirmed the axial orientation of the bromine atom as shown by the spectral measurements. These data were satisfactorily interpreted on the basis of the boat form (XVIIIb) of 2α-bromo-2β-methylcholestan-3-one (32, 33). The corresponding chair form (XVIIIa) is destabilized by the steric compression between the axial methyl groups at positions 2 and 10 and by the electrostatic interaction of the equatorial bromine and the carbonyl dipole. These unfavorable interactions are absent in the boat form.



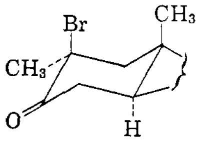
XVIIIa



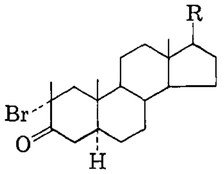
XVIIIb

The above assignment of the conformation was confirmed by the isolation of 2β-bromo-2α-methyl-cholestan-3-one (XIX) which, as expected, gave a strongly positive rotatory dispersion curve. The axial orientation of bromine in XIX also was demonstrated by the infrared and ultraviolet absorption spectra (32, 33).

Exactly similar findings were made in the androstane series (64). Bromination of 2α-methylandrostan-17β-ol-3-one yielded 2α-bromo-2β-methylandrostan-17β-ol-3-one (XX) which exhibited a rotatory dispersion curve characterized by a strong negative Cotton effect, and the infrared and ultraviolet spectral analyses also showed an axial bromine atom. Therefore ring A in XX has a boat conformation. The corresponding 17-acetate (XXI) also behaved similarly.

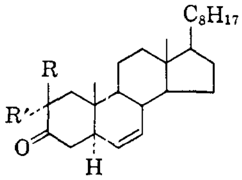


XIX

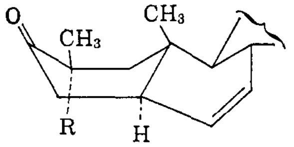


XX, R = OH
XXI, R = OCOCH$_3$

It is significant that the boat–chair equilibrium of ring A can be influenced by the presence of a double bond in ring B of a steroid. Methylation of cholest-6-en-3-one (XXII) afforded (78, 79) 2,2-dimethyl- (XXIII) 2β-methyl- (XXIV), and 2α-methyl-cholest-6-en-3-one (XXV). Chemical evidence and optical rotatory dispersion studies showed that in XXIII and XXIV ring A is in the boat conformation (XXVI). However, the corresponding saturated analogs, 2,2-dimethyl- and 2β-methylcholestan-3-one, were shown to have ring A in the chair conformation. Accordingly, the 6,7-double bond has a profound influence in stabilizing the boat form of ring A in XXIII and XXIV.

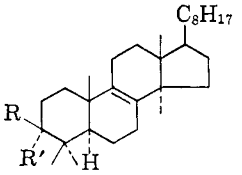


XXII, R, R' = H
XXIII, R, R' = CH$_3$
XXIV, R = CH$_3$, R' = H
XXV, R = H, R' = CH$_3$

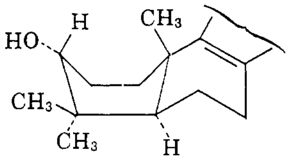


XXVI, R = H or CH$_3$

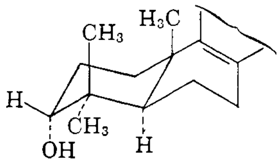
A similar case has been reported by Huffman (48). Reduction of lanost-8-en-3-one afforded an alcohol, considered to be lanost-8-en-3α-ol (XXVII), on the basis of differences in the infrared spectra of the product with the well-known lanost-8-en-3β-ol (XXVIII). The acetates of these two alcohols were also different. Assuming a chair conformation, the hydroxyl should be equatorial in XXVIII and axial in XXVII. However, both the alcohols gave a C–O stretching band at 9.76 μ, and their acetates showed a single strong band at 8.06 μ. These results indicated that the hydroxyl is equatorial (54) in XXVIII as well as in XXVII, and Huffman (48) was led to the conclusion that lanost-8-en-3α-ol has ring A in the boat conformation (XXVIIa) rather than the chair (XXVIIb). This conclusion was further supported by the sluggishness of XXVII to undergo dehydration, thereby excluding an axial position for the hydroxyl. On the other hand, analogous saturated triterpenoids are known to exist in the chair conformation. Here again the presence of a double bond in ring B forces ring A into a boat conformation. This subtle effect was attributed (48) to the inherent in-



XXVII, R = H; R' = OH
XXVIII, R = OH; R' = H

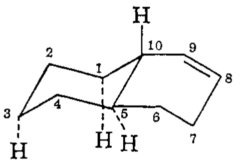


XXVIIa



XXVIIb

stability of the saturated carbocyclic ring in a *trans* fused Δ^1-octalin system (XXIX) (26, 82). The instability arises from an abnormal puckering of the saturated ring. As a result, the axial substituents at C-1, C-3 and C-5 are compressed to a large extent. Such a repulsive interaction would be considerably large

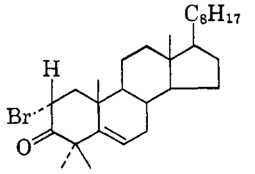


XXIX

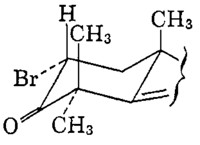
when groups larger than hydrogen are present at these positions. In the chair conformation of lanost-8-en-3α-ol (XXVIIb), the effect of the 8,9-double bond is to increase the non-bonded interaction between the C-3 hydroxyl and C-5 hydrogen. Such an interaction is relieved in the boat form (XXVIIa).

A similar explanation could be given to the preferred boat conformation of 2,2-dimethyl- (XXIII) and 2β-methylcholest-6-en-3-one (XXIV). Viewed as a *trans*-Δ^1-octalin system, the steric compression between the axial methyl groups at positions 2 and 10 in the chair form of XXIII or XXIV would be very high. Hence, the two ketones might be expected to adopt the boat conformation (XXVI) which is free from such interactions.

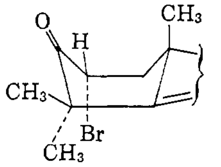
The boat conformation of ring A has been demonstrated in a Δ^5-unsaturated steroid also. Optical rotatory dispersion studies, as well as infrared and ultraviolet measurements have shown (27) that ring A in 2α-bromo-4,4-dimethylcholest-5-en-3-one (XXX) has a boat conformation with bromine in an axial orientation. The unfavorable electrostatic interaction between the equatorial bromine and the carbonyl dipole in the chair form (XXXa) is relieved in the boat form (XXXb). However, the saturated analogs, 2α-bromo-4,4-dimethylcholestan-3-one (77) and 2α-bromolanostan-3-one (15) are known to have ring A in the chair conformation with an equatorial bromine. The boat form of these compounds would be less favored because of the 1,2-interaction of the substituents at C-4 and C-5.



XXX

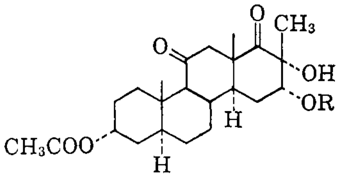


XXXa

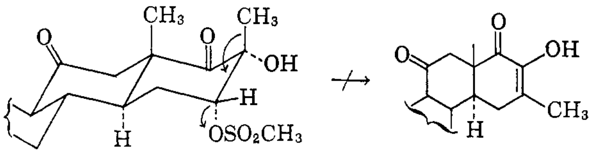


XXXb

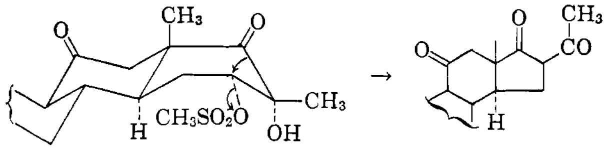
A boat conformation also has been suggested (83) for ring D of a D-homosteroid on the basis of chemical evidence: The dihydroxyketone (XXXI) of established structure (84) was converted into its mesylate (XXXII). The latter, on treatment with alkali, underwent ring contraction to afford the β-diketone (XXXIII). If the D-homo derivative (XXXII) had the chair conformation (XXXIIa) of ring D, the *trans* diaxial orientation of the C-17 methyl group and the departing mesylate group would be expected to facilitate the formation of the diosphenol (XXXIV).



XXXI, R = H
XXXII, R = SO_2Me



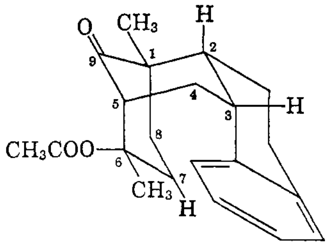
XXXIIa XXXIV



XXXIIb XXXIII

The formation of the diketone (XXXIII), rather than the diosphenol (XXXIV), was explained (83) on the basis of the boat conformation (XXXIIb) for ring D. This conformation satisfies the geometrical requirement of the reaction to give XXXIII. The 1,3-diaxial interaction of the methyl groups at C-17 and C-13 would cause the chair form less favored. However, the course of the reaction followed by the mesylate (XXXII) does not necessarily prove that the molecule exists in the normal state with ring D in the boat conformation. On the other hand, the normal chair form of ring D can flip into the boat form at the time of the reaction.

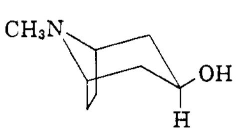
The ketol acetate, XXXV, was obtained (52) as an intermediate in the total synthesis of steroids. It has been suggested (53) that ring A or B of this and related compounds might exist in a boat conformation to relieve the severe interaction between the axial substituents at C-3 (aromatic ring) and C-7 (hydrogen).



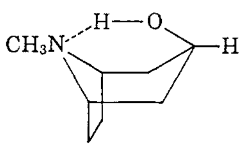
XXXV

IV. Boat Form in Heterocyclic Compounds

The principles of conformational analysis also are applicable to six-membered heterocyclic compounds containing oxygen, nitrogen, or sulfur in the ring (14, 57). It is well established that pyranoside sugars (72) and piperidines (7, 8, 18, 41, 42, 71) prefer the chair conformation rather than the boat. However, the existence of a boat form under favorable conditions cannot be excluded. Indeed, a few such examples could be cited. The infrared absorption (86) of ψ-tropine indicates an equilibrium composition of the chair (XXXVIa) and the boat (XXXVIb) conformation. This view also is strengthened by dipole moment measurements (22, 86). The boat form of ψ-tropine is stabilized largely by intramolecular hydrogen bonding (6, 80).

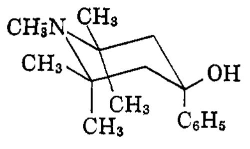


XXXVIa

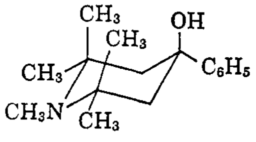


XXXVIb

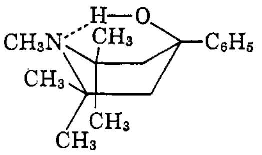
One might generally expect 4-piperidinols to be in the boat form, if there exists a strong intramolecular hydrogen bond. A shift in conformational equilibrium from chair to boat could be more effective, if unfavorable interactions present in the chair form are relieved during the process. For example, Lyle (62) observed that the properties of 1,2,2,6,6-pentamethyl-4-phenyl-4-piperidinol could be explained only on the basis of a boat conformation. The compound resisted acetylation and its infrared absorption spectrum showed intramolecular hydrogen bonding. However, the closely related 1-methyl-4-phenyl-4-piperidinol was acetylated readily and revealed no intramolecular hydrogen bonding. The severe non-bonded interactions of the three axial groups in either of the chair forms (XXXVIIa or XXXVIIb) and the stabilizing influence of hydrogen-bonding are factors which favor the boat form (XXXVIIc).



XXXVIIa

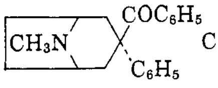


XXXVIIb

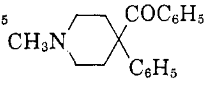


XXXVIIc

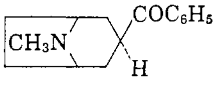
Bell and Archer (17) have shown that phenyl 3α-phenyl-3β-tropanyl ketone (XXXVIII) is best represented with the piperidine ring in a boat conformation. The ketone showed abnormal behavior in the ultraviolet and the infrared absorption in contrast to the normal absorption of the related compounds, 4-benzoyl-1-methyl-4-phenylpiperidine (XXXIX) and phenyl 3β-tropanyl ketone (XL). The absorption of the benzoyl chromophore in the ultraviolet region shown by XXXIX and XL was completely absent in XXXVIII. The infrared absorption of XXXVIII in methanol was characterized by the complete lack of absorption in the carbonyl stretching region, while in methylene chloride there was a peak at 6.02 μ. These observations revealed beyond doubt the existence of interaction between the lone-pair electrons of nitrogen and the carbonyl group in XXXVIII. A similar interaction has been observed in a number of medium ring compounds (61). Therefore, XXXVIII may be assumed to exist in the boat conformation (XLI). Since both XXXIX and XL behave normally, the 3α-phenyl and the ethylene bridge are necessary structural features that favor the boat form. Severe 1,3-diaxial interaction between the ethylene bridge and the axial phenyl would make the chair conformation (XLII) less stable.



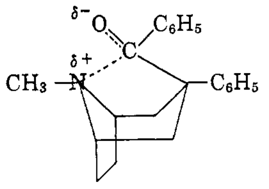
XXXVIII



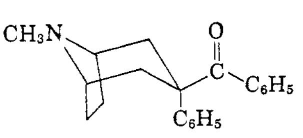
XXXIX



XL

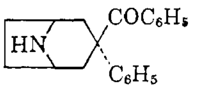


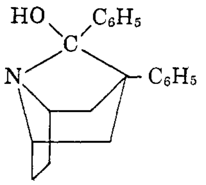
XLI



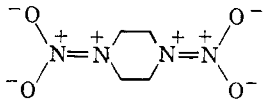
XLII

The spectral characteristics of the nortropane derivative, XLIII, showed (17) that it should be formulated as the carbinolamine (XLIV) with a complete reaction of the secondary amino group and the carbonyl group. This compound gave in the infrared a strong hydroxyl peak at 2.84 μ, and absorption was lacking in the 6μ region.


XLIII

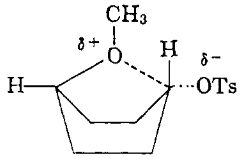

XLIV

George and Wright (44) found that N,N′-dinitropiperazine showed a dipole moment of 2.21 D (20°) which increased with temperature. Other similar N,N′-disubstituted piperazines also had a definite dipole moment. These observations were explained on the basis of the piperazines existing partly in the flexible form. Kumler and Huitric (58) have pointed out that the resonance form, XLV, should make a considerable contribution to the structure of N,N′-dinitropiperazine. Consequently, the nitrogen atoms in the ring acquire an sp^2 character, and a formal analogy exists between the piperazine and 1,4-cyclohexanedione.


XLV

V. BOAT FORM AS AN INTERMEDIATE

Apart from the compounds which prefer a boat conformation rather than a chair, it is possible for a six-membered ring with a normal chair conformation to undergo a reaction through a boat conformation. Thus Noyce, Thomas, and Bastian (69) observed an increase in the rate of solvolysis of *trans*-4-methoxycyclohexyl tosylate when compared to *cis*-4-methoxycyclohexyl tosylate, although the latter was expected to react faster. The higher rate of solvolysis of the *trans* isomer was attributed to the participation of the methoxyl group in an internally assisted reaction pathway which should involve the boat conformation (XLVI). Other similar examples of rate acceleration through 1,4-interaction across a boat form are known (69).


XLVI

The facile migration of acyl groups (N→O or O→N) (43, 68) in nor-ψ-tropine, as well as its reaction with *p*-nitrobenzaldehyde to give a tetrahydro-oxazine (45) undoubtedly take place through boat conformations. Some steroids are also known (29, 63, 75) to react through boat conformations. Cathylation (carbethoxylation) of equatorial alcohols, but not axial alcohols, is well known in steroids (39). However, the study (10) of some substituted 4-piperidinols of established conformation (9) indicated that equatorial as well as axial hydroxyl groups could be cathylated under comparable conditions. The hindered axial hydroxyl in the chair conformation probably reacts as an equatorial group in the boat conformation (*cf.* 40).

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