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CORRELATION BETWEEN THE STEREOCHEMISTRY OF QUINOLIZIDINE ALKALOIDS AND THEIR INFRARED SPECTRA FROM 2840–2600 CM^{-1}

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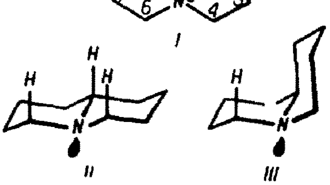
Abstract—The IR spectra from 2840–2600 cm^{-1} of a number of sparteine type quinolizidine alkaloids and their selectively α-deuterated derivatives have been examined. It was shown that a single absorption band or band complex arises from the stretching vibrations of one or more axially oriented $C_α$—H bonds. The intensity and general complexity of this absorption is roughly proportional to the number of these *trans*-diaxial α hydrogens and their steric environment. The characteristic absorption in the 2840–2600 cm^{-1} region has been correlated with different conformations of quinolizidine ring fusions. Steric factors influencing this absorption in sparteine type alkaloids are discussed. An attempt has been made to rationalize the nature of the specific interaction of $C_α$—H(a) bonds with the lone electron pair on nitrogen in the compounds investigated.

The IR spectra of numerous aliphatic amines and non-aromatic heterocyclic systems have been examined and absorption bands in the 2820–2760 cm^{-1} region have been attributed to C—H stretching vibrations in groups attached to a N atom. It has been shown that an N-Me group gives rise to a band in the 2805–2780 cm^{-1} region.[1–3] If two Me groups are attached to a N atom, two bands are found in the regions 2825–2810 cm^{-1} and 2775–2765 cm^{-1}. Structural modifications which involve the lone pair of electrons on the nitrogen, such as salt formation or coordination of the N atom to a metal, cause the disappearance of the bands.

From conformational studies on alkaloids containing one and/or two quinolizidine systems (I) it was shown that the lowering of the $C_α$—H stretching frequencies with reference to the normal C—H stretching region is due to a specific interaction between $C_α$—H bonds and the lone pair on the N atom. It has been confirmed that this interaction is highly stereospecific and that an analysis of the 2800–2700 cm^{-1} range is valuable for the assignment of the three dimensional relationship in the heterocyclic 2-ring system I.



I

II

III

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In 1957 an important IR criterion was reported by Bohlmann[4, 5] for the determination of *trans* (II) or *cis* (III) quinolizidine ring fusion. Only derivatives possessing a *trans* ring juncture with at least two axial H atoms on carbons adjacent to nitrogen show characteristic absorption bands in the 2800–2700 cm^{-1} region, according to Bohlmann. Such relationship of the electron pair to two hydrogens is not possible in *cis*-quinolizidines and it has been reported[5] that these IR bands were not found in their spectra. Bohlmann[5] also reported that the replacement of the lone pair of electrons on the N atom by a covalent bond, e.g. with oxygen in amine oxides, or if it is tied up in a lactam group in α-quinolizidones and its derivatives, results in a complete disappearance of absorption bands in the 2800–2700 cm^{-1} region. Ring deformation by a double bond at the ring juncture, as found in certain α,β-dehydroquinolizidines, also leads to a disappearance of the bands discussed.

Earlier spectroscopic observations on indole alkaloids led Wenkert and Roychandhuri[6] to suggest that bands at lower frequency are found in the 2840–2700 cm^{-1} region only if the $C_{(3)}$—H bond is α oriented. This criterion is related to Bohlmann's correlation, as was pointed out later by Rosen.[7]

Bohlmann's empirical correlation has been applied successfully in stereochemical studies of many natural and synthetic products.[8–17] However, in some cases the low intensity of the 2800–2700 cm^{-1} bands makes the method less reliable, and an uncritical application of the criterion as it was formulated originally* might lead to erroneous conclusions.[10, 19–24]

The quinolizidine ring system I may in principle exist in either *cis* (III) or *trans* (II) forms comparable to those found in decalin, except that in this case the interconversion of the two isomers (II $\rightleftharpoons$ III) involves an inversion of the configuration at the N atom. The two forms can therefore not be isolated separately, but are in a rapid equilibrium in solution at room temperature. From conformational studies on piperidines it could be estimated that the equilibrium in quinolizidine itself will favour the *trans* isomer by about 4·6 Kcal/mole.[24,]† One can predict that this equilibrium will be influenced by additional factors if the quinolizidine moiety is incorporated into larger fused systems. This is the case in sparteine type alkaloids. Here two quinolizidine systems are fused in position 1,3 which results in definite, highly rigid skeletal structures. The stereochemistry of sparteine alkaloids is well known and their configuration has been correlated with IR absorption bands in the region 2800–2700 cm^{-1}. However, in this series of compounds one can also observe species in which a deformation of ideal chair forms leads to unexpected IR results. The main factor which modifies the skeleton in this way is a set of large repulsive non-bonded interactions which exist predominantly in α-isosparteine and its derivatives.[26] In the sparteine alkaloid series it is the *cis*-quinolizidine system C/D which is most susceptible to conformational changes. In sparteine the 1,3-fusion

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* With respect to the configuration of quinolizidine derivatives, Bohlmann reported that lupanine as well as other alkaloids possessing a lactam group in a *trans* quinolizidine system and a basic nitrogen in a *cis* quinolizidine system, do not show absorption bands in the 2800–2700 cm^{-1} region. It was later shown that these bands were indeed present in the lupanine spectrum[10] and this view was confirmed by Bohlmann *et al.* in a more recent publication.[18] The stereochemistry of lupanine has been studied in detail recently and it was shown that ring C is present in the boat form.[19] This finding is also in agreement with the present view on the conformation of ring C in the sparteine skeleton.[18]

† Eliel *et al.*[25] give the values 2·6 kcal/mole.

guarantees the existence of *cis*-quinolizidine in which conformational changes of the type all-chair ⇌ all-chair (as in *cis* decalin) are impossible. The 1,3 ring fusion does not, however, exclude the possibility of nitrogen inversion, leading to a boat form of ring C. Bohlmann's IR correlation[5] and our modification of this rule[10] did not take into account that in *cis*-quinolizidine with ring C in a boat form, there are three α-H atoms anti and in a diaxial relation to the nitrogen lone electron pair, as in *trans*-quinolizidine. We believe that this is the reason why the conformation of ring C in numerous sparteine type alkaloids was not determined for a long time.

TABLE 1. CONFORMATIONAL FEATURES OF SPARTEINE DERIVATIVES INVESTIGATED

Compound	Configuration of quinolizidine system		Number of C_α—H(a) (C_α—D(a)) bonds *trans* with reference to the free electron pair on nitrogen	
	Rings A/B	Rings C/D	In NCH_2, (NCD_2) groups	In NCH, (NCD) groups
Lupinine (IV)	*trans*	—	2	1
15-Oxosparteine (V)	*trans*	*cis* (lactam)	2	1
17-Oxosparteine (VI)	*trans*	*cis* (lactam)	2	1
6-Deutero-17-oxosparteine (VII)	*trans*	*cis* (lactam)	2	(1)
α-Isolupanine (VIII)	*trans*	*trans* (lactam)	2	1
11-Deutero-α-isolupanine (IX)	*trans*	*trans* (lactam)	2	(1)
Aphylline (X)	*trans* (lactam)	*cis* (C chair)	1	—
17-β-Deutero-aphylline (XI)	*trans* (lactam)	*cis* (C chair)	(1)	—
Lupanine (XII)	*trans* (lactam)	*cis* (C boat)	2	1
17-d_2-Lupanine (XIII)	*trans* (lactam)	*cis* (C boat)	1 (1)	1
17-β-Deutero-lupanine (XIV)	*trans* (lactam)	*cis* (C boat)	2	1
17-α-Deutero-lupanine (XV)	*trans* (lactam)	*cis* (C boat)	1 (1)	1
Sparteine (XVI)	*trans*	*cis*	4	2
6-Deutero-sparteine (XVII)	*trans*	*cis*	4	1 (1)
2-d_2-Sparteine (XVIII)	*trans*	*cis*	3 (1)	2
2,6-d_3-Sparteine (XIX)	*trans*	*cis*	3 (1)	1 (1)
10-d_2-Sparteine (XX)	*trans*	*cis*	3 (1)	2
17-d_2-Sparteine (XXI)	*trans*	*cis*	3 (1)	2
15-d_2-Sparteine (XXII)	*trans*	*cis*	3 (1)	2
6,17-d_3-Sparteine (XXIII)	*trans*	*cis*	3 (1)	(1)
2,17-d_4-Sparteine (XXIV)	*trans*	*cis*	2 (2)	2
2,6,17-d_5-Sparteine (XXV)	*trans*	*cis*	2 (2)	(1)
α-Isosparteine (XXVI)	*trans*	*trans*	4	2
6,11-d_2-α-Isosparteine (XXVII)	*trans*	*trans*	4	(2)
2,6,11,17-d_6-α-Isosparteine (XXVIII)	*trans*	*trans*	2 (2)	(2)
2-d_2-α-Isosparteine (XXIX)	*trans*	*trans*	3 (1)	2
2,11-d_3-α-Isosparteine (XXX)	*trans*	*trans*	3 (1)	1 (1)
2,6,11-d_4-α-Isosparteine (XXXI)	*trans*	*trans*	3 (1)	(2)

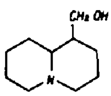
In a previous paper[10] we have suggested that stereochemical studies of quinolizidine derivatives must take into consideration not only the presence or absence of absorption bands in the 2800–2700 cm^{-1} region, but that these bands must also be interpreted in terms of the intensity and the shape of the whole band complex. It has also been observed that one C_α—H(a) bond is sufficient for an absorption in the 2800–2700 cm^{-1} region. This modified approach to the empirical IR correlation turned out to be very useful; in particular, the *cis*-quinolizidine conformation in sparteine-N-oxides[11] as well as in lupanine, sparteine and aphylline[19] was established.

In more recent papers, the correlation of quinolizidine conformations with NMR spectra are reported.[27,28] This method has been applied successfully in studies on the stereochemistry of different quinolizidine derivatives[13,17,27,29] including sparteine[18] and some of its α-oxoderivatives.[19,30]

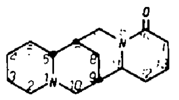
In spite of its great utility Bohlmann's IR correlation requires further modification and rationalization which should allow the exclusion of erroneous structural conclusions and permit the assignment of individual components of the band complex to vibrations of specific chemical bonds. With this in mind the spectra of numerous sparteine alkaloids and their selectively α-deuterated derivatives were determined, using a high resolution spectrometer and an expanded frequency scale. The compounds examined (Table 1) possess definite configurations and under normal conditions they serve as stable conformational models of the quinolizidine system.

RESULTS AND DISCUSSION

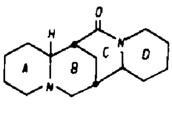
trans-*Quinolizidine system.* Lupinine (IV) may be regarded as a model of an isolated *trans*-quinolizidine system, where three C_α—H bonds are in a *trans* planar and diaxial position with reference to the lone electron pair on nitrogen. In the 2840–2600 cm^{-1} region the IR spectrum of IV shows two prominent absorption bands at 2806·5 and 2763·5 cm^{-1} and a weak absorption at 2677 cm^{-1}. Similar absorption bands are found in the spectra of 15-oxosparteine (V) and 17-oxosparteine (VI) at 2800 and 2761 cm^{-1}. The skeleton of V and VI is built up of two quinolizidine systems, one with a *trans* A/B configuration and one with a *cis* C/D configuration. In the C/D system the electron pair on $N_{(16)}$ is involved in a lactam group and does not contribute to the absorption in the 2840–2600 cm^{-1} region, and also does not influence the ν C_α—H(a) vibrations in A/B significantly, as can be concluded from the similarity of the spectra of V and VI with that of an isolated *trans*-quinolizidine system represented by IV.



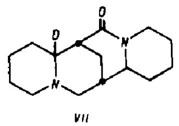
IV



V



VI



VII

Substitution of the methine hydrogen of *trans*-quinolizidine by deuterium, as in 6-deutero-17-oxosparteine (VII), leads to characteristic spectral changes which allow an approximate assignment of the absorption due to the methine ν C_α—H vibration (Fig. 1). Deuterium substitution at $C_{(6)}$ results in an intensity decrease of the band at 2761 cm^{-1} and in the disappearance of a shoulder at 2726 cm^{-1}. Furthermore, the main bands at 2800 and 2761 cm^{-1} shift to lower frequency by ca. 2–3 cm^{-1}. In the ν C_α—D(a) region a broad irregular absorption of low intensity appears at 1930–2060 cm^{-1}, on which small peaks at 1991 and 2014 cm^{-1} can be distinguished.

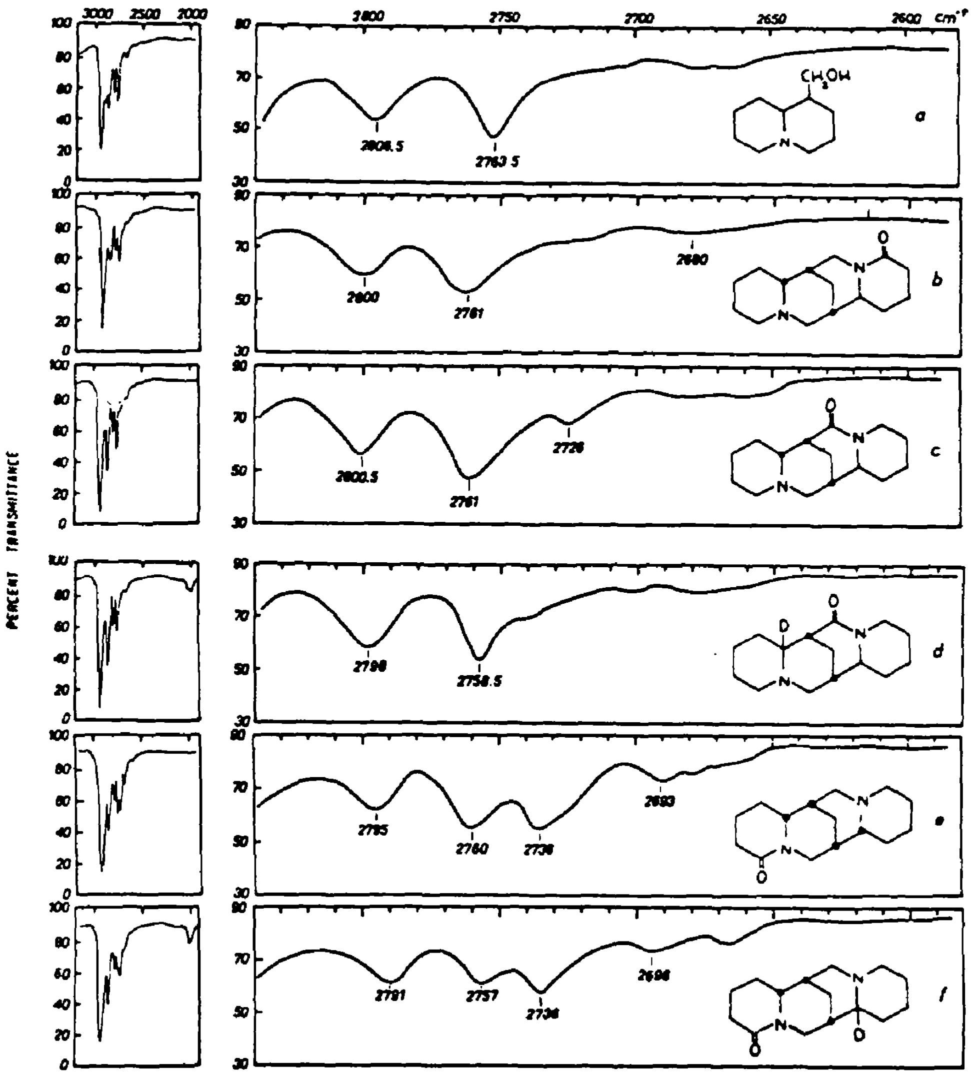
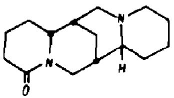
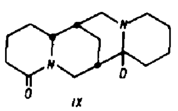


FIG. 1 IR spectra of (a) lupinine (IV), (b) 15-oxosparteine (V), (c) 17-oxosparteine (VI), (d) 6-deutero-17-oxosparteine (VII), (e) α-isolupanine (VIII), and (f) 11-deutero-α-isolupanine (IX) in C_2Cl_4.

From the above we conclude that the main bands at 2800 and 2761 cm^{-1} are due to stretching vibrations of C_α—H(a) bonds in methylene groups at $C_{(2)}$ and $C_{(10)}$. These bands are overlapped by a broad absorption of low intensity which contributes less to the 2840–2600 cm^{-1} absorption complex and is assigned to the ν $C_{(6)}$—H vibration. The ν C_α—H(a) vibrations are mutually coupled, in particular these of methylene groups at $C_{(2)}$ and $C_{(10)}$, which leads to two separate absorption bands probably due to asymmetric and symmetric stretching modes. These conclusions will be supported by further observations discussed in this paper.



VIII

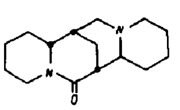


IX

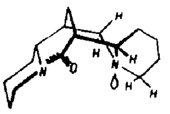
Another compound with a *trans*-quinolizidine system is α-isolupanine (VIII). In addition to the two bands at 2795 and 2760 cm^{-1}, the spectrum of VIII shows a band of medium intensity at 2736 cm^{-1} (Fig. 1), unlike the cases already discussed. Comparing the spectrum of VIII with that of 11-deutero-α-isolupanine (IX), it is seen that the absorption due to the methine ν CH vibration lies in the range 2780–2700 cm^{-1}, the corresponding ν C_α—D(a) vibration giving rise to a peak at ca. 2002 cm^{-1}. In deuterated IX two of the three main absorption bands, namely those at 2791 and 2757 cm^{-1}, are shifted to lower frequency by ca. 3–4 cm^{-1} with reference to the non-deuterated VIII. The band at 2736 cm^{-1} does not change on deuteration of VIII in the $C_{(11)}$ position.

From the results discussed above we conclude that the bands at 2795 and 2760 cm^{-1} are due to ν C_α—H(a) vibrations in methylene groups at $C_{(15)}$ and $C_{(17)}$. The origin of the additional band at 2736 cm^{-1} is not clear. It is remarkable that this band appears only in the spectra of compounds which contain two *trans*-quinolizidine systems as present in α-isosparteine (XXVIa), where serious non-bonded interaction between H(e) on $C_{(10)}$ and H(a) on $C_{(12)}$, as well as between H(a) on $C_{(5)}$ and H(e) on $C_{(17)}$ might be expected.

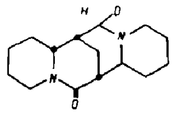
cis-*Quinolizidine*. In previous work Bohlmann has suggested[4,5] that *cis*-quinolizidine with a chair/chair conformation, where only one C_α—H bond is *trans* planar and diaxial with reference to the nitrogen lone electron pair, does not show absorption bands in the 2840–2600 cm^{-1} region. On this basis the authors distinguished *trans*-quinolizidine from *cis*-quinolizidine. However, several exceptions to this rule were also reported and our observations[10,19] have later confirmed that one C_α—H bond *trans* planar to the free electron pair on nitrogen, as present in chair/chair *cis*-quinolizidine, is sufficient for an absorption band in the region 2840–2600 cm^{-1}.



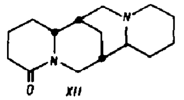
X



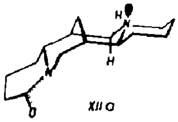
Xa



XI



XII



XIIa

This finding is important not only from a practical viewpoint but also has theoretical significance. The reason for the earlier conclusion that at least two C_α—H(a) bonds are necessary to produce a 2840–2600 cm^{-1} band complex can be traced to the use of spectrometers with low resolving power, making detection of the weak ν C_α—H(a) absorption band in *cis*-quinolizidine spectra difficult, particularly since this band appears at a relatively high frequency and is largely overlapped by the normal ν_{sym} C—H band of the other CH_2 groups. Furthermore, confusion arose because of an erroneous interpretation of the spectra of compounds containing a *cis*-quinolizidine ring fusion. Thus it was suggested[5] that in lupanine (XII) as well as in

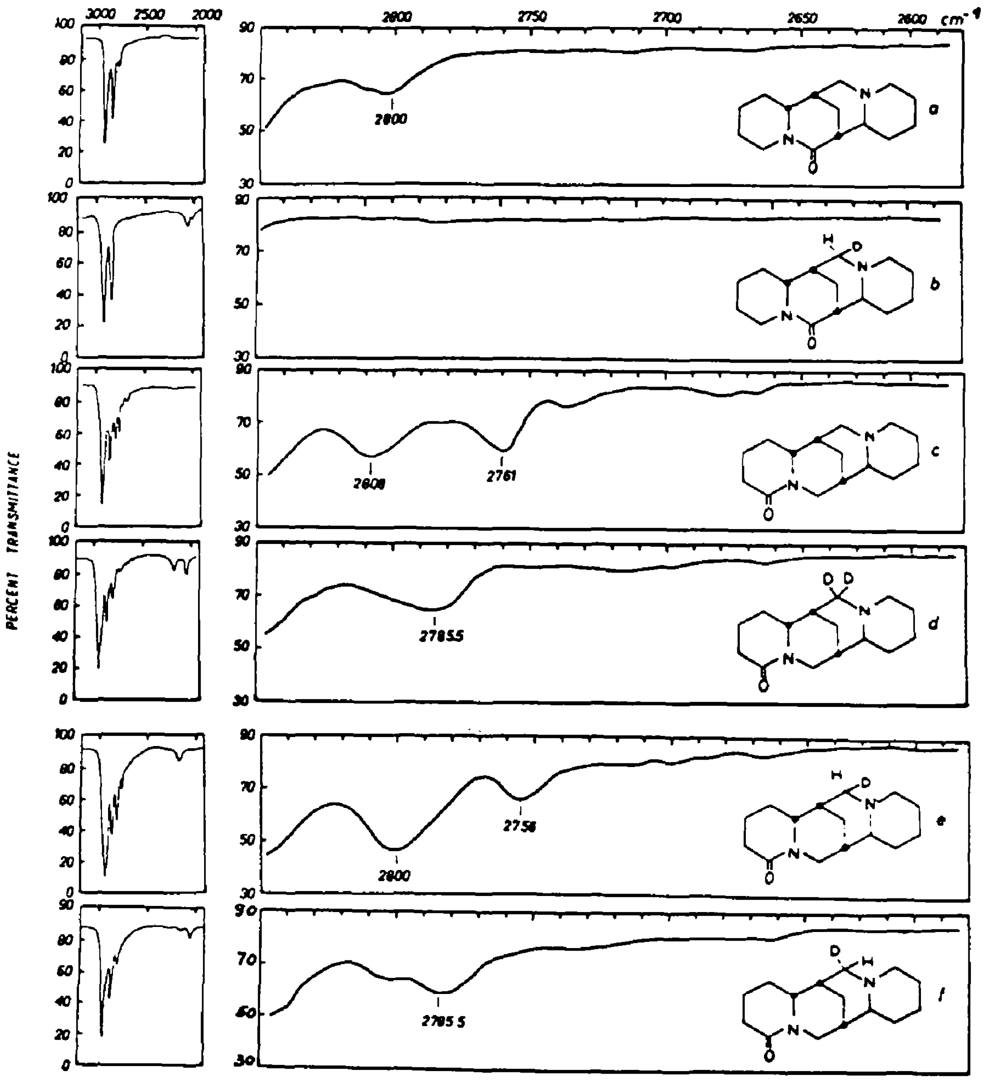
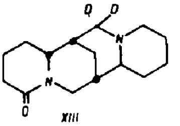


FIG. 2 IR spectra of (a) aphylline (X), (b) 17-β-deuteroaphylline (XI), (c) lupanine (XII), (d) 17-d_2-lupanine (XIII), (e) 17-β-deuterolupanine (XIV), and (f) 17-α-deuterolupanine (XV) in C_2Cl_4.

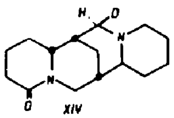
sparteine (XVI) rings C and D are present in a chair conformation (one C_α—H(a) bond), while recent detailed investigations[19] have proven that in both compounds in solution ring C exists predominantly in a boat conformation (three C_α—H(a) bonds), as shown in XIIa.

Aphylline (X and Xa) may be considered as a model compound with an all-chair quinolizidine ring fusion.[19] The IR spectrum of X shows a weak absorption band at 2800 cm^{-1} which is partially overlapped by the ν_{sym} C—H band centred at 2857 cm^{-1}. The band at 2800 cm^{-1} is absent in 17 β-deuteroaphylline (XI) and therefore it can be assigned to ν C_α—H(a) vibrations at $C_{(17)}$ (Fig. 2).

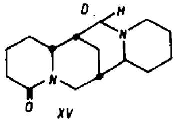
The skeleton of sparteine type alkaloids with *cis*-C/D ring fusion may undergo inversion at $N_{(16)}$ which results in a conformational change of ring C from a chair into a boat form. In the first form there is only one C_α—H(a) bond which is situated at $C_{(17)}$, and which is *trans*-planar and diaxial in relation to the electron pair on $N_{(16)}$, while in the second form there are three such C_α—H(a) bonds at $C_{(11)}$, $C_{(15)}$ and $C_{(17)}$. Thus it is possible to distinguish between these conformations by means of IR spectroscopy.



XIII



XIV



XV

An example of a skeleton with *cis*-C/D ring fusion and boat/chair conformation may be lupanine (XII). The band complex in the 2840–2600 cm^{-1} region of XII consists of two main bands at 2808 and 2761 cm^{-1} which are assigned to ν C_α—H(a) vibrations in methylene groups at $C_{(15)}$ and $C_{(17)}$. Substitution of one of the axially oriented hydrogens by deuterium, as in 17-d_2-lupanine (XIII) or 17-α-deuterolupanine (XV), causes the nearly complete disappearance of both bands compensated by the appearance of a single band at 2785·5 cm^{-1}, i.e. in the middle between the two bands mentioned before. This indicates that the two ν C_α—H(a) vibrations at $C_{(15)}$ and $C_{(17)}$ are mutually coupled. The spectrum of 17-β-deuterolupanine (XIV), where the deuterium atom remains in an equatorial and *cis*-position with reference to the lone electron pair on $N_{(16)}$, shows a modified band complex in relation to that of XII. This is due to the mass effect of D(e) which, however, does not change the coupling described above (Fig. 2).[*]

Fused quinolizidine systems; sparteine. The C–N skeleton of sparteine isomers is built up of two quinolizidine systems fused in position 1,3. In sparteine (XVI) a *trans*-quinolizidine system A/B is attached to a *cis*-quinolizidine system C/D, with ring C in a boat conformation as in XII. Thus the band complex of XVI in the

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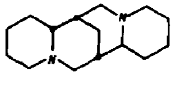
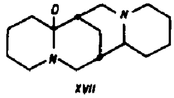
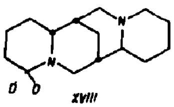
[*] It is expected that important information on the equilibrium between the two main lupanine conformers may be derived from a detailed analysis of band positions and intensities in the C–D region of XIII, XIV and XV. Such investigations are in progress.



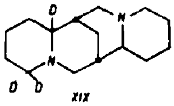
XVI



XVII



XVIII



XIX

2840–2600 cm^{-1} region can be considered as a summation of the respective band complexes of IV or VI with that of XII. The spectrum of XVI shows two strong absorption bands at 2795 and 2761 cm^{-1} and a shoulder at 2823 cm^{-1}. An additional shoulder is observed at 2726 cm^{-1} and a weak band at 2679 cm^{-1}. It can be assumed that the band at 2795 cm^{-1} together with the shoulder at 2823 cm^{-1} arise from the overlapping of two bands which appear in the spectrum of VI at 2800 cm^{-1} and in the spectrum of XII at 2808 cm^{-1}. The band at 2761 cm^{-1} is probably also due

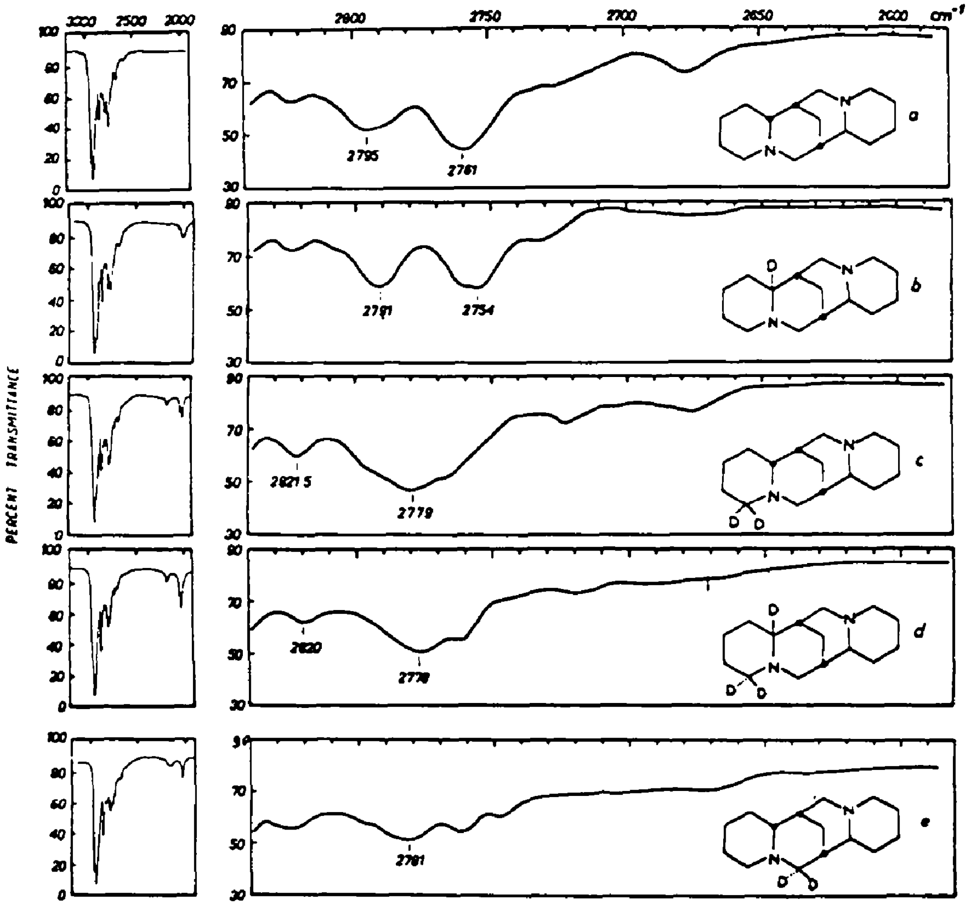
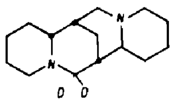
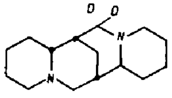


FIG. 3 IR spectra of (a) sparteine (XVI), (b) 6-deuterosparteine (XVII), (c) 2-d$_2$-sparteine (d) 2,6-d$_3$-sparteine (XIX) and (e) 10-d$_2$-sparteine (XX) in C$_2$Cl$_4$.

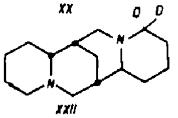
to the summation of two unresolved absorption bands; in the spectra of VI and XII prominent bands are found at a similar frequency. The assumption that the 2840–2600 cm^{-1} band complex of XVI could originate from the simple summation of a *trans*-quinolizidine band complex with that of a boat/chair *cis*-quinolizidine system is supported by the fact that the XVI band complex is approximately equal to the sum of intensities of the respective VI and XII band complexes. The spectrum of 6-deutero-sparteine (XVII) gives evidence on the band position of ν $C_{(6)}$—H vibrations. This band is broad and overlapped by the strong absorption band at 2761 cm^{-1}. The spectrum of XVII shows a broad ν $C_{(6)}$—D absorption with remarkable fine structure of small peaks which can be distinguished at 2014, 2004 and 1992 cm^{-1}. The observation that the broad ν $C_{(6)}$—H absorption is centred at ca. 2760 cm^{-1} may be confirmed by a comparison of other deuterated sparteines such as 2-d_2-sparteine (XVIII), 2,6-d_3-sparteine (XIX), 17-d_2-sparteine (XXI), and 6,17-d_3-sparteine (XXIII) (Fig. 3).



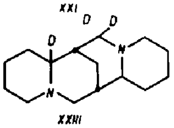
XX



XXI

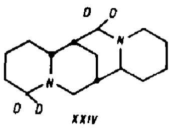


XXII

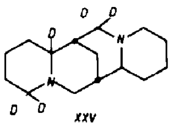


XXIII

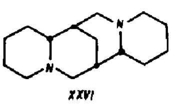
From the above spectral observations on single quinolizidine systems it can be expected that in XVI the ν C—H(a) vibration in methylene groups adjacent to the same nitrogen will be mutually coupled. This assumption may be confirmed by the following observation: If deuterium substitution takes place in position $C_{(2)}$ or $C_{(10)}$, the coupling between ν $C_{(2)}$—H(a) and ν $C_{(10)}$—H(a) vibrations is removed and a new absorption band appears at 2781 cm^{-1}, as seen in the spectra of XVIII and 10-d_2-sparteine (XX). The coupling between ν $C_{(15)}$—H(a) and ν $C_{(17)}$—H(a) vibrations in the *cis*-quinolizidine systems XVIII and XX still remains intact, as seen from the distinct shoulders at 2824 and 2762 cm^{-1} (Fig. 3). Similar relations are observed if the spectrum of XVII is compared with that of XIX.



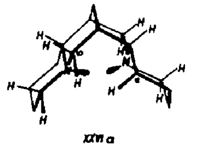
XXIV



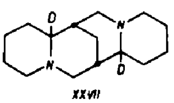
XXV



XXVI



XXVIa



XXVII

Characteristic spectral changes are observed if deuterium substitution is carried out in methylene groups adjacent to $N_{(16)}$, i.e. in the *cis*-quinolizidine fragment of XVI. In this case, the coupling between ν $C_{(15)}$—H(a) and ν $C_{(17)}$—H(a) vibrations is removed, while it will still exist in the *trans*-quinolizidine system A/B. A comparison of the spectra of XVI with those of XXI and XXII shows that the result is a disappearance of the shoulder at 2824 cm^{-1} and a decrease of the band at 2761 cm^{-1}, with simultaneous formation of a new band at ca. 2780 cm^{-1}, i.e. between the two bands at ca. 2795 and 2760 cm^{-1} which are characteristic of the *trans*-quinolizidine system A/B (Fig. 4). A similar situation is found in the spectrum of 6,17-d$_3$-sparteine (XXIII) if compared with that of XVII (Fig. 4).

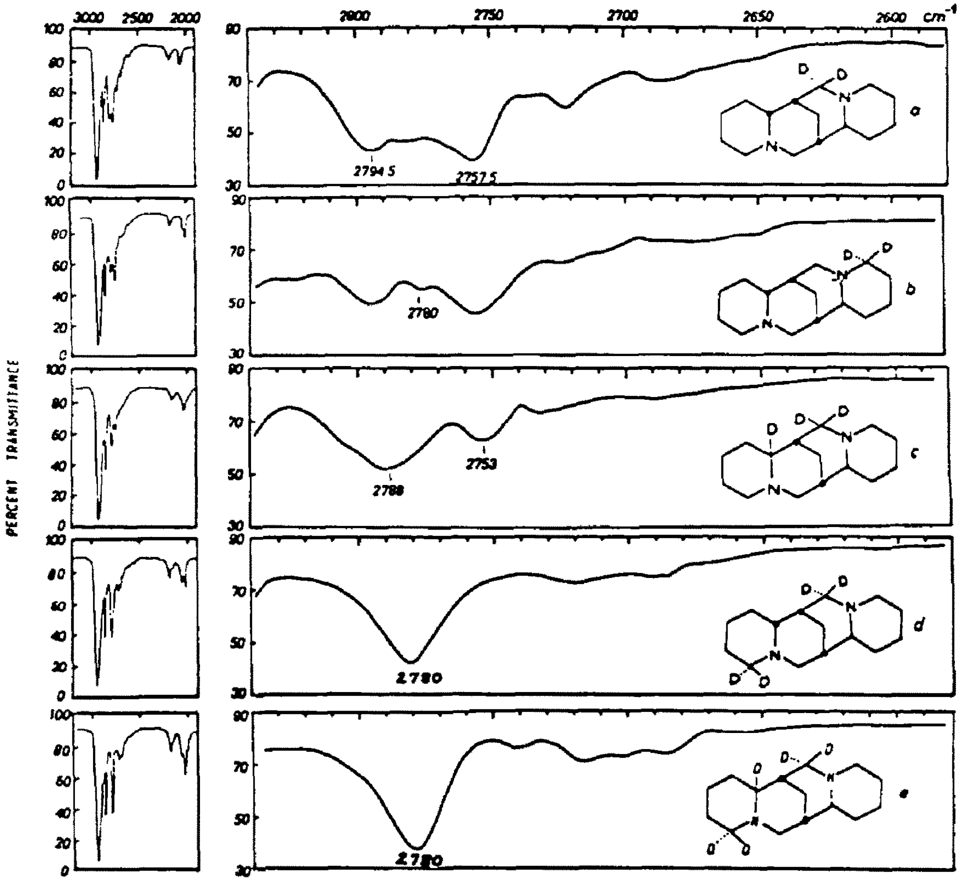


FIG. 4 IR spectra of (a) 17-d$_2$-sparteine (XXI), (b) 15-d$_2$-sparteine (XXII), (c) 6,17-d$_3$-sparteine (XXIII), (d) 2,17-d$_4$-sparteine (XXIV), and (e) 2,6,17-d$_5$-sparteine (XXV) in C_2Cl_4.

The hypothesis presented above may be confirmed by the very interesting spectral changes which are observed in the spectra of deuterated sparteines where deuterium substitution was carried out in C$_\alpha$-methylene groups of both the *trans*-quinolizidine A/B and the *cis*-quinolizidine C/D parts of the molecule. These compounds are 2,17-d$_4$-sparteine (XXIV) and 2,6,17-d$_5$-sparteine (XXV). The spectra of XXIV and XXV shows strong single bands at ca. 2780 cm^{-1} which are assigned to uncoupled ν C$_\alpha$—H(a) vibrations of methylene groups at C$_{(10)}$ and C$_{(15)}$ (Fig. 4). The weak absorption in the spectra of XXIV and XXV at ca. 2700 cm^{-1} is unidentified. It is presumed that this absorption is due to overtones of C_α—H(a) deformation modes which lie at ca. 1350 cm^{-1}.

α-Isosparteine (XXVI and XXVIa). In XXVI, which has the conformation XXVIa, two *trans*-quinolizidine systems are fused in position 1,3. The ideal chair conformation of the 6-membered rings in the skeleton of XXVI is somewhat deformed by the repulsive interaction between the lone electron pairs on $N_{(1)}$ and $N_{(16)}$, as well as between H atoms at $C_{(10)}$ and $C_{(12)}$ on one side and $C_{(5)}$ and $C_{(17)}$ on the other. In connection with this it cannot be expected *a priori* that the 2840–2600 cm^{-1} band

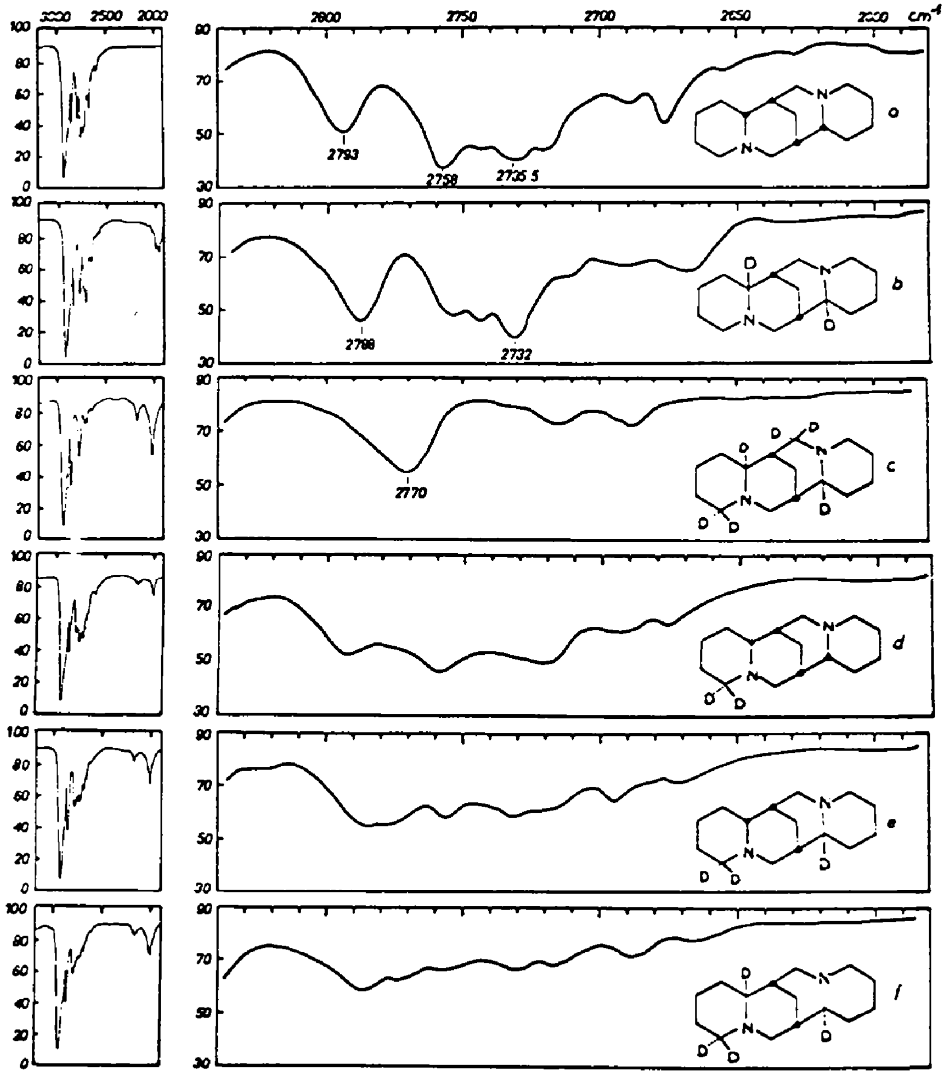
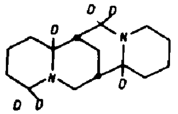
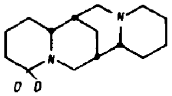


FIG. 5 IR spectra of (a) α-isosparteine (XXVI), (b) 6,11-d$_2$-α-isosparteine (XXVII), (c) 2,6,11,17-d$_6$-α-isosparteine (XXVIII), (d) 2,d$_2$-α-isosparteine (XXIX), (e) 2,11-d$_3$-α-isosparteine (XXX) and (f) 2,6,11-d$_4$-α-isosparteine (XXXI) in C_2Cl_4.

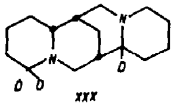
complex of XXVI can be rationalized by a simple summation of two *trans*-quinolizidine band complexes. A certain similarity is found between the spectra of XXVI and VIII where a deformation of the ideal all-chair skeleton also occurs. The 2840–2600 cm^{-1} band complex of XXVI has the strongest bands at 2793, 2758 and 2735 cm^{-1}, i.e. at about the same frequencies as found in the spectrum of VIII. The band complex of XXVI, however, is much more intense than that of VIII and the band at 2735 cm^{-1} has additional shoulders at ca. 2745 and 2720 cm^{-1}. Furthermore, in the spectrum of XXVI two bands are present at 2690 and 2675 cm^{-1} which are absent in the spectrum of VIII (Fig. 5).



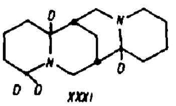
XXVIII



XXIX



XXX



XXXI

An analysis of the spectrum of α-isosparteine in which the methine hydrogens at $C_{(6)}$ and $C_{(11)}$ are substituted by deuterium shows the following features: (i) a considerable decrease in the intensity of the band at 2758 cm^{-1} and a complete disappearance of the shoulder at 2720 cm^{-1}, (ii) a decrease of the band at 2675 cm^{-1}, and (iii) a downward shift of the bands at 2793 and 2735 cm^{-1} by about 3–5 cm^{-1}. The ν C_α—D band of 6,11,d_2-α-isosparteine (XXVII) is centred at ca. 2000 cm^{-1}, and shows remarkable fine-structure (Fig. 5). From the above it can be deduced that the remaining bands in the spectrum of XXVII at 2788, 2755 and 2732 cm^{-1} are due to ν C_α—H(a) vibrations in methylene groups. These vibrations at $C_{(2)}$ and $C_{(10)}$ on one side and at $C_{(15)}$ and $C_{(17)}$ on the other are mutually coupled. Deuterium substitution at $C_{(2)}$ and $C_{(17)}$, as in 2,6,11,17-d_6-α-isosparteine (XXVIII), removes the coupling in both *trans*-quinolizidine systems, as is indicated by the very strong single ν C_α—H(a) band at 2770 cm^{-1} (Fig. 5). It is assumed that the unidentified bands in the 2700 cm^{-1} region in the spectra presented in Fig. 5, are due to overtones of C_α—H(a) deformation modes which appear at ca. 1350 cm^{-1}.

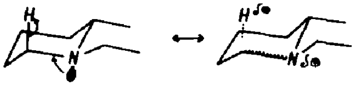
If deuterium substitution is carried out in only one methylene group, e.g. at $C_{(2)}$, then coupling is removed in the A/B system, but still exists intact in the C/D-ring system. In this case the 2840–2600 cm^{-1} band complex consists of three main bands which are characteristic for the deformed *trans*-quinolizidine C/D. These overlap the single band which is due to ν $C_{(10)}$—H(a) vibrations in the A/B system. The irregular shape of the band complexes of 2-d_2-α-isosparteine (XXIX), 2,11-d_3-α-isosparteine (XXX) and 2,6,11-d_4-α-isosparteine (XXXI) may be regarded as a transition between the band complex of XXVI and that of XXVIII (Fig. 5).

CONCLUSIONS

1. The absorption which appears in the spectra of quinolizidine and its derivatives in the 2840–2600 cm^{-1} region arises from the stretching vibrations of one or more

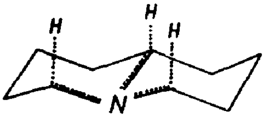
axially oriented C_α—H bonds. The intensity and shape of the band complex depends on the number of those bonds and their steric environment in the molecule.

2. It is suggested that the lower frequency of ν C_α—H(a) bands with reference to the "normal" ν CH region is due to a specific charge delocalization from the *trans*-planar lone electron pair on nitrogen to the C_α—H(a) bonds, as indicated in XXXII.*



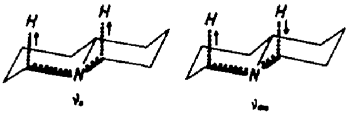
XXXII

3. In *trans*-quinolizidine, all three axial C_α—H bonds participate in the charge delocalization of the type XXXII and the whole oscillating system is coupled mechanically (see XXXIII).



XXXIII

This conclusion is supported by spectral changes in the 2840–2600 cm^{-1} region which are observed after deuterium substitution of one of the axial C_α—H bonds. These spectral changes are insignificant if deuterium substitution takes place in the C_α-methine group, but they are dramatic if an axially oriented C_α-methylene hydrogen is subject to deuterium substitution. Axial CH bonds in both methylene groups adjacent to nitrogen have identical force constants and the same symmetry; thus two absorption bands are found in the spectrum of *trans*-quinolizidine systems at



XXXIV

2800 and 2761 cm^{-1} respectively, due to vibrational coupling. The first band can be assigned to the asymmetric and the second band to the symmetric stretching vibration, as indicated in XXXIV. Vibrational coupling between two C_α—H(a) bonds in

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* This could also be described as hyperconjugation. A mechanism for this increase in charge on the C_α—H(a) proton has been proposed in Ref. 27.

methylene groups is only slightly affected if one of the equatorially oriented geminal methylene hydrogens is substituted by deuterium. Deuterium substitution in an axial position removes the coupling completely and a single band due to an uncoupled C_α—H(a) methylene hydrogen appears at ca. 2780 cm^{-1}.

4. In sparteine and α-isosparteine the band complex in the 2840–2600 cm^{-1} region can be regarded as a summation of two respective quinolizidine band complexes. However, in the latter case the 2840–2600 cm^{-1} absorption is significantly modified by additional intramolecular steric factors.*

5. In compounds containing a *cis*-quinolizidine ring fusion two conformations are considered, the all-chair conformer and the boat-chair conformer. The first has only one C_α—H(a) bond which gives rise to a single band in the 2840–2600 cm^{-1} region. In the second conformer three C_α—H(a) bonds are present, similar to those found in *trans*-quinolizidine. The steric environments in boat–chair *cis*-quinolizidine are, however, different from those in *trans*-quinolizidine if examined in the sparteine series. Consequently vibrational coupling within the two systems will not be exactly equal and certain differences in their 2840–2600 cm^{-1} absorption complexes will be observed.†

6. As far as the shape of the 2840–2600 cm^{-1} band complex of compounds investigated is concerned, the following four fundamental types can be distinguished:

(i) The *normal* trans-*quinolizidine type* which consists of two main bands at ca. 2800 and 2761 cm^{-1} (the latter being stronger), present in IV, V, VI and all *trans*-quinolizidine derivatives in which the general geometry of the oscillator XXXIII is not disturbed.

(ii) The *deformed* trans-*quinolizidine type* with three main absorption bands at 2795, 2760 and 2736 cm^{-1} respectively. This band complex is found in the spectra of VIII and XXVI.

(iii) The *all-chair* cis-*quinolizidine type* which has only a single band due to the presence of only one C_α—H(a) bond in the molecule. This conformation exists in X.

(iv) The *boat–chair* cis-*quinolizidine type*, consisting of two main bands at ca. 2808 and 2761 cm^{-1} respectively (the former being stronger), as in XII.

7. One of the four fundamental band complexes mentioned above appears unchanged in the spectrum only if none of the three axial and two equatorial C_α hydrogens in a given quinolizidine system is substituted by other atoms or groups. In this paper the results of deuterium substitution at C_α are discussed in detail. From these it can be determined whether a C_α—D bond is axially or equatorially oriented. The influence of other C_α substituents on quinolizidine band complexes in the 2840–

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* This deformation is probably due to an interaction of the lone electron pair on $N_{(1)}$ with that on $N_{(16)}$, but some other steric factors must be involved too, since VIII—where only one nitrogen has basic properties—also shows the deformed trans-quinolizidine band complex. The Dreiding model of XXVI reveals significant repulsive interaction between $C_{(10)}$—H(e) and $C_{(12)}$—H(a) on one side and between $C_{(5)}$—H(a) and $C_{(17)}$—H(e) on the other. This interaction which also exists in VIII, modifies the geometry of XXXIII somewhat and probably this is the origin of the band found in the spectra of XVI and VIII at ca. 2736 cm^{-1}, in addition to the bands at 2800 and 2761 cm^{-1}.

† It is assumed that these differences are caused by repulsive interaction between the $C_{(8)}$ hydrogen and the lone electron pair on $N_{(16)}$ as well as between $C_{(7)}$—H and $C_{(17)}$—H(e) (see XIIa).

2600 cm^{-1} region has not been investigated, but from some remarks in the literature[5,21] it is obvious that alkyl substituents can change those bands drastically.[*]

Furthermore, we accept that the specific charge delocalization (XXXII) might be influenced by substituents at C atoms other than C_α, especially if such substituents are in a co-axial position to C_α—H(a) bonds.

8. Variations in the 2840–2600 cm^{-1} absorption can arise from non-bonded interactions between closely situated atoms and the lone electron pair on nitrogen. For example, we have observed that hydrogen bonding with quinolizidine nitrogen as a hydrogen bond acceptor does not change the band complex seriously, except if proton tunnelling takes place. In the case of very short hydrogen-bonds, as found in monocations of sparteine and α-isosparteine-N-oxides, no absorption is observed in the 2840–2600 cm^{-1} region. It should be pointed out that hydrogen bonding sometimes contributes to a conformational change within a *cis*-quinolizidine system. In that case spectral changes in the 2840–2600 cm^{-1} region are significant, e.g. in sparteine monoperchlorate.

The empirical correlation between the general complexity and fine structure of the 2840–2600 cm^{-1} absorption and the conformation of quinolizidine alkaloids can provide valuable stereochemical evidence. However, it is important to interpret the IR data very critically and on the basis of well chosen model compounds. For example, the considerable divergence of opinion on the stereochemistry of alkyl quinolizidine derivatives arose from an over-simplified interpretation of the 2840–2600 cm^{-1} absorption which was limited to the conclusion of the "presence or absence" of the band complex. We hope that the results discussed in this paper will contribute to further determinations of the stereochemistry of quinolizidine derivatives. The ultimate usefulness of the 2840–2600 cm^{-1} absorption complex for diagnostic purposes will be reached if the problem of the specific charge delocalization in the co-planar system XXXIII will be explained theoretically.

EXPERIMENTAL

IR spectra. Preliminary IR spectra were obtained with a Perkin Elmer Model 237 grating spectrophotometer with a linear frequency scale. The high resolution measurements were made with a Beckman IR-7 IR spectrophotometer with a NaCl foreprism and a 75 lines/mm grating blazed at 12μ, operating in the third grating order. The spectra were recorded at a nominal slit width of ca. 1 cm^{-1}, using a frequency scale of 10 cm^{-1}/inch. The frequency calibration of this instrument[31,32] as well as other details of the instrumental procedure have been described in previous papers.[33] KBr cells with a path length of 0·1 cm were used. The concentration of tetrachloroethylene solns of the compounds examined was 0·2 M. Reagent grade solvent was dried over P_2O_5 and distilled through a 50-theoretical plate spinning band column. All the quinolizidine derivatives were distilled or sublimed over a short path under ca. 10^{-3} torr press just before the spectra were recorded.

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[*] From one of Bohlmann's papers[5] it is seen that the substitution of the methine hydrogen by a Me group in 10-methylquinolizidine results in the almost complete disappearance of the absorption in the 2840–2600 cm^{-1} region, while a deuterium atom in $C_{(10)}$ position does not change the *trans*-quinolizidine band complex significantly. We assume that in 10-methyl-quinolizidine serious non-bonded interactions between the Me hydrogens and the remaining two C_α—H(a) hydrogens forces the system XXXIII to adopt a new geometry, where C_α—H(a) bonds will be somewhat dislocated from their ideal axial and co-planar position with reference to the lone electron pair on nitrogen. Consequently the specific charge delocalization of the type XXXII which gives rise to absorption in the 2840–2600 cm^{-1} region will be affected. We believe that from a systematic IR study of various quinolizidine derivatives with C_α alkyl groups, further diagnostic correlations concerning the steric situation of these groups can be obtained.

Lupinine (IV), 15-*oxosparteine* (V), 17-*oxosparteine* (VI), α-*isolupanine* (VIII), *aphylline* (X), *lupanine* (XII), *sparteine* (XVI) *and* α-*isosparteine* (XXVI). The alkaloids were samples used in previous investigations by two of us (J.S. and M.W.) and were isolated from plant material or partially synthesized. All compounds were purified by common methods and showed physical properties (m.p., b.p., $[\alpha]_D$, n_D, IR, UV and NMR spectra) which agreed well with literature values. The elemental analyses were satisfactory, and the physical properties of characteristic salts formed were also in good agreement with literature data.

17-β-*Deuteroaphylline* (XI), 17-d_2-*lupanine* (XIII), 17-β-*deutero-lupanine* (XIV) *and* 17-α-*deutero-lupanine* (XV). The compounds were those described in a recent paper.[19]

Deuterated 17-*oxosparteine*, α-*isolupanine*, *sparteines and* α-*isosparteines*. A general method was used to obtain these compounds.[5] α-Oxosparteines or α,β-dehydrosparteines were reduced with suitable deuterated reducing agents. α-Oxosparteines were reduced with $LiAlD_4$ while the dehydrobases were reduced with the same reagent or with $NaBD_4$. The intermediate dehydrobases were prepared from sparteine type alkaloids by the common mercuric acetate $[Hg(OAc)_2]$ method. In detail, the following pathways were followed:

6-*Deutero*-17-*oxosparteine* (VII). VI $\xrightarrow{Hg(OAc)_2}$ Δ^5-dehydro-VI $\xrightarrow{NaBD_4}$ VII.

11-*Deutero*-α-*isolupanine* (IX). VIII $\xrightarrow{Hg(OAc)_2}$ Δ^{11}-dehydro-VIII $\xrightarrow{NaBD_4}$ IX.

6-*Deutero-sparteine* (XVII). XVI $\xrightarrow{Hg(OAc)_2}$ Δ^5-dehydro-XVI $\xrightarrow{NaBD_4}$ XVII.

2-d_2-*Sparteine* (XVIII). XII $\xrightarrow{LiAlD_4}$ XVIII.

2,6-d_3-*Sparteine* (XIX). XVIII $\xrightarrow{Hg(OAc)_2}$ Δ^5-dehydro-XVIII $\xrightarrow{NaBD_4}$ XIX.

10-d_2-*Sparteine* (XX). X $\xrightarrow{LiAlD_4}$ XX.

17-d_2-*Sparteine* (XXI). VI $\xrightarrow{LiAlD_4}$ XXI.

15-d_2-*Sparteine* (XXII). V $\xrightarrow{LiAlD_4}$ XXII.

6,17-d_3-*Sparteine* (XXIII). XXI $\xrightarrow{Hg(OAc)_2}$ Δ^5-dehydro-XXI $\xrightarrow{NaBD_4}$ XXIII.

2,17-d_4-*Sparteine* (*F*XIV). 17-Oxolupanine $\xrightarrow{LiAlD_4}$ XXIV.

2,6,17-d_5-*Sparteine* (XXV). XXIV $\xrightarrow{Hg(OAc)_2}$ Δ^5-dehydro-XXIV $\xrightarrow{NaBD_4}$ XXV.

6,11-d_2-*Isosparteine* (XXVIII). XVI $\xrightarrow{Hg(OAc)_2}$ $\Delta^{5,11}$-didehydro-XVI $\xrightarrow{LiAlD_4}$ XXVIII.

2,6,11,17-d_6-α-*Isosparteine* (XXVIII). XXIV $\xrightarrow{Hg(OAc)_2}$ $\Delta^{5,11}$-didehydro-XXIV $\xrightarrow{LiAlD_4}$ XXVIII.

2-d_2-α-*Isosparteine* (XXIX). VIII $\xrightarrow{LiAlD_4}$ XXIX.

2,11-d_3-α-*Isosparteine* (XXX). XII $\xrightarrow{Hg(OAc)_2}$ Δ^{11}-dehydro-XII $\xrightarrow{NaBD_4}$ XXX.

2,6,11-d_4-α-*Isosparteine* (XXXI). XVIII $\xrightarrow{Hg(OAc)_2}$ $\Delta^{5,11}$-didehydro-XVIII → XXXI.

The initial alkaloids, intermediate dehydrobases, and deuterated products were analysed in the usual way. Physical properties (m.p., b.p., $[\alpha]_D$, n_D, IR spectrum), elemental analyses of the bases, and salt characteristics agreed well with literature values. In some of the deuterated bases the deuterium content was determined and results of 97–98% deuterium were found.

Acknowledgement—This work was supported financially by the National Research Council of Canada. One of us (J.S.) expresses his appreciation for the award of a postdoctoral fellowship.

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[1] R. D. Hill and G. D. Meakins, *J. Chem. Soc.* 761 (1958).

[2] F. Dalton, R. D. Hill and G. D. Meakins, *Ibid.* 2927 (1960).

[3] J. T. Braunholtz, E. A. V. Ebsworth, F. G. Mann and N. Sheppard, *Ibid.* 1462 (1957).

[4] F. Bohlmann, *Angew. Chem.* **69**, 641 (1957).

[5] F. Bohlmann, *Chem. Ber.* **91**, 2157 (1958).

[6] E. Wenkert and D. K. Roychandhuri, *J. Am. Chem. Soc.* **78**, 6417 (1956).

[7] W. E. Rosen, *Tetrahedron Letters* 481 (1961).

[8] A. R. Katritzky, *Physical Methods in Heterocyclic Chemistry* Vol. II; p. 246. Academic Press, New York (1963) and additional refs cited there.

[9] C. Y. Chen and R. J. W. Le Fèvre, *Tetrahedron Letters* 1611 (1965).

[10] M. Wiewiórowski and J. Skolik, *Bull. Acad. Polon. Sci., Ser. Sci. Chim.* **10**, 1 (1962).

[11] M. Wiewiórowski and P. Baranowski, *Ibid.* **10**, 537 (1962).

[12] F. Bohlmann and D. Schumann, *Tetrahedron Letters* 2432 (1965).
[13] H. S. Aaron, G. E. Wicks, Jr. and Ch. P. Rader, *J. Org. Chem.* **29**, 2248 (1964).
[14] Ch. P. Rader, R. L. Young, Jr. and H. S. Aaron, *Ibid.* 1536 (1965).
[15] T. M. Moynehan, K. Schofield, R. A. Y. Jones and A. R. Katritzky, *J. Chem. Soc.* 2637 (1962).
[16] S. Saito, K. Kotera, N. Shigematsu, A. Ide, N. Sugimoto, Z. Hoiri, M. Hanoka, Y. Yamawaki and Y. Tamura, *Tetrahedron* **19**, 2085 (1963).
[17] W. A. Ayer, J. K. Jenkins, K. Piers and S. Valerde-Lopez, *Canad. J. Chem.* **45**, 445 (1967).
[18] F. Bohlmann, D. Schumann and Ch. Arndt, *Tetrahedron Letters* 2705 (1965).
[19] M. Wiewiórowski, O. E. Edwards and M. D. Bratek-Wiewiórowska, *Canad. J. Chem.* **45**, 1447 (1967).
[20] L. Blahaa, B. Kakáč and J. Weichet, *Coll. Czech. Chem. Commun.* **27**, 857 (1962).
[21] C. D. Johnson, R. A. Y. Jones, A. R. Katritzky, C. R. Palmer, K. Schofield and R. J. Wells, *J. Chem. Soc.* 6797 (1965).
[22] T. Takemoto, Y. Kondo and K. Kondo, *J. Pharm. Soc. Japan* **83**, 162 (1963).
[23] M.-M. Janot, R. Goutarel, E. W. Warnhoff and A. Le Hir, *Bull. Soc. Chim. Fr.* 637 (1961).
[24] H. S. Aaron, *Chem. & Ind.* 1338 (1965).
[25] E. L. Eliel, N. L. Allinger, S. J. Angyal and G. A. Morrison, *Conformational Analysis* p. 252. Interscience, New York (1965).
[26] M. Przybylska and W. H. Barnes, *Acta Cryst.* **6**, 377 (1953).
[27] H. P. Hamlow, S. Okuda and N. Nakagawa, *Tetrahedron Letters* 2553 (1964).
[28] F. Bohlmann, D. Schumann and H. Schulz, *Ibid.* 173 (1964).
[29] M. Uskoković, H. Bruderer, C. von Planta, T. Williams and A. Brossi, *J. Am. Chem. Soc.* **86**, 3364 (1964).
[30] F. Bohlmann and D. Schumann, *Tetrahedron Letters* 2435 (1965).
[31] P. J. Krueger, *Appl. Opt.* **1**, 443 (1962).
[32] P. J. Krueger and G. H. Schulze, *Rev. Sci. Instr.* **34**, 88 (1963).
[33] P. J. Krueger and H. D. Mettee, *Canad. J. Chem.* **42**, 326 (1964).