[CONTRIBUTION FROM THE DIVISION OF CHEMISTRY OF THE NATIONAL RESEARCH COUNCIL OF CANADA]

The Infrared Absorption Spectra of Alkaloids[1]

BY LÉO MARION, D. A. RAMSAY AND R. NORMAN JONES

Although several applications of infrared spectrometry to the detection of functional groups in alkaloids are to be found in the recent literature,[2] no systematic examination of the infrared spectra of the alkaloids has been reported.

This paper is concerned with a comparative study of the infrared absorption spectra of a variety of alkaloids in the regions characteristic of the principal structural groups. Particular attention has been devoted to the regions 3700–3200 cm.$^{-1}$ in which both the hydroxyl and the imino groups absorb, and 1780–1620 cm.$^{-1}$ in which the variously substituted carbonyl groups absorb.[3] The correlations which have been derived between the spectra and molecular structures of various nitrogenous compounds (*e.g.*, penicillin[4,5]), and the steroids,[6] encouraged the view that similar correlations might be established for the alkaloids.

Experimental

The spectra were determined on a Perkin–Elmer 12B single beam spectrometer using a calcium fluoride prism and a 7-cycle GM amplifier. Chloroform was used as a solvent since it is transparent in the infrared regions of principal interest (3700-3100, 3000-2700, 1800-1540 cm.$^{-1}$) and dissolves most alkaloids readily. The chloroform was washed several times with water to remove ethanol, dried by repeated shaking with anhydrous sodium sulfate and distilled, the middle fraction being collected.[7] The formation of phosgene by photolysis produces an absorption band at 1810 cm.$^{-1}$ and the solvent was discarded as soon as this band appeared.

Standard solutions of the alkaloids (usually 3 mg. per ml.) were employed to give some significance to the band intensities, the absorptions being measured in a sodium chloride cell of thickness 1 mm. To make allowance for the appreciable variations in molecular weights of the alkaloids, apparent molecular extinction coefficients[8] at the absorption maxima were calculated for the principal bands. These intensities are probably accurate to ± 10%. The estimated errors in the frequencies reported are ± 5 cm.$^{-1}$ for the region 3700-2700 cm.$^{-1}$ and ± 2 cm.$^{-1}$ for the region 1800-1540 cm.$^{-1}$.

Results and Discussion

Forty-seven alkaloids were investigated in chloroform solution under the conditions specified above. The principal bands will be discussed in order of decreasing frequency.

A. Hydroxyl Bands (O–H Stretching Vibration).—It is well established[3,5] that unassociated hydroxyl groups show sharp absorption bands in the region 3700–3500 cm.$^{-1}$ while hydrogen bonding produces a broadening of these bands and a shift to lower frequencies (usually 3500–3200 cm.$^{-1}$).

Fifteen of the alkaloids contained hydroxyl groups and of these thirteen produced sharp bands in the region 3625–3540 cm.$^{-1}$ while lupinine and cevine produced a broad absorption in the region of 3400 cm.$^{-1}$ (see Table I and Fig. 2). The apparent molecular extinction coefficients of the sharp bands ranged from 30–90 with the exception of hunnemanine which produced a value of 160. This high intensity and low frequency may be associated with the phenolic character of the hydroxyl group. The remaining thirty-two alkaloids, which did not contain hydroxyl groups, showed no band in the region 3700–3500 cm.$^{-1}$ with an apparent molecular extinction coefficient greater than 10.

TABLE I

OH STRETCHING BANDS IN SOME ALKALOIDS IN CHLOROFORM SOLUTION

Compound	OH frequency, cm.$^{-1}$	E_a^{14}
Non-associated hydroxyl groups		
Quinine	3625	61
Dihydrolycopodine	3625	75
Chelidonine	3625	30
Yohimbine	3625	35
ψ-Conhydrine	3620	69
l-Hyoscyamine	3620	50
Tropine	3620	61
Cinchonidine	3620	82
Jervine	3615	90
Ochrobirine	3580	81
α-Methylmorphimethine	3580	70
Codeine	3580	64
Hunnemanine	3540	160
Associated hydroxyl groups		
Cevine	3520, 3400	
Lupinine	~3400	

Hence the presence of a sharp band in the region 3625–3540 cm.$^{-1}$ with an apparent molecular ex-

---

[1] Published as Contribution No. 2274 from the laboratories of the National Research Council of Canada. Presented in part at a Symposium on Alkaloid Chemistry held at the University of New Brunswick, August, 1949.

[2] See for instance (a) Adams and Govindachari, THIS JOURNAL, **71**, 1182 (1949); (b) Gates, Woodward, Newhall and Kunzli, *ibid.*, **72**, 1141 (1950).

[3] Barnes, Liddel and Williams, *Ind. Eng. Chem., Anal. Ed.*, **15**, 659 (1943).

[4] Thompson, Brattain, Randall and Rasmussen, "The Chemistry of Penicillin," Ch. XIII, Princeton University Press, Princeton, N. J.

[5] Randall, Fuson, Fowler and Dangl, "Infrared Determination of Organic Structures," Van Nostrand Co., Inc., New York, N. Y., 1949.

[6] Jones, Humphries and Dobriner, THIS JOURNAL, **72**, 956 (1950), and earlier publications.

[7] Chloroform purified as described above possesses an absorption band at 3625 cm.$^{-1}$. This band is weak and of variable intensity and has been attributed to traces of residual water in the solvent. Solutes containing a non-associated hydroxyl group also give a band near 3625 cm.$^{-1}$, from which the solvent absorption can be subtracted. In a few cases, principally of hygroscopic solutes containing associated hydroxyl groups, the intensity of the absorption band at 3625 cm.$^{-1}$ may be diminished in the presence of the solute, and if this occurs it is difficult to evaluate the solute absorption in the region between 3700 and 3550 cm.$^{-1}$. In explanation of this "chloroform effect" it is suggested that the hygroscopic solute combines with part of the residual water in the chloroform, with shift of the band position.

[8] The apparent molecular extinction coefficient E_a^s is defined as

$$E_a^s = (1/cl) \log_{10}(T_0/T)_\nu$$

where c is the concentration of the solute in moles per liter; l is the cell length in cm.; T and T_0 designate the intensity of the radiation transmitted by the solution and solvent, respectively, when the spectrometer is set at the frequency ν, and s is the slit width in wave numbers. This differs from the molecular extinction coefficient commonly employed in ultraviolet spectrophotometry in that it does not assume the radiation to be strictly monochromatic. E_a^s varies with the slit width and with the optical characteristics of the spectrometer.

tinction coefficient of 30–160 may be accepted as evidence of a hydroxyl group, though the absence of such a band does not entirely exclude the possibility of a hydroxyl group being present. A broad band in the region of 3400 cm.$^{-1}$ may indicate hydroxyl groups in a state of hydrogen bonding.

B. Imino Bands (N–H Stretching Vibration).—Imino groups are known to produce sharp absorption bands between 3500 and 3200 cm.$^{-1}$ when unassociated, and broad absorption bands between 3300 and 3000 cm.$^{-1}$ when associated.[3,5]

Sixteen of the alkaloids investigated contained imino groups. Eight of these contained the indole nucleus and produced sharp absorption bands between 3480 and 3460 cm.$^{-1}$ with apparent molecular extinction coefficients ranging from 140–210 (see Table II). Physostigmine and gelsemine which contain secondary amido groups also give sharp bands between 3480 and 3440 cm.$^{-1}$ with slightly lower intensities. Ergotinine which contains one indole nucleus and two secondary amido groups produced a sharp band at 3480 cm.$^{-1}$ with an apparent molecular extinction coefficient of 340 together with a broad associated band at 3200 cm.$^{-1}$.

TABLE II

NH STRETCHING BANDS IN SOME ALKALOIDS

Compound	NH frequency cm.$^{-1}$	E_a^{12}
Indole derivatives[c]		
Gramine	3480	170
Isoevodiamine	3480	210
Yohimbine	3480	180
Ergotinine	3480	340[a]
Harman	3475	150
Harmaline	3470	140
Evodiamine	3470	170
Rutaecarpine	3465	190
N-Acetylharmaline	3460	210
Secondary amides[c]		
Physostigmine	3470	100
Gelsemine	3445	130
Piperidine derivatives		
ψ-Conhydrine[d]	3290[b]	
Piperidine[e]	3280	
Cytisine[d]	3280	
Other alkaloids		
Jervine[d]	3225	

[a] This compound contains one indole NH group and two secondary amido groups. [b] This compound has an additional broad band at ~ 3110 cm.$^{-1}$. [c] Chloroform solution. [d] Nujol mull. [e] Liquid film.

Piperidine and three other alkaloids containing the piperidine ring, *viz.*, anabasine, cytisine and ψ-conhydrine-, produced no appreciable absorption in the region 3500–3100 cm.$^{-1}$ using the standard conditions of concentration and cell thickness. In all four cases, however, broad bands were observed in the region of 3280 cm.$^{-1}$ using liquid films (0.025 mm.) or suspensions in Nujol (see Fig. 1). This corresponds to an increase in path length of ~10. Jervine also behaved in a similar manner (Fig. 2).

While a sharp absorption band between 3480 and 3440 cm.$^{-1}$ with an apparent molecular extinction coefficient of 100–210 indicates the presence of an indole imino group or a secondary amido group. the absence of such a band does not exclude the possibility that the molecule may contain other types of NH groups (*e.g.*, a piperidine ring).

C. Carbonyl Bands (C=O Stretching Vibrations).—Compounds containing carbonyl groups produce intense absorption bands which generally occur in the region 1850–1620 cm.$^{-1}$.[5] These bands are useful for the identification of carbonyl groups and for characterizing the type of carbonyl present.[6]

Twenty-eight of the alkaloids possessed a single carbonyl group and, with two exceptions—rutaecarpine and N-acetylharmaline—each produced a single absorption band in the region of 1780–1620 cm.$^{-1}$ with an apparent molecular extinction coefficient between 300 and 1200 (see Table III). Additional weak bands were sometimes observed in the region 1640–1620 cm.$^{-1}$ but these bands lay outside the intensity range for the carbonyl bands, and may probably be attributed to phenyl ring vibrations (see below). Rutaecarpine produced two absorption bands of similar intensity at 1677 and 1665 cm.$^{-1}$ but the bands were incompletely resolved and it is possible that one of these bands corresponds to

TABLE III

ABSORPTION BANDS BETWEEN 1800 AND 1550 CM.$^{-1}$ FOR SOME ALKALOIDS IN CHLOROFORM SOLUTION

Compound	Bands attributed to the carbonyl group, cm.$^{-1}$	E_a^4	Other[a] bands, cm.$^{-1}$
Adlumidine	1778	600	
Bicuculline	1776	730	
Annotinine	1776	590	
Hydrastine	1775	450	
Adlumine	1762	890	1615
Physostigmine	1734	550	1615
Ergotinine[b]	1728 1658	1160 1650	1605
Gelsemine	1720	710	1619
l-Hyoscyamine	1716	430	1604
Yohimbine	1712	340	
Jervine	1705	480	1630
Lycopodine	1693	400	
Cevine	1692	340	1613 1600
Rutaecarpine	1677	760	1665 1600
Isoevodiamine	1676	1200	1601
N-Acetylharmaline	1668	540	1630 1576
Strychnine	1665	510	1600
Cryptocavine	1661	310	1603
Protopine	1660	340	1617
Hunnemanine	1658	330	1620
Cryptopine	1658	320	1602
Allocryptopine	1658	320	1620
Cytisine	1653	750	1566
N-Methylcytisine	1653	750	1567
Thermopsine	1653	570	1566
Anagyrine	1652	660	1570
Evodiamine	1649	770	
Oxysparteine	1636	630	
Piperine	1635	570	1614 1588
Aphyllidine	1628	750	
Lupanine	1622	750	
α-Methylmorphimethine			1637
Harmaline			1629
Harman			1625 1602 1573
Quinine			1624 1594
Papaverine			1620 1591 1570
Codeine			1605
Chelidonine			1604
Gramine			1600
Anabasine			1592 1576
Cinchonidine			1593 1573

[a] For assignments see text. [b] This compound contains four carbonyl groups.

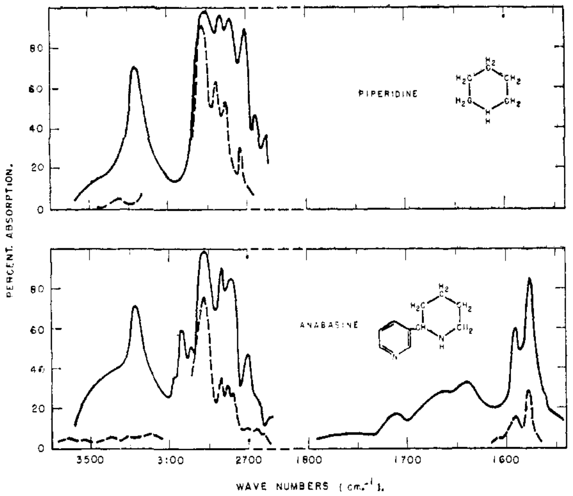


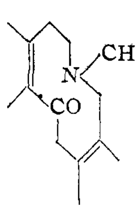
Fig. 1.—Infrared absorption spectra of piperidine and anabasine in the regions 3700–2700 and 1800–1550 cm.$^{-1}$: —, liquid film (0.025 mm.); – – – – –, chloroform solution.

a C=N stretching vibration. Acetylharmaline gave two strong bands at 1668 and 1630 cm.$^{-1}$, the former being almost certainly the C=O stretching frequency and the latter a phenyl ring frequency. Ergotinine contains four carbonyl groups and produced two bands at 1728 and 1650 cm.$^{-1}$ both with double the normal intensity. Seventeen of the remaining nineteen alkaloids which contain no carbonyl groups produced no strong absorption bands in the region 1780–1620 cm.$^{-1}$.

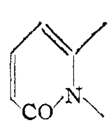
The presence of a band in the region 1780–1620 cm.$^{-1}$ with an apparent molecular extinction coefficient between 300 and 1200 in general indicates the presence of a carbonyl group. This is particularly useful for detecting carbonyl groups in compounds where the carbonyl group is resistant to chemical attack as in the protopine alkaloids.

The molecular extinction coefficients fall into the same range as for the steroids (350–1350) and for a variety of esters (350–770).[9] Hence it appears that carbonyl groups may be recognized not only by characteristic band frequencies but also by characteristic band intensities.

Correlations between the carbonyl frequencies and molecular structures of the alkaloids are not as well defined as in the case of the steroids.[6] This is due to the more diverse types of chemical structure found in the alkaloids. Nevertheless similarities of chemical structure in the neighborhood of the carbonyl group are found to be paralleled by similarities in carbonyl frequency. Thus the five lactone alkaloids listed in Table III—adlumidine, bicuculline, annotinine, hydrastine and adlumine—all show absorption bands in the region 1778–1762 cm.$^{-1}$. The protopine alkaloids—cryptocavine, protopine, hunnemanine, cryptopine and allocryptopine—containing the ten-membered ring system I absorb in the region 1661–1658 cm.$^{-1}$ with similar intensity. Cytisine, N-methylcytisine, thermopsine and anagyrine which contain the partial structure II absorb at 1653–1652 cm.$^{-1}$. Other similarities have been noted but the number of compounds investigated is insufficient to justify the establishment of correlations.



I



II

The two steroid alkaloids, jervine and cevine, gave spectra which call for separate comment. The curves of these compounds are shown in Fig. 2. The bands at 1705 cm.$^{-1}$ (E^{1}_{1} 480) in jervine and at 1692 cm.$^{-1}$ (E^{1}_{1} 340) in cevine are typical carbonyl maxima, and indicate the presence of a carbonyl group in each of these alkaloids. Although chemical evidence indicating the presence of a carbonyl group in jervine has been put forward,[10] the presence of a carbonyl group in cevine has not hitherto been suspected. The displacement of the band in cevine is not readily explained, but it could arise from internal hydrogen bonding with one of the hydroxyl groups.

D. Other Bands. (i) **CH Stretching.**—These vibrations produce absorption bands above 3000 cm.$^{-1}$ when the carbon atom is unsaturated and between 3000 and 2800 cm.$^{-1}$ when the carbon atom is saturated.[3] The former bands are obscured by the chloroform absorption between 3100 and 3000 cm.$^{-1}$ but may be observed in other transparent media. Thus a thin film of anabasine shows a band at 3030 cm.$^{-1}$ due to the CH linkages of the pyridine nucleus which is absent from the spectrum of piperidine (see Fig. 1). The bands between 3000 and 2800 cm.$^{-1}$ may be observed in chloroform solution, but although each alkaloid produces several absorption bands in this region, it has not been possible to assign these bands to specific groups in the molecule.

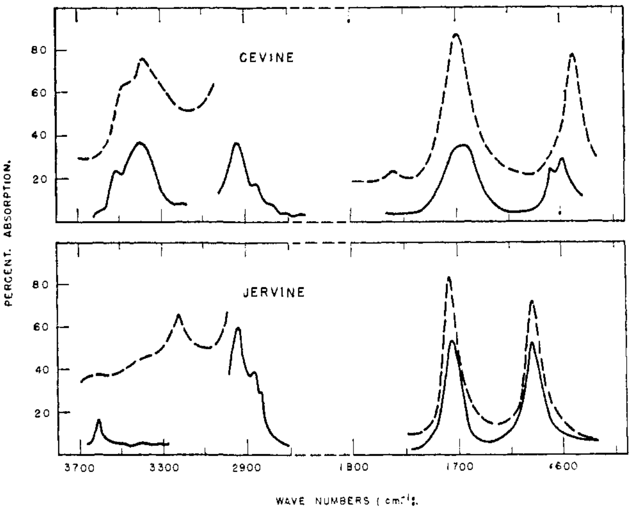


Fig. 2.—Infrared absorption spectra of cevine and jervine: —, chloroform solution; – – – – –, Nujol mull.

---

(9) Hampton and Newell, *Anal. Chem.*, **21**, 914 (1949).

(10) Jacobs and Craig, *J. Biol. Chem.*, **170**, 635 (1947).

(ii) **Carbonyl Overtone.**—Since carbonyl groups produce strong absorption bands in the region 1780–1620 cm.$^{-1}$, weak overtone bands may be expected at approximately twice this frequency range, *viz.*, 3560–3240 cm.$^{-1}$. Such bands overlap the regions of the OH and NH stretching bands and may confuse the interpretation of weak bands in this region, though no cases of this have yet been encountered.

(iii) **Bands between 1640 and 1550 Cm.$^{-1}$.**—Bands of moderate intensity are frequently observed in the region 1640–1550 cm.$^{-1}$ (see Table III). Such bands generally indicate unsaturation in the molecule (C=C, C=N stretching vibrations), though there is the possibility that they could be caused by NH bending vibrations.[5] Phenyl rings generally give absorption bands in the ranges 1640–1615 or 1605–1600 cm.$^{-1}$ while alkaloids containing aromatic nitrogen rings (*e. g.* pyridine, quinoline rings) generally give bands between 1600 and 1560 cm.$^{-1}$. Thus the bands at 1592 and 1576 cm.$^{-1}$ present in the spectrum of anabasine but absent from the spectrum of piperidine (see Fig. 1) may be assigned to the pyridine ring. Similarly the band between 1570 and 1566 cm.$^{-1}$ found in the spectra of cytisine, N-methylcytisine, thermopsine and anagyrine may be assigned to the α-pyridone ring (II). The observation of bands in this region gives an indication of the types of structure which might be present but does not permit an unambiguous choice to be made owing to the multiple interpretations possible (*viz.*, cevine and jervine).

(iv) **Bands at Lower Frequencies.**—The spectra included in this survey do not extend beyond 1540 cm.$^{-1}$ due to the strong absorptions of the chloroform. Satisfactory spectra are obtained, however, by using Nujol mulls[2a] or thin films of the alkaloids. A great deal of complex structure is found in the region 1500–600 cm.$^{-1}$, and as yet the assignment of bands in this region to specific groups in the molecule is comparatively undeveloped. The chief value of such spectra lies in this high specificity, which offers a very delicate method for the identification of individual alkaloids. Thus they have been used to confirm the identity of monolupine, rhombinine and anagyrine.[11]

Acknowledgments.—The authors wish to thank Mr. R. Lauzon for technical assistance in the measurement of the spectra.

Summary

1. The infrared absorption spectra of forty-seven alkaloids have been investigated in the region 3700–1540 cm.$^{-1}$ in dilute chloroform solution.

2. Hydroxyl groups may generally be detected by the appearance of a sharp band in the region 3625–3540 cm.$^{-1}$ with an apparent molecular extinction coefficient of 30–160 though there are exceptions.

3. Imino groups produce a sharp band in the region 3480–3440 cm.$^{-1}$ with an apparent molecular extinction coefficient of 100–210 when the imino group is present in an indole nucleus or secondary amido group. When the imino group is present in a piperidine ring, however, the absorption is much weaker but may be observed at increased path lengths.

4. Carbonyl groups may be detected by the appearance of a strong band in the region 1780–1620 cm.$^{-1}$ with an apparent molecular extinction coefficient from 300–1200. Certain correlations have been established between the carbonyl frequency and the type of carbonyl group present.

5. Phenyl rings generally give absorption bands in the region 1640–1600 cm.$^{-1}$ while aromatic nitrogen rings generally give bands between 1600 and 1560 cm.$^{-1}$.

6. The presence of a carbonyl group both in cevine and jervine is indicated by the infrared absorption spectra.

[11] Marion and Ouellet, THIS JOURNAL, **70**, 3076 (1948).

OTTAWA, CANADA RECEIVED MAY 27, 1950

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF MICHIGAN]

Energetics of the Adsorption of Aliphatic Amines by Silica Gel[1]

BY DONALD G. DOBAY,[2] YING FU AND F. E. BARTELL

In a previous communication[3] adsorption isotherms of diethylamine, *n*-butylamine and di-*n*-butylamine on silica gel at 25° were presented and their significance as relating to the nature of the adsorption process discussed. In the present paper these adsorption systems will be considered from the basis of energy changes.

Isosteric Heats, $\overline{\Delta H}$, $\overline{\Delta F}$ and $\overline{\Delta S}$ of Adsorption.—In order to determine the isosteric heats, adsorption isotherms for these amines at 40° were obtained and the pressure range employed was from zero to a value higher than that corresponding to the inception of the hysteresis effect. These data are given in the first column of Table I. The isosteric heats were calculated by means of the Clapeyron equation

$$\mathrm{d}Q/\mathrm{d}(x/m) = RT_1T_2\log_e(p_1/p_2)/(T_1 - T_2) \quad (1)$$

where $\mathrm{d}Q/\mathrm{d}(x/m)$ represents the differential isosteric heats of adsorption and the p-values represent the pressures at which equal amounts of the amines were adsorbed by the solid at the two different temperatures. This method of calculating the isosteric heats requires that the surface area of the solid be considered as being independent of the temperature. While this is not strictly true, the

---

[1] A portion of the material in this paper is from a dissertation submitted to the Horace H. Rackham School of Graduate Studies by Donald G. Dobay in partial fulfillment of the requirements for the degree of Doctor of Philosophy, September, 1948.

[2] Linde Air Products Company, Tonawanda, N. Y.

[3] Bartell and Dobay, THIS JOURNAL, **72**, 4388 (1950).