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ALKALOIDS OF *GLYCOSMIS ARBOREA*—II[1]

STRUCTURE OF ARBORINE

D. CHAKRAVARTI,[2] R. N. CHAKRAVARTI,[3] L. A. COHEN,[4]
B. DASGUPTA,[3] S. DATTA[3] and H. K. MILLER[4]

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Abstract—On the basis of a critical study of the ultra-violet and the infra-red absorption spectra of arborine, dihydroarborine, 1,2-dimethylquinazol-4-one, 2-ethyl-1-methylquinazol-4-one, 2,3-dihydro-1,2-dimethylquinazol-4-one and 2,3-dihydro-2-ethyl-1-methylquinazol-4-one, it has been shown that arborine is 2-benzyl-1-methylquinazol-4-one and not the tautomeric form, 2-benzylidene-1-methylquinazol-4-one. This has been confirmed on the basis of the nuclear magnetic resonance spectrum of arborine. Incidentally, it has been shown that 'glycosine' of Chatterjee and Ghosh Majumdar is not a new alkaloid and this name should be deleted from the literature.

THE present authors have recently been able to clarify the position with regard to the structure of arborine. In view of some unusual claims and misrepresentations in the literature, however, it is desirable to present a review on the whole position in proper sequence before describing the results worked out recently.

The alkaloid, arborine, was isolated by Chakravarti and Chakravarti[5–8] from the leaves of the plant known in Bengali as *Ash-shoura*. It grows as a roadside shrub in the suburbs of Calcutta, and is extensively used in the Ayurvedic system of medicine as a febrifuge and as an anthelmintic. The botanical name of this plant is stated as *Glycosmis pentaphylla* Correa in standard books on Indian medicinal plants and for this reason this particular name was mentioned in the earliest publication by Chakravarti and Chakravarti.[5] In view of the work of Narayanswami,[9] however, the name of the plant was changed to *Glycosmis arborea* Correa in all the later publications by Chakravarti *et al.*

The main points of difference between the two species will be evident from the botanical characteristics[9,10] of the plants as presented below:

G. pentaphylla. Inflorescence, short axillary panicles; ovary fusiform, stalked, smooth, pitted glandular; leaflets entire, elliptic, obtusely acuminate; fruit globose, pitted glandular (Fig. 1).

G. arborea. Panicles as long as or longer than leaf rachis, ovary ovoid, sessile, papillose; leaflets crenate, dentate or serrate, oblong lanceolate, never entire; fruit globose, mamillate (Fig. 2).

[1] Part I: (Mrs.) D. Chakravarti, R. N. Chakravarti and S. C. Chakravarti, *J. Chem. Soc.* 3337 (1953).
[2] Address: Bethune College, Calcutta-6.
[3] Address: School of Tropical Medicine, Calcutta-12.
[4] Address: National Institutes of Health, Bethesda.
[5] R. N. Chakravarti and S. C. Chakravarti, *Proc. 38th Indian Sci. Cong.* Part III, 79 (1951).
[6] S. C. Chakravarti, D. Phil. Thesis entitled *Alkaloids of* Glycosmis arborea *Correa.* Calcutta University, June (1951).
[7] R. N. Chakravarti and S. C. Chakravarti, *Proc. 39th Indian Sci. Cong.* Part III, 100 (1952).
[8] R. N. Chakravarti, and S. C. Chakravarti, *J. & Proc. Inst. Chemists (India)* **24**, 96 (1952).
[9] V. Narayanswami, *Records of the Botanical Survey of India* **14**, No. 2 (1941).
[10] Herbarium sheets of *G. arborea* and *G. pentaphylla*, received from Dr. C. B. Sulochana, Coimbatore, are in accord with the observations of Narayanswami.[9]

According to Narayanswami[9] the plant *Ash-shoura* growing around Calcutta is *G. arborea*. In fact, this species occurs widely throughout India, whereas *G. pentaphylla* occurs only in the Eastern and the Western Ghats and in Orissa, although it is much more common in the Malayan peninsula.

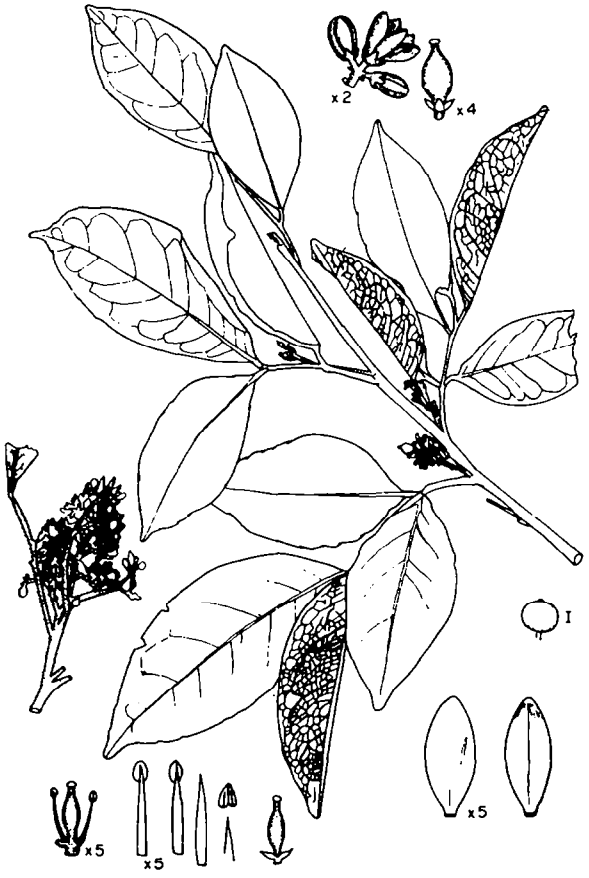


FIG. 1. *Glycosmis pentaphylla* Correa.

Arborine,[5–8] m.p. 155–156°, was found to be optically inactive. It was characterized by the preparation of the hydrochloride (m.p. 215° with partial melting at 106–108°), hydrobromide (m.p. 75–76°), hydriodide (m.p. 95–96°), nitrate (m.p. 116–117°), chloroplatinate, chloroauriate, picrate (m.p. 172–173°), styphnate (m.p. 194–195°), picrolonate (m.p. 171°) and methiodide (m.p. 126–127°). On distillation with sodalime, it yielded methylaniline and toluene along with ammonia, and on hydrolysis with alkalis, it yielded N^2-methylanthranilamide, N-methylanthranilic acid, phenylacetic acid, ammonia and a very weak acid, m.p. 221–222° termed arboricine. Also on catalytic hydrogenation in the presence of a platinum catalyst, arborine afforded a product, m.p. 199–200°. The latter on hydrolysis with hydrochloric acid gave N^2-methylanthranilamide, N-methylanthranilic acid and phenylacetaldehyde.

The structure of arborine was established by Chakravarti *et al.*[1,11] The correct molecular formula[12] for arborine was found to be $C_{16}H_{14}ON_2$ and that of arboricine, $C_{16}H_{18}O_2N$. The hydrogenated product of arborine was found to be a dihydroarborine, $C_{16}H_{16}ON_2$. On the basis of the results of degradation, arborine was considered to be

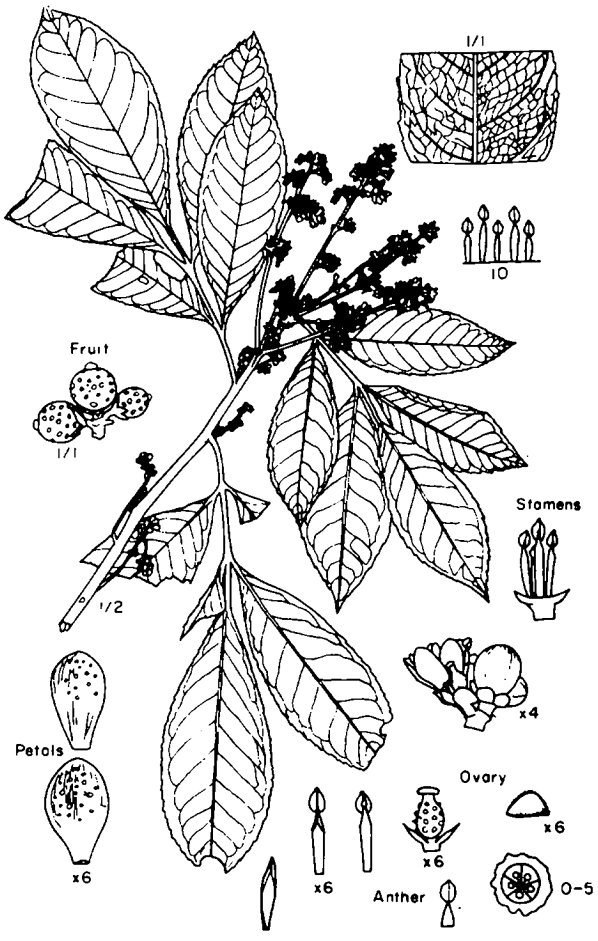


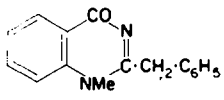
FIG. 2. *Glycosmis arborea* Correa.

2-benzyl-1-methylquinazol-4-one (I). This structure was established by a direct synthesis of arborine starting from N^2-methylanthranilamide and phenylacetic acid through the intermediate product, N^2-methyl-N^2-phenylacetylanthranilamide (II). Arboricine was shown to be 1,2-dihydro-4-hydroxy-1-methyl-2-oxo-3-phenylquinoline (III) (or its diketo tautomer) by synthesis of the product from ethyl phenylmalonate and methylaniline. The formation of arboricine (III) during the alkaline hydrolysis of

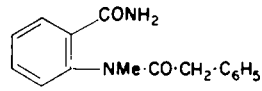
[11] This paper was received for publication in London partly on March 23rd 1953, and partly on April 30th 1953.

[12] Arborine was at first[7] ascribed a double formula, $C_{31}H_{36}O_2N_4$.

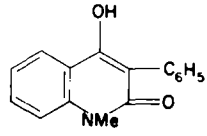
arborine (I) was indicated as taking place through the intermediate amide (II) and the corresponding acid.



I



II



III

According to Robinson[13] arborine, from the standpoint of biogenesis 'is obviously a condensation product of anthranilic acid (N-methylated), ammonia, and phenylacetic acid and was synthesized in accordance with this by its discoverers'.

It may be mentioned in this connection that Chatterjee and Ghosh Majumdar,[14] in their earlier attempt to verify the presence of arborine in the plant, could only isolate two minor alkaloids, namely skimmianine[15] and glycosminin. This was rather curious as arborine is found in the leaves to the extent of about 0·5 per cent, whereas the two minor alkaloids were found to be present to the extent of about 0·03 per cent and 0·003 per cent respectively. Moreover, leaves of the plant received from this group of workers were also successfully used for the isolation of arborine by Chakravarti and Chakravarti.[16]

Later,[17] Chaterjee and Ghosh Majumdar[18] claimed the isolation of a *new* alkaloid, glycosine, $C_{15}H_{12}ON_2$ from the same plant. Melting points of arborine and glycosine and those of their derivatives are given in Table 1.

Similarity between the two products side by side with the fact that both are obtained from the same plant[19] leads to the obvious conclusion that arborine and glycosine are identical, and this was pointed out by Chakravarti *et al.*[20] in a short communication. It was also pointed out in this note[20] that the molecular formula of glycosine (arborine) should be $C_{16}H_{14}ON_2$ and not $C_{15}H_{12}ON_2$, as suggested by

[13] R. Robinson, *The Structural Relations of Natural Products.* Clarendon Press, Oxford (1955), being the *First Weizmann Memorial Lecture* p. 95. December (1953).

[14] A. Chatterjee and S. Ghosh Majumdar, *Science and Culture* **17**, 306 (1952) (communicated on 1st December, 1951).

[15] This product was given a new name, pentaphylline, although found[14] to be identical with skimmianine.

[16] R. N. Chakravarti and S. C. Chakravarti, *Science and Culture* **18**, 539 (1953) (communicated on 12th November, 1952).

[17] The second note[18] of Chatterjee and Ghosh Majumdar was communicated about *four months after* the communication of the earlier note[16] by Chakravarti and Chakravarti but was published *one month earlier* by the authorities of *Science and Culture.*

[18] A Chatterjee and S. Ghosh Majumdar, *Science and Culture* **18**, 505 (1953) (communicated on 4th March, 1953).

[19] The position with regard to the botanical name of the plant used by Chakravarti *et al.* has been clarified earlier in this communication. As regards the plant used by Chatterjee and Ghosh Majumdar, fragments of leaves as received from the senior worker were found[18] to have 'crenations and serrations' characteristic[9] of *G. arborea and not G. pentaphylla.*

[20] (Mrs.) D. Chakravarti, R. N. Chakravarti and S. C. Chakravarti, *Science and Culture* **18**, 553 (1953) (communicated on 22nd April, 1953).

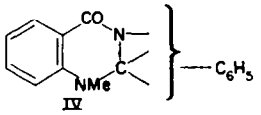
Chatterjee and Ghosh Majumdar.[18] It was observed[20,21] that arborine on catalytic hydrogenation yields dihydroarborine, $C_{16}H_{16}ON_2$, m.p. 199–200°, that arborine should be represented by the 2-benzylquinazol-4-one structure (I) and that this structure for arborine had already been confirmed by Chakravarti *et al.* by a direct synthesis of the product from phenylacetic acid and N^2-methylanthranilamide.

Nevertheless Chatterjee and Ghosh Majumdar[22] continued to represent glycosine as $C_{15}H_{12}ON_2$. It was stated that glycosine yields N-methylanthranilic acid on hydrolysis with alkali, indicating a 4-quinazolone structure. Although this finding is simply a

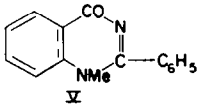
TABLE 1.

	m.p. of Base	m.p. of Hydrochloride	m.p. of Picrate
Arborine[1,5,7]	155–156°	215° (decomp)	173°
Glycosine[18]	155–156°	209–210° (decomp)	171–172°

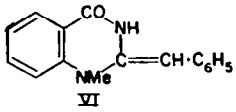
confirmation of the same result observed in the case of arborine by Chakravarti *et al.*[20] these workers[22] still designated glycosine as a new alkaloid quite different from arborine. On the basis of hydrolysis characteristics, it was stated that 'glycosin is probably a 3-substituted 4-quinazolone compound which again cannot explain the presence of a —CONH group in glycosin as indicated by its I.R.' data. The partial structure IV was proposed in this communication but it is not at all clear how this can be developed to a 3-substituted 4-quinazolone, since IV leads to only one complete structure V, which differs from that proposed by Chakravarti *et al.* only by the missing CH_2 in accordance with the incorrect molecular formula proposed for glycosine.[18,20] In the subsequent note of Chatterjee and Ghosh Majumdar[23] the molecular formula of glycosine was changed from $C_{15}H_{12}ON_2$ to $C_{16}H_{14}ON_2$ and the preparation of dihydroglycosine (m.p. 196°, dihydroarborine of Chakravarti *et al.* m.p. 199–200°) by catalytic hydrogenation was described. They also proposed the structure VI which is simply the tautomeric form of I, for glycosine and claimed the synthesis of glycosine by a method



IV



V



VI

similar to that of Chakravarti *et al.*[20] using phenylacetic acid and N^2-methylanthranilamide. This belated adoption of the earlier work of Chakravarti *et al.* was made without reference[24] to the latter.

[21] (Mrs.) D. Chakravarti, R. N. Chakravarti and S. C. Chakravarti, *Experientia* **9**, 333 (1953) (communicated on April 18, 1953).

[22] A. Chatterjee and S. Ghosh Majumdar, *Science and Culture* **18**, 604 (1953) (communicated on 18th May 1953).

[23] A. Chatterjee and S. Ghosh Majumdar, *J. Amer. Chem. Soc.* **75**, 4365 (1953) (communicated on 22nd July 1953).

[24] The position in this respect is somewhat better in the detailed paper by Chatterjee and Ghosh Majumdar[25] on the subject. No mention has been made in this paper about their earlier [23] claim for the synthesis of glycosine.

[25] A. Chatterjee and S. Ghosh Majumdar, *J. Amer. Chem. Soc.* **76**, 2459 (1954).

Since it is obvious that arborine and glycosine are identical, as was repeatedly pointed out by Chakravarti *et al.*[1,20] the repeated claims of Chatterjee and Ghosh Majumdar[18,22,23] for the recognition of glycosine as a new alkaloid are evidently untenable. As the name 'arborine' was proposed much earlier by Chakravarti and Chakravarti,[7] who isolated it for the first time,[5] it is not at all necessary to retain the name 'glycosine' for this alkaloid. In any case 'glycosine' is not a suitable name for any new product in view of the fact that this name was used for the first time, about a century ago, by Debus[26,28] to designate 2,2'-diiminazolyl.[27] In the unlikely event that it is possible for Chatterjee and Ghosh Majumdar to establish that the plant used by them was different from that used by Chakravarti *et al.*, it must be pointed out that the isolation of arborine from it was first carried out by Chakravarti and Chakravarti,[16,17] who used a specimen of the plant received by them from Chatterjee. It may be noted in this connection that authentic leaves of *G. pentaphylla* of South India,[29] having no 'crenations and serrations', were also successfully used by Chakravarti *et al.*[30] for isolation of arborine.

Chatterjee and Ghosh Majumdar,[23] however, made the interesting observation that arborine undergoes oxidative cleavage during oxonolysis and periodic acid oxidation with formation of benzaldehyde, and this constitutes the only original finding of any significance in the whole series of publications of Chatterjee and Ghosh Majumdar as quoted in this paper. In view of this, it is necessary to consider the structure VI for arborine side by side with the tautomeric structure I. The fact that arborine, on hydrolysis with alkali, yields phenylacetic acid[1,7,20] indicates the presence of a benzyl group ($C_6H_5 \cdot CH_2$—) in the alkaloid, which is in favour of I. As stated above, however, ozonolysis and periodic acid oxidation of arborine yields benzaldehyde[23] and this observation has recently been confirmed by the present authors. In addition, it has been observed that oxidation of arborine with 6 per cent hydrogen peroxide also yields benzaldehyde. These latter findings indicate the presence of a benzylidene group ($C_6H_5 \cdot CH=$) in the alkaloid, which is in favour of VI. The synthesis of arborine from phenylacetic acid and N^2-methylanthranilamide[1,20] apparently supports structure I, but this may as well be explained on the basis of VI for arborine. As has been stated above, I and VI are tautomers and hence appropriate physical data can be more profitably utilized than chemical reactions in order to determine the actual structure of arborine.

With the above object in view, 1,2-dimethylquinazol-4-one and 2-ethyl-1-methylquinazol-4-one were prepared as models and the spectral data of these were compared with those of arborine. Similarly, 2,3-dihydro-1,2-dimethylquinazol-4-one and 2,3-dihydro-2-ethyl-1-methylquinazol-4-one were compared with dihydroarborine. For the preparation of the alkyl quinazolones a convenient method was to react N^2-methylanthranilamide with the appropriate acid anhydride. 1,2-Dimethylquinazol-4-one (cf. Weddige[31]) and 2-ethyl-1-methylquinazol-4-one were obtained in this way, and on catalytic hydrogenation in presence of a platinum catalyst afforded dihydro-derivatives.

[26] H. Debus, *Liebigs Ann.* **107**, 199 (1859).
[27] K. Lehmstedt, *Liebigs Ann.* **456**, 253 (1927).
[28] E. H. Rodd, *Chemistry of Carbon Compounds* Vol. IV, part A, pp. 292, 294. Elsevier, Amsterdam (1957).
[29] Authentic leaves of *G. pentaphylla* of South India were received from Dr. C. B. Sulochana, Coimbatore in 1953.
[30] Chakravarti *et al.*, unpublished results.
[31] A. Weddige, *J. Pr. Chem.* (2) **36**, 154 (1887).

The ultra-violet absorption spectra of the above products were studied at concentrations of the order of 2–4 mg per litre. Comparison of the U.V. curves of dihydroarborine, 2,3-dihydro-1,2-dimethylquinazol-4-one and 2,3-dihydro-2-ethyl-1-methylquinazol-4-one with that of N^2-methylanthranilamide in ethanol (Fig. 3) clearly indicates a close similarity in the unsaturated systems of all these products. Intro-

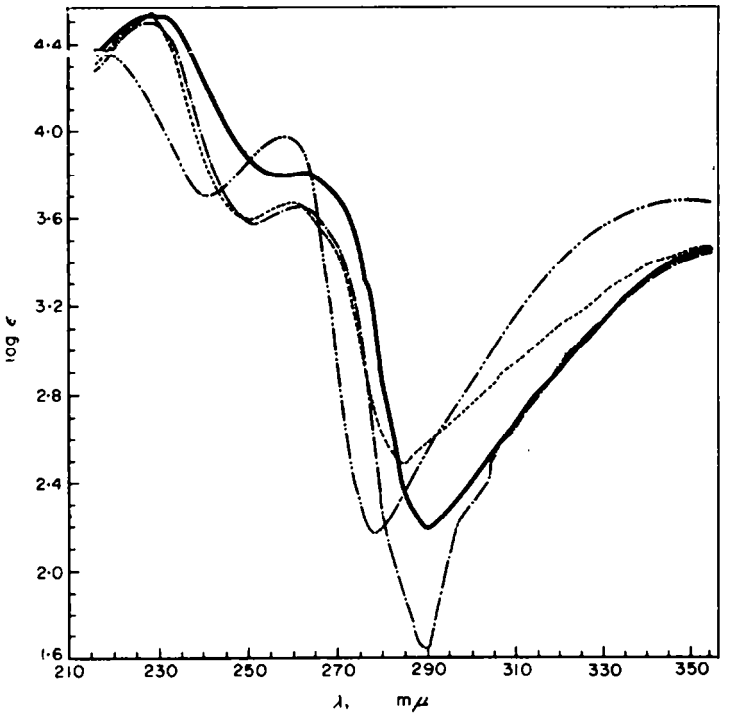


FIG. 3. U.V. curve of dihydroarborine ———, 2,3-dihydro-1,2-dimethylquinazol-4-one . . . . , 2,3-dihydro-2-ethyl-1-methylquinazol-4-one – · – · – · –, and N^3-methylanthranilamide – · · – · · – · · – in ethanol.

duction of the double bond in the 2,3-position, as in arborine, 1,2-dimethylquinazol-4-one and 2-ethyl-1-methylquinazol-4-one, brings about a large change in the U.V. picture. It is evident that the similarity of the U.V. absorption curves of the set of three is still maintained both in ethanolic (Fig. 4) and in chloroform (Fig. 5) solutions, but these curves are found to differ greatly from those of the respective dihydro-derivatives and from that of N^2-methylanthranilamide. This fact naturally leads to the conclusion that although the unsaturated system present in the dihydroquinazolones and the quinazolones may differ considerably, those of 1,2-dimethylquinazol-4-one, 2-ethyl-1-methylquinazol-4-one and arborine are quite similar and that the second benzene nucleus of arborine (i.e. the one in the benzyl group in structure I or the one in the benzylidene group in structure VI) makes no major contribution in the spectra in the ultra-violet region of the alkaloid. As the two 1,2-dialkylated 4-quinazolones have no enolizable proton, there are no tautomeric forms in these cases and they should be represented by structure VII (R = Me, Et), and arborine, on account of its close similarity with the 1,2-dialkylated 4-quinazolones, may be represented by a similar structure VII ($R = -CH_2 \cdot C_6H_5$), both in chloroform and in ethanolic solutions.

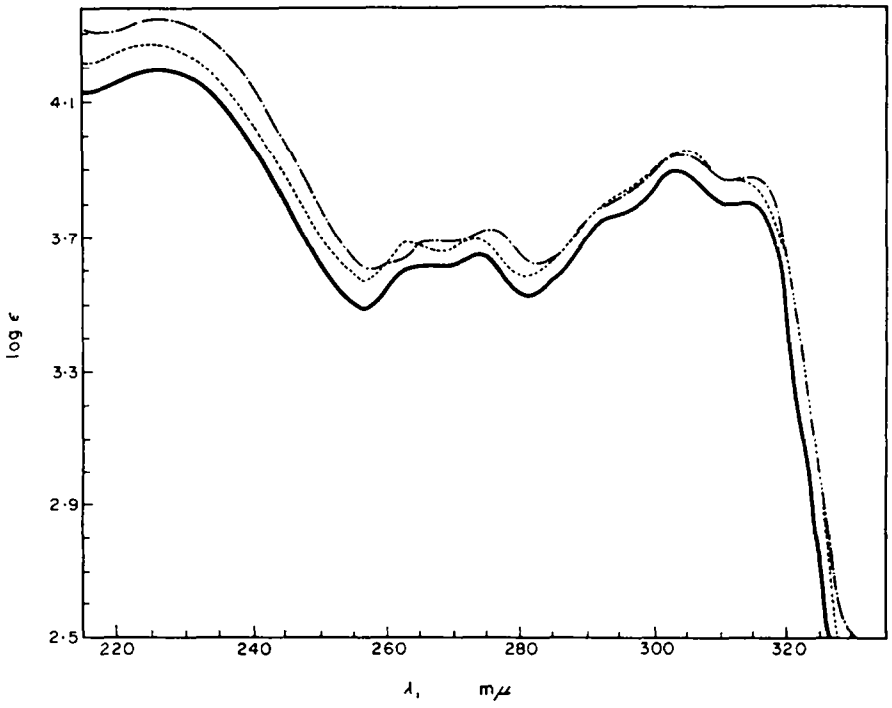


FIG. 4. U.V. curve of arborine – . – . – . –, 1,2-dimethylquinazol-4-one ———, and 2-ethyl-1-methylquinazol-4-one . . . . . in ethanol.

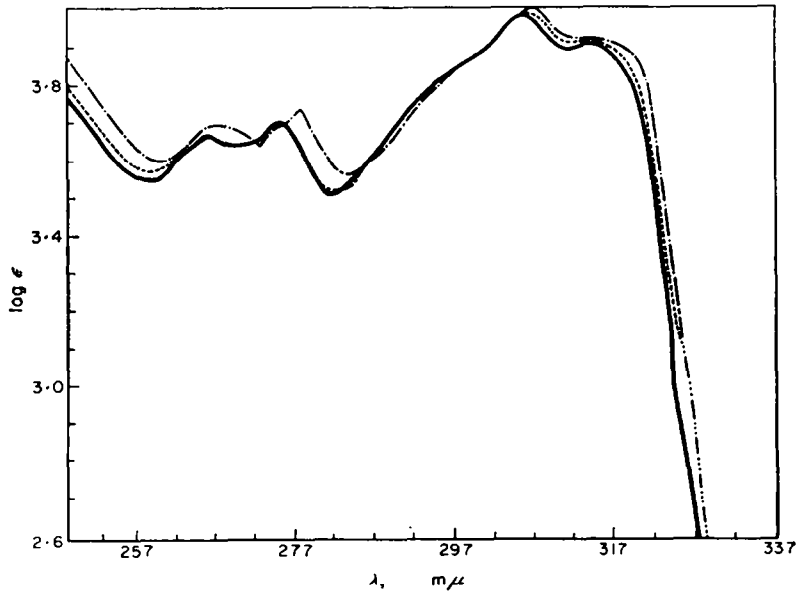
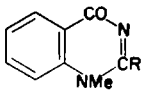


FIG. 5. U.V. curve of arborine – . – . – . –, 1,2-dimethylquinazol-4-one ———, and 2-ethyl-1-methylquinazol-4-one . . . . . in chloroform.

The U.V. spectra of arborine, 1,2-dimethylquinazol-4-one and 2-ethyl-1-methylquinazol-4-one were also studied both in acidic and in alkaline solutions. The solvent,



VII

for the purpose, was prepared by diluting 1 ml aqueous N HCl and 1 ml aqueous N NaOH respectively to 10 ml with ethanol. As is evident from the similar nature of the U.V. curves of the set of three in decinormal aqueous alcoholic hydrochloric acid (Fig. 6) and in decinormal aqueous alcoholic sodium hydroxide solution (Fig. 7), the similarity in the U.V. light absorption systems of the three products are

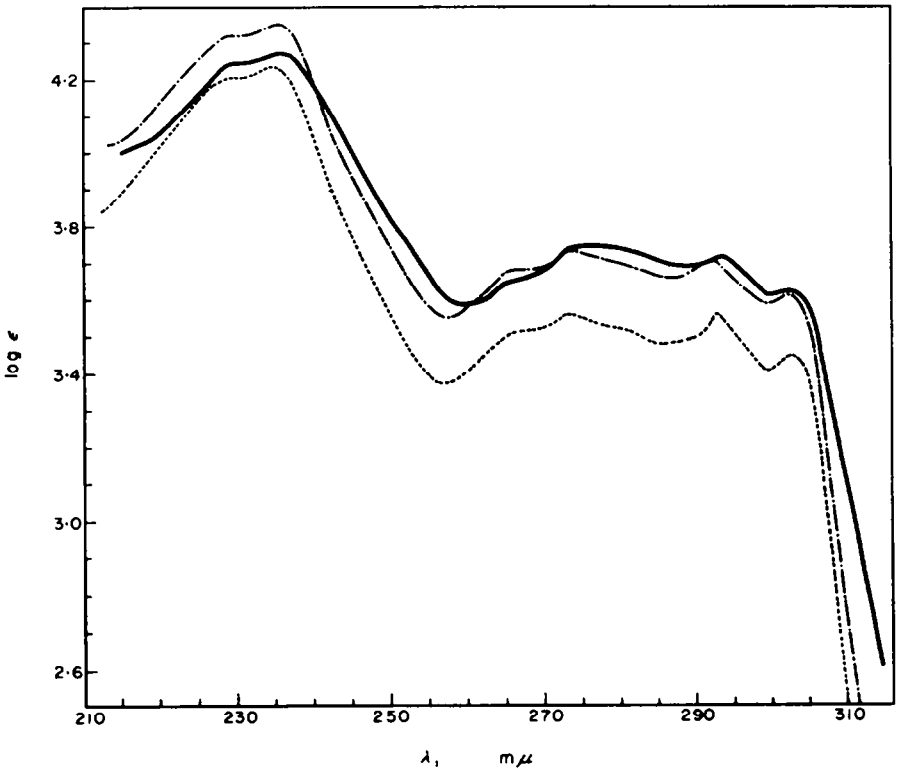


FIG. 6. U.V. curve of hydrochlorides of arborine ———, 1,2-dimethylquinazol-4-one . . . . ., and 2-ethyl-1-methylquinazol-4-one – . – . – . – in 0·1 *N* aqueous alcoholic hydrochloric acid solution.

maintained in these solutions, indicating that arborine is possibly 2-benzyl-1-methylquinazol-4-one (I). It may, however, be pointed out that 3-methylquinazol-4-one[32] shows U.V. spectrum similar to those of the quinazolone derivatives mentioned above, indicating that the spectra of quinazol-4-one derivatives in such cases remain more or less the same, irrespective of whether the double bond is in the 1,2-position or in the 2,3-position. Introduction of the benzylidene group as in structure VI, however, may

[32] (Miss) J. M. Hearn, R. A. Morton and J. C. E. Simpson, *J. Chem. Soc.* 3319 (1951).

be expected to cause a much greater change in the unsaturated system of the alkylated quinazolones mentioned above.

For further clarification of the position, a study of the infra-red spectra of the related products was undertaken. It may be mentioned in this connection that according to Chatterjee and Ghosh Majumdar,[25] arborine (glycosine) 'shows absorption bands at 3 μ (—NH or OH group or both), at 6·1 μ (aromatic amido group) and at

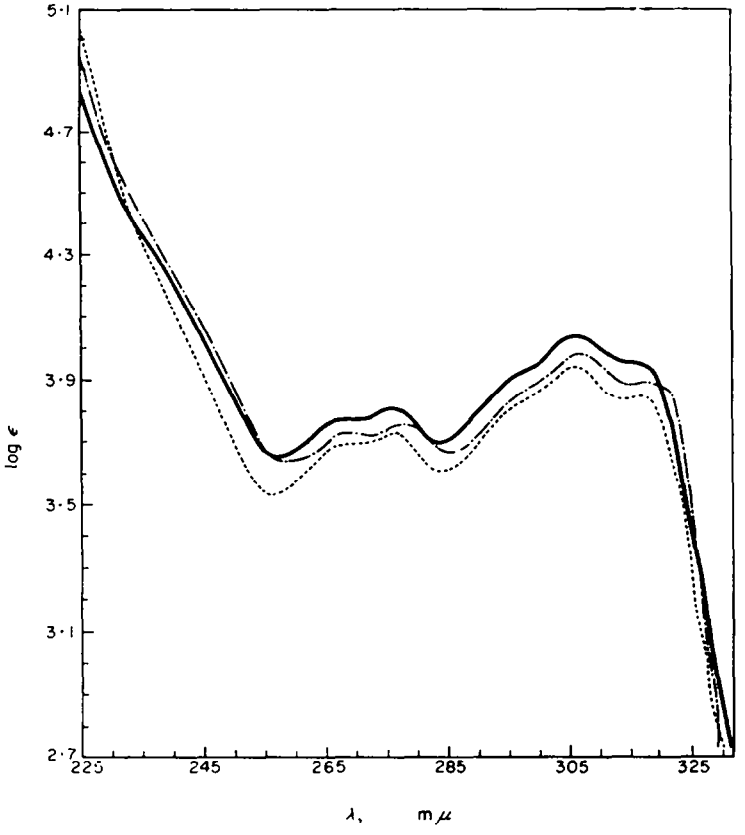


FIG. 7. U.V. curve of arborine – · – · – · –, 1,2-dimethylquinazol-4-one . . . . ., and 2-ethyl-1-methylquinazol-4-one ——— in 0·1 *N* aqueous alcoholic sodium hydroxide solution.

6·2 μ (—C=C— group)'. In the present instance, the infra-red spectra were observed in the solid phase using potassium bromide pellets, and also in chloroform solution; other solvents were employed in a few instances. The solution path length was approximately 0·50 mm (in some cases, 1 mm); solutions were observed at approximate concentrations of 30 mg substance/ml chloroform, and dilutions were made to give concentrations of 6 mg substance/ml chloroform, as intensities required. In some cases, the spectra were recorded at three different concentrations. All values for wavelengths were obtained after making corrections for atmospheric water vapour, atmospheric carbon dioxide, and ammonia vapour in a 10·0 cm gas cell at atmospheric pressure (approximately 760 mm Hg).

For determination of the I.R. spectra, the specimens, after crystallization, were dried at 100° and mailed to Bethesda from Calcutta. These were then desiccated over

phosphoric anhydride at atmospheric pressure. Nevertheless all the samples showed considerable absorption (Figs. 8 to 23) in the N–H and O–H stretching region of the infra-red (Table 2). According to Jones and Sandorfy[33] the ranges for N–H and O–H bonding centre types are as in Table 3. In view of the frequency overlap for such bonding species, it is seen that the presence of associated solvent containing —OH or water would render any unequivocal differentiation between N—H or O—H stretching impossible in this region. The wavelengths for maximum absorption for O—H and N—H stretching[33] are quoted in Table 4.

TABLE 2.

Substance	Chloroform solution				Potassium bromide pellet			
	ν cm^{-1}	λ max (μ)	ν cm^{-1}	λ max (μ)	ν cm^{-1}	λ max (μ)	ν cm^{-1}	λ max (μ)
1,2-Dimethylquinazol-4-one	3676	2·72	3413	2·93	3472	2·88	3401*	2·94*
2-Ethyl-1-methylquinazol-4-one	3413	2·93	~3289*	~3·04*	3425	2·92	~3257*	~3·07*
Arborine	3663	2·73	3425	2·92	3534	2·83	3414	2·93
Dihydroarborine	3413	2·93	3289	3·04	3425	2·92	~3279*	~3·05*
2,3-Dihydro-1,2-dimethylquinazol-4-one	3425	2·92	~3300*	~3·03*	3448	2·90	~3289*	~3·04*
2,3-Dihydro-2-ethyl-1-methylquinazol-4-one	2425	2·92	~3300*	~3·03*	3436	2·91	3247	3·08

N.B. In this and the subsequent tables (*) indicates 'Shoulder' and (~) indicates 'approximately'.

TABLE 3.

Bonding centre type	ν cm^{-1}	λ max (μ)
OH····O—	3500–3200	2·86–3·13
OH····O=C	3300–2830	3·03–3·53
NH····O=C	3300–3240	3·03–3·09
NH····N—	3300–3150	3·03–3·17

Absorption in the 2·5 μ to 3·3 μ region is found to be practically identical for 1,2-dimethylquinazol-4-one and arborine. This observation indicates one or more of the following possibilities:

(a) both substances possess the same type of functional centres capable of proton bonding.

(b) both substances contain solvent or water of crystallization.

(c) both substances contain N—H or O—H groups.

To test for the presence of solvation, each sample was dried at 125–130°/0·005 mm for three hours, then quickly weighed and the spectrum redetermined in chloroform

[33] R. N. Jones and C. Sandorfy, *Technique of Organic Chemistry* Vol. IX. p. 510. Interscience, (1956).

solution (Figs. 24 to 27). The ratios of the optical density of each 'solvent' band to the corresponding C—H stretching frequency maximum was determined by a relative base line method (Table 5). A decrease in this ratio would indicate that the absorption in the 2·5–3·3 μ region was probably due to a hydroxylic solvent of crystallization.

TABLE 4.

Mode of motion	Species type	ν cm^{-1}	λ max (μ)
O—H stretch	Free OH group	3636–3610	2·75–2·77
N—H stretch	Free NH of N—mono-substituted amide	3500–3400	2·86–2·94[24]
N—H stretch	NH stretch in solid spectra of amide	3330–3280	3·00–3·05
N—H stretch	NH stretch in solid spectra of amide	3100–3060	3·23–3·27

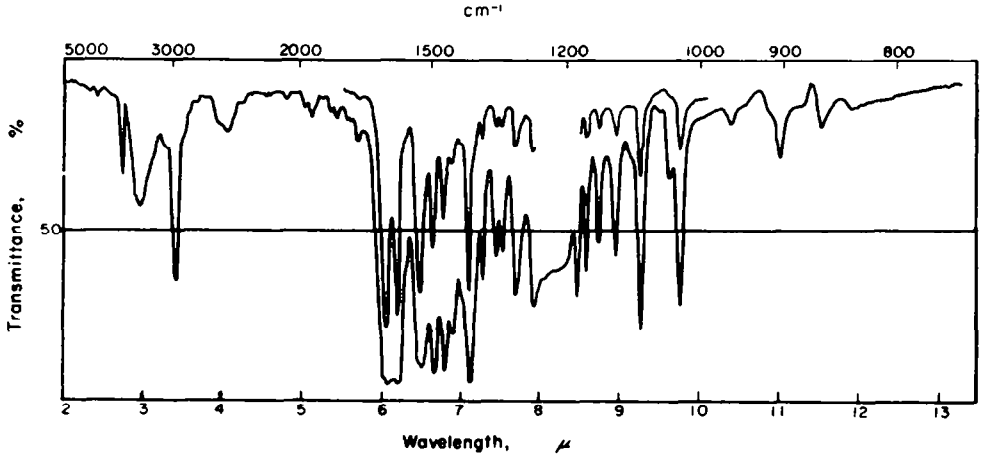


FIG. 8. I.R. curve of 1,2-dimethylquinazol-4-one in $CHCl_3$.

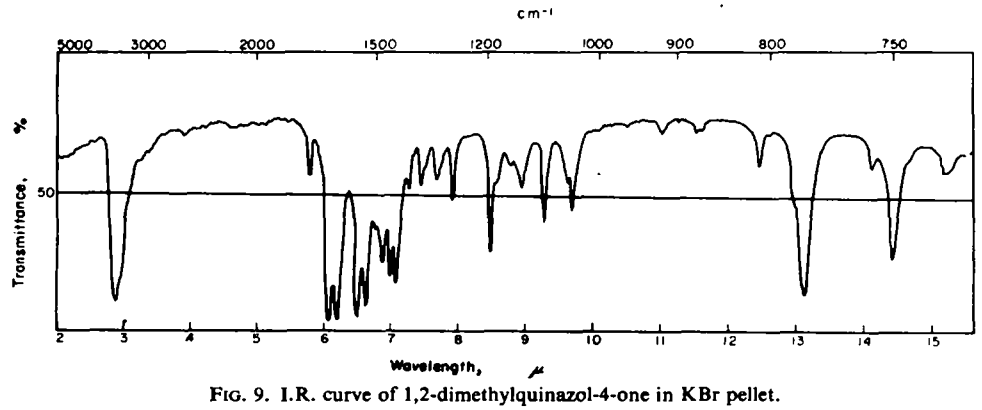


FIG. 9. I.R. curve of 1,2-dimethylquinazol-4-one in KBr pellet.

[24] The intensity of this band diminishes with increased amide concentration in chloroform solution, and the absorption is absent from the solid phase spectra.

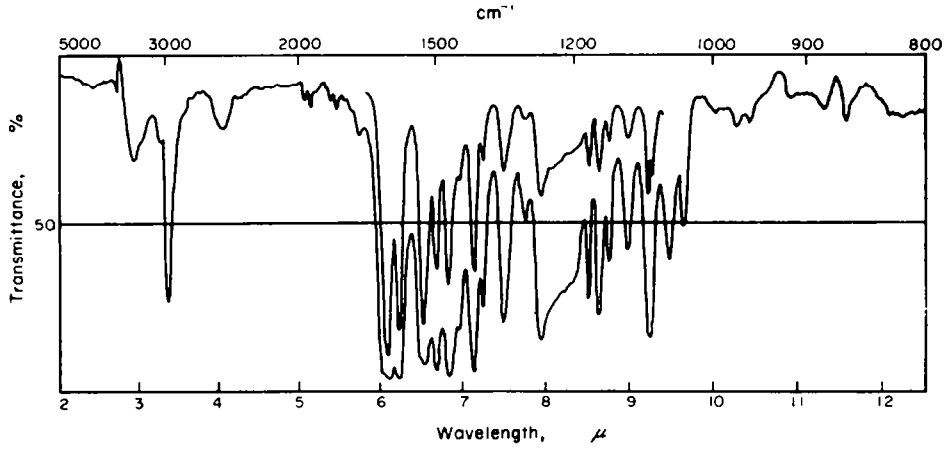


FIG. 10. I.R. curve of 2-ethyl-1-methylquinazol-4-one in $CHCl_3$.

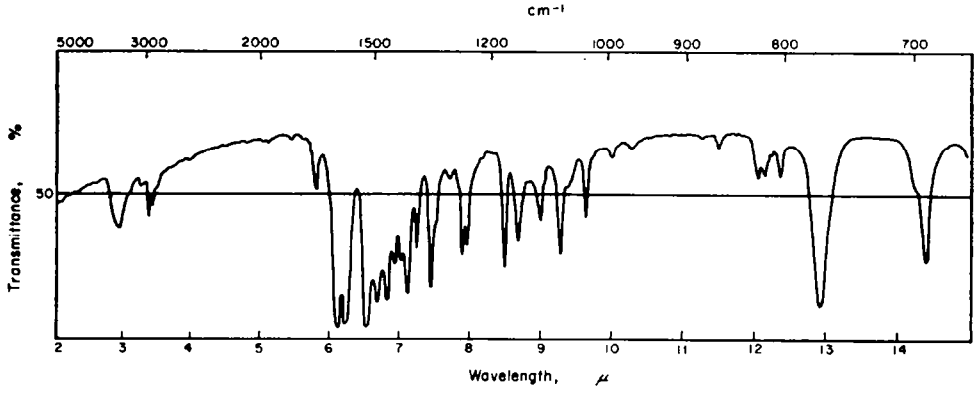


FIG 11. I.R. curve of 2-ethyl-1-methylquinazol-4-one in KBr pellet.

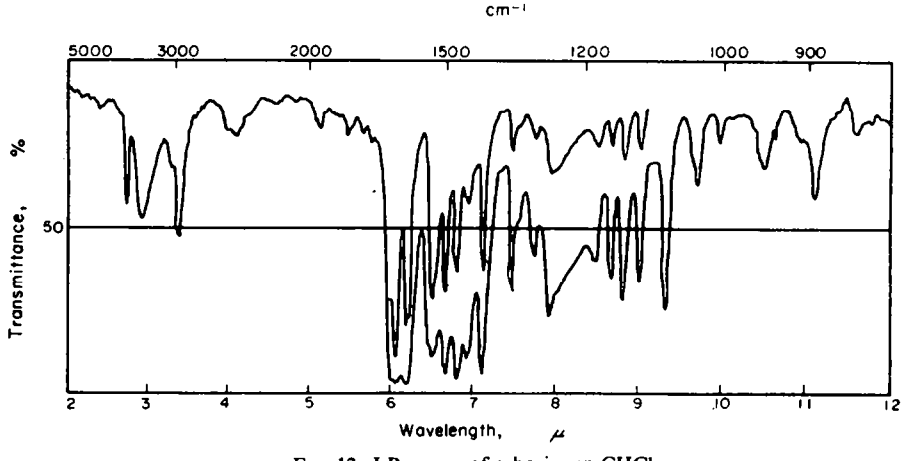


FIG. 12. I.R. curve of arborine in $CHCl_3$.

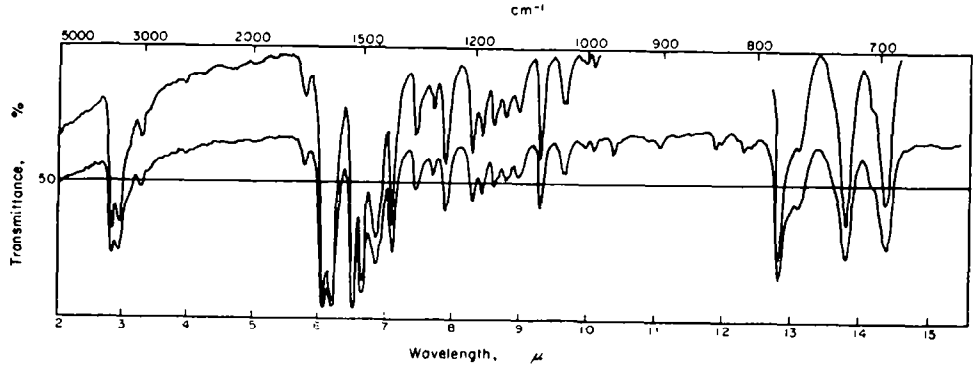


FIG. 13. I.R. curve of arborine in KBr pellet.

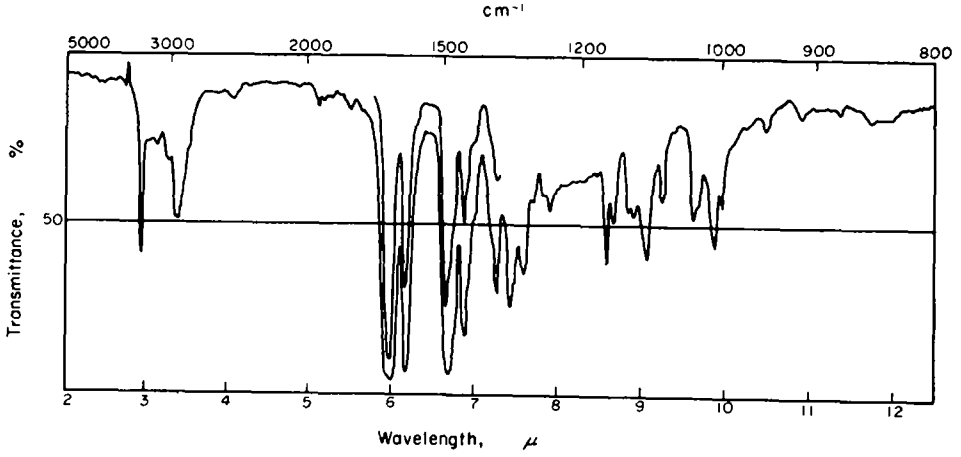


FIG. 14. I.R. curve of dihydroarborine in $CHCl_3$.

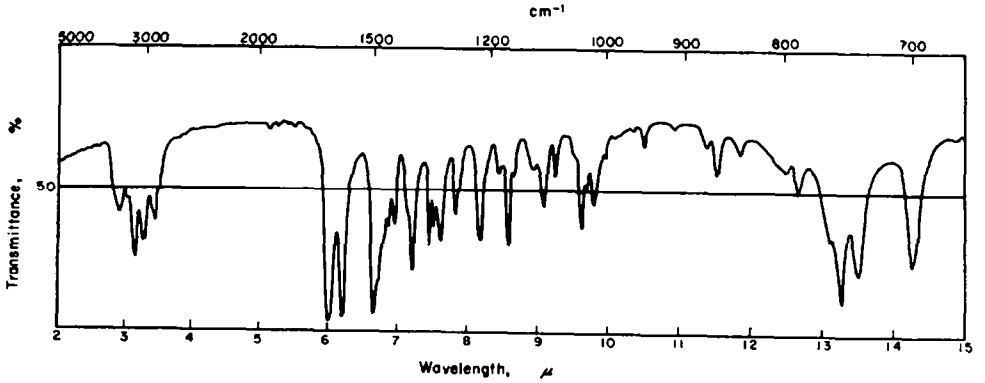


FIG. 15. I.R. curve of dihydroarborine in KBr pellet.

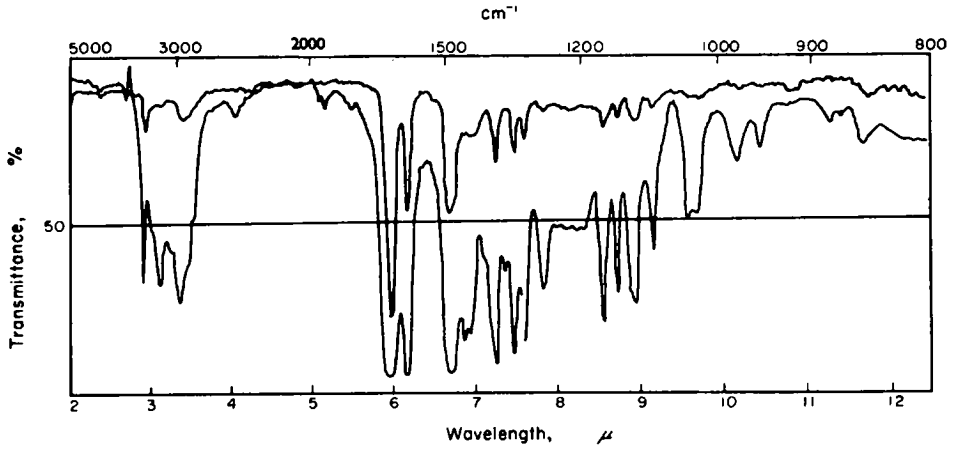


FIG. 16. I.R. curve of 2,3-dihydro-1,2-dimethylquinazol-4-one in $CHCl_3$.

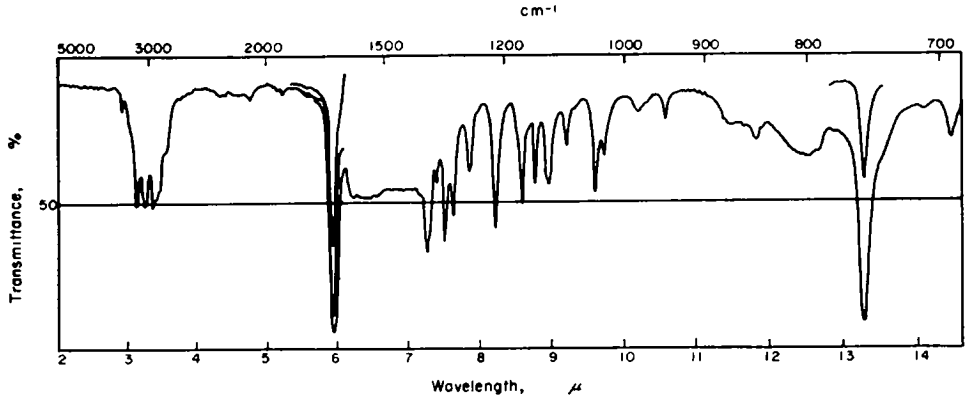


FIG. 17. I.R. curve of 2,3-dihydro-1,2-dimethylquinazol-4-one in CS_2.

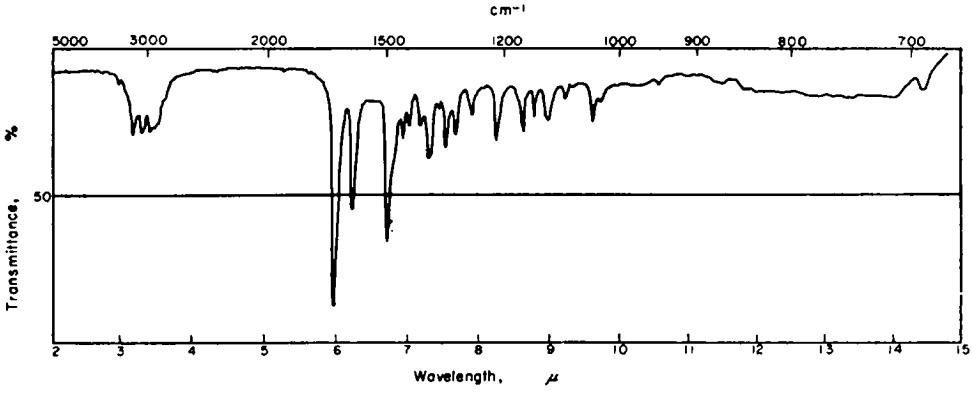


FIG. 18. I.R. curve of 2,3-dihydro-1,2-dimethylquinazol-4-one in CCl_4.

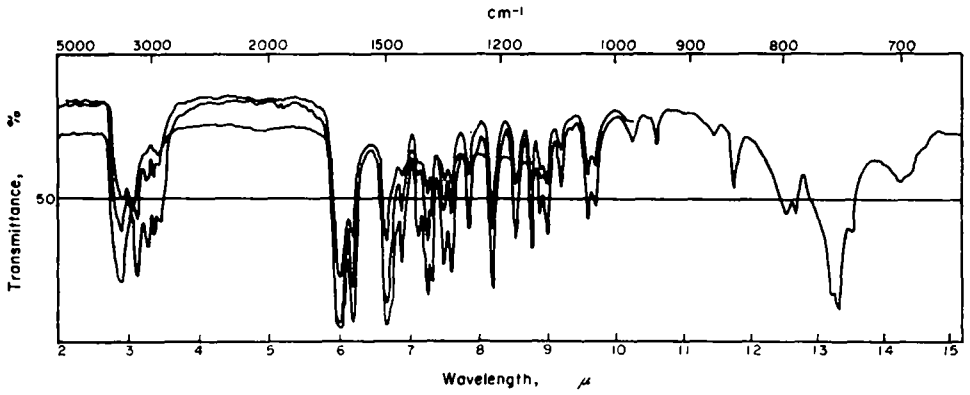


FIG. 19. I.R. curve of 2,3-dihydro-1,2-dimethylquinazol-4-one in KBr pellet.

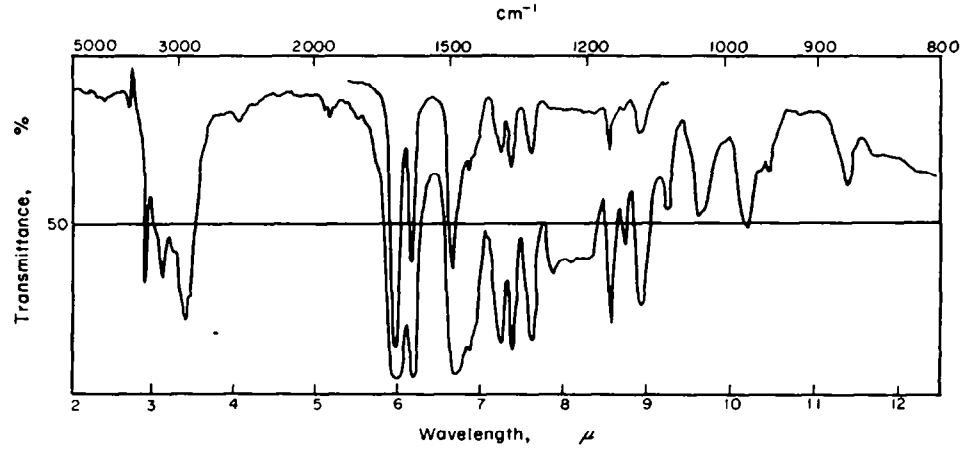


FIG. 20. I.R. curve of 2,3-dihydro-2-ethyl-1-methylquinazol-4-one in $CHCl_3$.

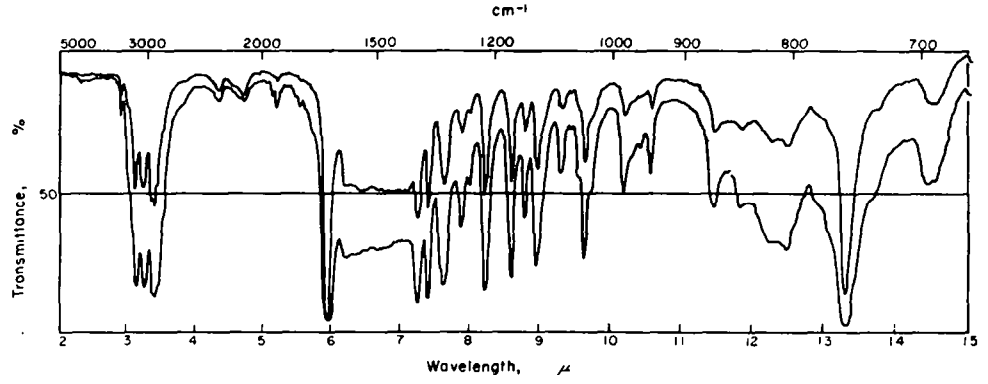


FIG. 21. I.R. curve of 2,3-dihydro-2-ethyl-1-methylquinazol-4-one in CS_2.

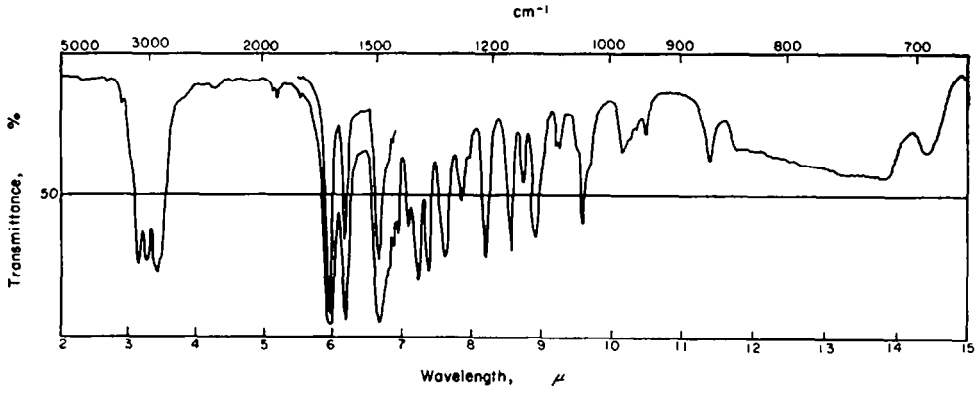


FIG. 22. I.R. curve of 2,3-dihydro-2-ethyl-1-methylquinazol-4-one in CCl_4.

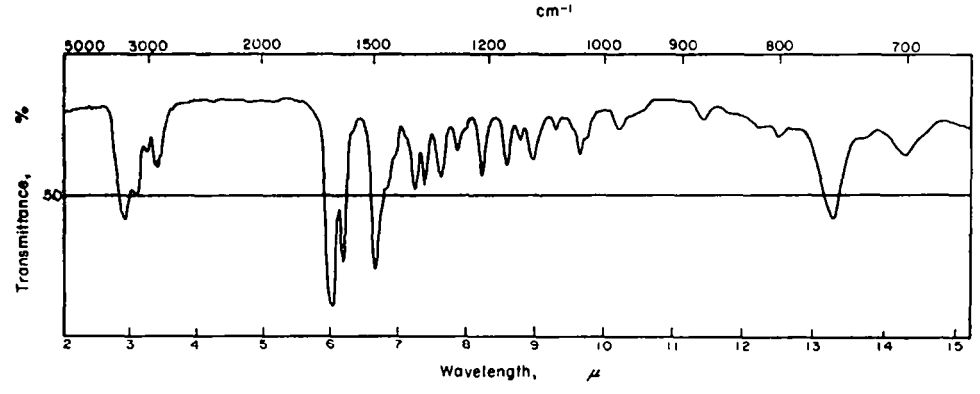


FIG. 23. I.R. curve of 2,3-dihydro-2-ethyl-1-methylquinazol-4-one in KBr pellet.

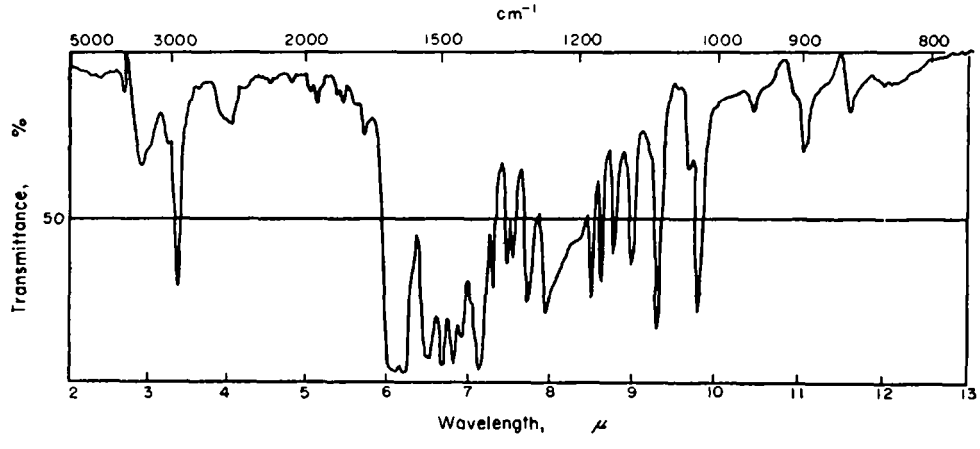


FIG. 24. I.R. curve of specially dried sample of 1,2-dimethylquinazol-4-one in $CHCl_3$.

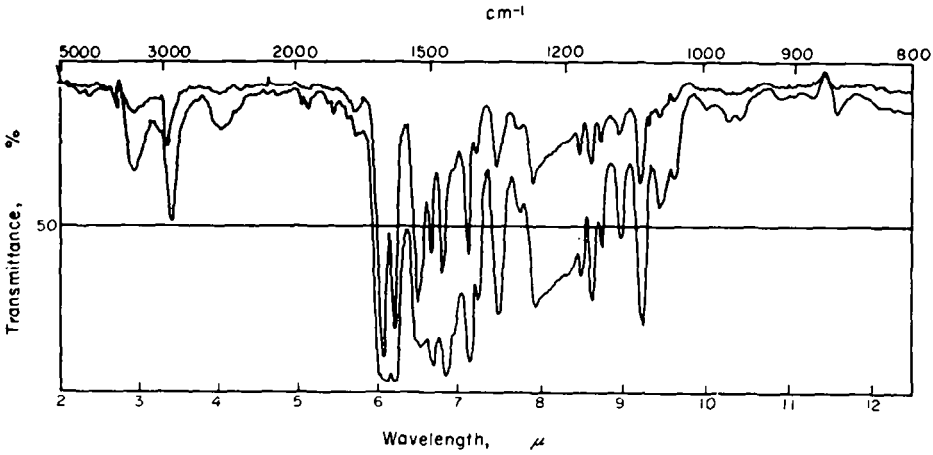


FIG. 25. I.R. curve of specially dried sample of 2-ethyl-1-methylquinazol-4-one in $CHCl_3$.

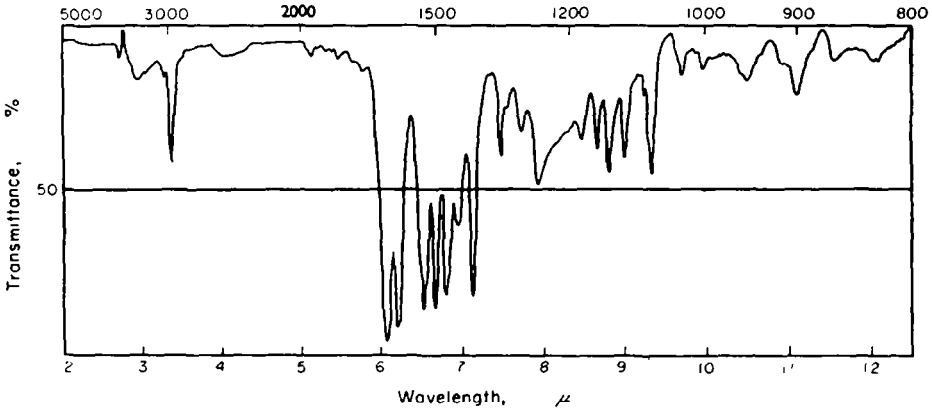


FIG. 26. I.R. curve of specially dried sample of arborine in $CHCl_3$.

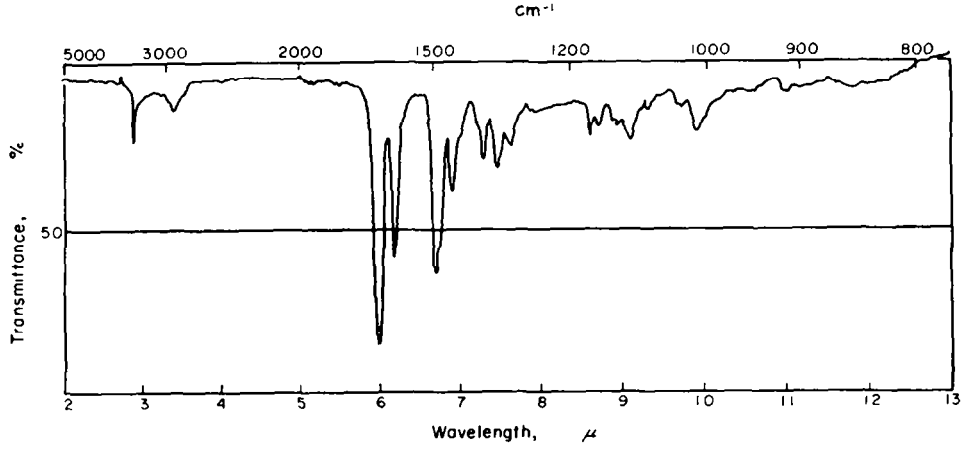


FIG. 27. I.R. curve of specially dried sample of dihydroarborine in $CHCl_3$.

This method, as here applied, may be considered sufficiently accurate to give the direction of the ratio shifts. In the case of 2-ethyl-1-methylquinazol-4-one, the drying procedure gave optical density ratios for wet and dried materials which did not show a decrease after drying. Comparison of the spectra of the wet (Figs. 8, 10, 12, 14) and

TABLE 5. N—H STRETCHING REGION ABSORPTION FOR WET AND DRY SAMPLES

Substance	Arbitrary base line data band (μ)	Base line points: 2·60 and 3·70 μ	
		Wet O.D. (band) / O.D. (C—H St)	*Dry O.D. (band)* / O.D. (C—H St)
1,2-Dimethyl-quinazol-4-one	2·72 2·94	0·314 0·468	0·056 0·293
2-Ethyl-1-methyl-quinazol-4-one	2·74 2·94	0·018 0·227	0·073 0·374
Arborine	2·72 2·95	0·548 0·705	0·094 0·266
Dihydroarborine	2·93	1·62	2·17

dried (Figs. 24 to 27) materials in chloroform solution did not disclose any profound changes in the region 5·0 to 15 μ indicating that besides the change in the solvate structure, the drying procedure did not bring about any other more serious change in the molecules.

For 1,2-dimethylquinazol-4-one, 2-ethyl-1-methylquinazol-4-one and arborine, the drying procedure employed did not completely remove all absorption from the N—H stretching region. After the above drying procedure, absorption still remained in all three compounds as a broad absorption maxima in the 2·95 μ region in chloroform solution, while the absorption at 2·74 microns, although much decreased in intensity, also remained. Band contour changes were observed in the 2·95 μ band for 1,2-dimethylquinazol-4-one, 2-ethyl-1-methylquinazol-4-one and arborine. The formation of a shoulder was observed at approximately 3·04 μ in the case of 1,2-dimethylquinazol-4-one and arborine, and partial disappearance of a shoulder at the same wavelength occurred in the case of 2-ethyl-1-methylquinazol-4-one. Such changes are most probably due to different hydrate or solvate structures arising from the drying operation. These data demonstrate the difficulties in the interpretation of N—H stretching absorption in the presence of water of crystallization or hydroxylic solvation. It is, however, important to note in this connection that absorptions in the N—H stretching region, as presented in Table 2, in the case of 1,2-dimethylquinazol-4-one and 2-ethyl-1-methylquinazol-4-one cannot be due to NH or OH groups as these compounds do not contain any such group, actual or potential. Also, in the case of arborine it cannot be assumed that absorptions in the N—H stretching region are necessarily due to the presence of NH or OH groups; the circumstances noted in the above models may well be operative.

Absorptions in the 1400 to 1750 cm^{-1} region of the infra-red for the various specimens are presented in Table 6. Culbertson *et al.*[35] determined the infra-red spectra

[35] H. Culbertson, J. G. Decius and B. E. Christensen, *J. Amer. Chem. Soc.* **74**, 4834 (1952).

TABLE 6.[86] 1400 to 1750 cm^{-1} REGION ABSORPTION COMPLEX FOR QUINAZOL-4-ONES

Substance	ν cm^{-1}	λ max	ν cm^{-1}	λ max	ν cm^{-1}	λ max	ν cm^{-1}	λ max	ν cm^{-1}	λ max	ν cm^{-1}	λ max	ν cm^{-1}	λ max
1,2-Dimethylquinazol-4-one (in $CHCl_3$)	1742	5·74	1645	6·08	1603	6·24	1536	6·51	1497	6·68	1468	6·81	1443	6·93
1,2-Dimethylquinazol-4-one (in KBr)	1724	5·80	1642	6·09	1608	6·22	1534	6·52	1504	6·65	1453	6·88	1431	6·99
1,2-Dimethylquinazol-4-one (in Nujol)[85]	—	—	1637	6·11	1597	6·26	1534	6·52	1498	6·68	—	—	—	—
2-Ethyl-1-methylquinazol-4-one (in $CHCl_3$)	1739	5·75	1645	6·08	1608	6·22	1534	6·52	1497	6·68	1466	6·82	1439	6·97
2-Ethyl-1-methylquinazol-4-one (in KBr)	1715	5·38	1626	6·15	1608	6·22	1527	6·55	1493	6·70	1458	6·86	1441	6·94
Arborine (in $CHCl_3$)	1730	5·78	1642	6·09	1610	6·21	1531	6·53	1497	6·68	1466	6·82	1437	6·96
Arborine (in KBr)	1721	5·81	1645	6·08	1603	6·24	1531	6·53	1502	6·66	1456	6·87	—	—
Dihydroarborine (in $CHCl_3$)	—	—	1667	6·00	1613	6·20	—	—	1493	6·70	1468	6·81	—	—
Dihydroarborine (in KBr)	—	—	1653	6·05	1605	6·23	—	—	1497	6·68	1451	6·89	1435	6·97
2,3-Dihydro-1,2-dimethylquinazol-4-one (in $CHCl_3$)	—	—	~1664	~6·01	~1613	~6·20	—	—	~1484	~6·74	1449	6·90	1435	6·97
2,3-Dihydro-1,2-dimethylquinazol-4-one (in KBr)	—	—	1658	6·03	1610	6·21	—	—	1493	6·70	1447	6·91	~1441	~6·94
2,3-Dihydro-2-ethyl-1-methylquinazol-4-one (in $CHCl_3$)	—	—	1664	6·01	1613	6·20	—	—	1495	6·69	1447	6·91	—	—
2,3-Dihydro-2-ethyl-1-methylquinazol-4-one (in KBr)	—	—	1658	6·03	1610	6·21	—	—	1497	6·68	—	—	—	—

[86] Shoulders have not been included in this Table.

of a number of quinazolones and quinazolines, including 1,2-dimethylquinazol-4-one. His data for the latter are also included in Table 6. The differences between the data of the present authors and those of Culbertson, for 1,2-dimethylquinazol-4-one, arise from the fact that the values of Culbertson were obtained using slit widths approximately three times wider than those used for the quoted observed values and also that the substance in the literature was observed as a Nujol mull. No corrections for wavelength or frequency were given.[35] Except in those cases where pressure or chemical reaction with potassium bromide occurs, spectra observed in Nujol are usually the same as those observed in potassium bromide, when the regions of Nujol absorption are taken into consideration. Different crystalline forms obtained by crystallization from different solvents also cause large differences in the spectra of solids.

Culbertson *et al.*[35] assign values of absorption bands associated with the $\diagdown C{=}N-\diagup$ linkage in quinazolines as shown in Table 7. His greatest interest was in the region 1500 to 1700 cm^{-1} (6·67 to 5·88 μ), where absorption arises from $C{=}O$, $C{=}N-$ and $C{=}C$ groups, and in the case of amide linkage, from N—H and possibly C—N linkages also. The complexities and difficulties involved in interpretation of the 1500 to 1700 cm^{-1} region in amide spectra are ably discussed by Bellamy.[37] In connection

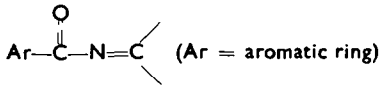
TABLE 7. $C{=}N$-ABSORPTION ASSIGNMENTS OF CULBERTSON *et al.*[35]

Substance	$C{=}N$-Absorption	
	ν cm^{-1}	λ max (μ)
2-Methylquinazol-4-one	1625	6·15
3-Methylquinazol-4-one	1612	6·20
2,3-Dimethylquinazol-4-one	1593	6·28
1,2-Dimethylquinazol-4-one	1597	6·26
Quinazol-4-one	1664, 1608	6·01, 6·22
Quinazol-2-one	1645, 1608	6·08, 6·22

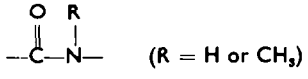
with these considerations, observations of the 1500 to 1700 cm^{-1} (6·67 to 5·88 μ) region in the infra-red for arborine and dihydroarborine indicates that hydrogenation causes disappearance from the complex of an absorption at 6·52 μ (1531 cm^{-1}), as is evident from Table 6. It is important to note that whereas arborine, 1,2-dimethylquinazol-4-one and 2-ethyl-1-methylquinazol-4-one all have an absorption peak in this region, dihydroarborine, 2,3-dihydro-1,2-dimethylquinazol-4-one and 2,3-dihydro-2-ethyl-1-methylquinazol-4-one have none in this region. This fact naturally suggests that an absorption close to 1531 cm^{-1} may represent the contribution of the $C{=}N$-linkage in the quinazol-4-one absorption complex.

[37] L. J. Bellamy, *Infra-red Spectra of Complex Molecules* (2nd Ed.) pp. 203–221. John Wiley, New York 1958).

A survey of the spectra of Culbertson *et al.*[35] of quinazolines and quinazolones indicates that the 1531 cm^{-1} (6·52 μ) absorption might occur only in those substances in which the system:



exists, since all other materials which contain >C=N— not so linked do not show an absorption peak at this frequency. In all the cases considered by Culbertson *et al.* the presence of the linkage:



is also attended by the absence of the 1531 cm^{-1} (6·52 μ) absorption. This fact, coupled with the observations concerning 1,2-dimethylquinazol-4-one, 2-ethyl-1-methylquinazol-4-one and arborine on the one hand, and 2,3-dihydro-1,2-dimethylquinazol-4-one, 2,3-dihydro-2-ethyl-1-methylquinazol-4-one and dihydroarborine on the other, suggests that arborine exists in the form as 2-benzyl-1-methylquinazol-4-one (I) containing the grouping Ar—C(=O)—N=C<, and not as VI which does not contain this grouping. Intensity data for the 1531 cm^{-1} (6·52 μ) absorption relative to the 1653 cm^{-1} (6·05 μ) and 1605 cm^{-1} (6·23 μ) absorption maxima tend to substantiate this view, since for all the molecules which contain the linkage Ar—C(=O)—N=C< these relative intensities are uniformly constant in the solid phase, and the order of intensities is not altered in chloroform solution. It is to be noted in this connection that, though intensity data are helpful here, there is no precise relation between intensity of absorption and molecular constitution in this series of compounds.

Consideration of the absorptions of the hydrogenated derivatives of arborine and of the alkylated quinazolones in conjunction with those of the parent products indicates that in these instances the absorption, noted in all spectra of the materials examined, at approximately 1466 cm^{-1} (6·68 μ) is less intimately involved with the —C(=O)—N=C< linkage system than are the absorptions of the complex which occur in the region of 1608 cm^{-1} (6·22 μ), 1451 cm^{-1} to 1468 cm^{-1} (6·89 to 6·81 μ), and 1453 to 1443 cm^{-1} (6·97 to 6·93 μ). In dihydroarborine, the carbonyl absorption is shifted to 1667 cm^{-1} (6·00 μ) from the value 1642 cm^{-1} (6·09 μ) observed in the unsaturated system present in arborine. This is a shift of 25 cm^{-1}, and is of the same order of magnitude as that noted by Culbertson *et al.*,[35] for carbonyl groups linked with >C=N-system as compared with the phenyl ring conjugation. Similar shifts have

also been noted in the absorptions in this region in the cases of the alkylated dihydroquinazol-4-ones (cf. Table 6).

The 1610 cm^{-1} (6·21 μ) absorption in arborine shows splitting at 1603 cm^{-1} (6·24 μ) in chloroform solution, but not in the solid state (KBr pellet) spectrum. This may be interpreted as caused by some effect other than a shifted absorption due to an exocyclic double bond (1625 cm^{-1}, 6·15 μ), since the only other sign of splitting in 1603 cm^{-1} absorption is seen in the case of 2-ethyl-1-methylquinazol-4-one. In dihydroarborine the intensity of the 1613 cm^{-1} (6·20 μ) absorption is appreciably altered, which is an indication that the unsaturated linkage contributes to the intensity in this region.

Arborine and the dialkylated quinazol-4-ones show absorption in the region 1730–1742 cm^{-1} (5·78–5·74 μ) in chloroform solution and in the region 1715–1724 cm^{-1}

The complex structure embracing the regions C and D may be interpreted as follows:

C—This signal is due to the five benzyl-aromatic protons.

D (Complex)—This is due to the four aromatic quinazolone protons.

As regards the possibility for the tautomeric form VI for arborine, it may be pointed out that the N—H proton, if present, might be difficult to locate (region F of Fig. 28) as a result of confusion with the C—D complex. There should not, however, be any

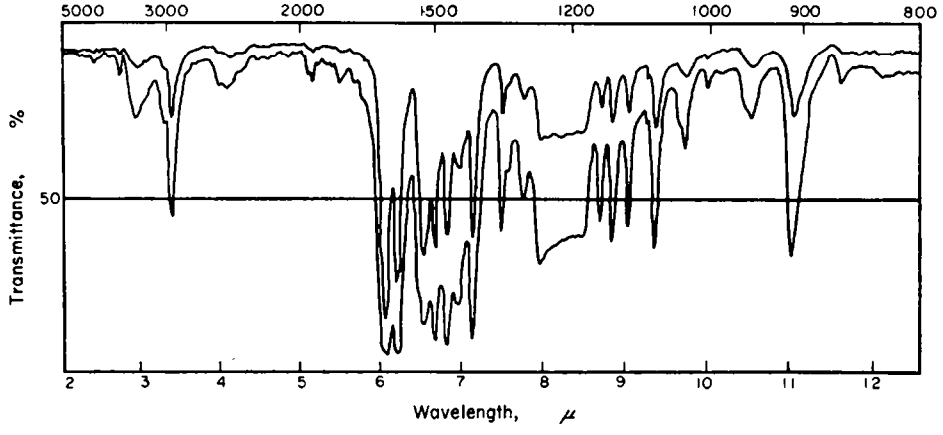


FIG. 29. I.R. curve of arborine in $CHCl_3$ using the specimen recovered by removal of deuterochloroform after the N.M.R. spectra determination.

doubt as to the absence of the vinyl proton in view of the absence of vinyl absorption in the appropriate region (region E of Fig. 28). Thus the integrated area count for the protons gives strong support to the 2-benzyl-1-methylquinazol-4-one structure (I) for arborine.

As a further check, after determination of the N.M.R. spectrum the arborine used for the purpose was recovered by evaporation of the deuterochloroform. The recovered arborine was then used for the infra-red determination. This I.R. absorption curve (Fig. 29) for arborine was found to be the same as that of arborine as obtained previously (Fig. 12), practically in all detail except for an intensity difference and small wavelength shift for the absorption in the region of 900 cm^{-1}. This difference is most probably due to traces of deuterochloroform remaining in the product after evapora-

above, it may be stated that support is given to the view that arborine exists as 2-benzyl-1-methylquinazol-4-one (I) and not as the tautomeric form VI.

Nuclear magnetic resonance data were obtained on Varian equipment utilizing deuterochloroform as solvent and tetramethylsilane as an internal standard. The sample was excited with a sixty megacycle radio frequency, using a side band of approximately six hundred cycles.

There are fourteen protons in arborine. Disregarding for the moment the possibility of tautomerism between structure I and structure VI, nine protons are located on aromatic nuclei, four of these on an ortho-substituted aromatic ring and five on a monosubstituted aromatic ring. These protons are in different positions, though in similar chemical environments. The three protons located on the N-methyl carbon atom are another group of protons located at a chemically different site in the molecule. Both the aromatic and the methyl protons cannot be involved in a tautomeric process. However, if the tautomerism does indeed occur, two protons represented as attached in one tautomeric form (I) to the methylene of the benzyl group, and in another form VI as attached to a nitrogen atom and to a vinyl carbon atom, give rise to two distinct chemical environments which are easily recognized by nuclear magnetic resonance technique.

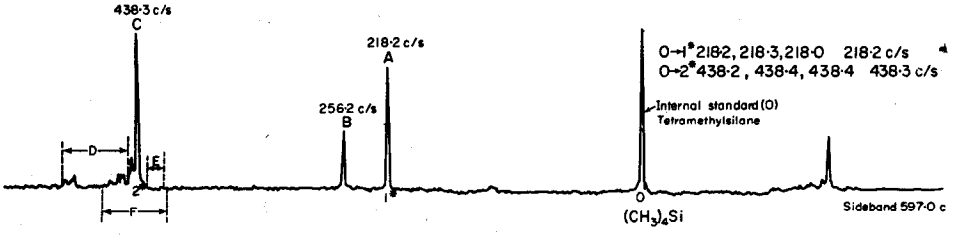


FIG. 28. Nuclear magnetic resonance curve of arborine in deuterochloroform with tetramethyl silane as internal standard.

TABLE 8.

Peak label	X-axis cycles/sec	Proton assignments	Approximate integrated area (P.U.)	No. of protons
0	0	CH_3 protons in $(CH_3)_4Si$	—	—
A (1*)	218·2	protons of N—CH_3 group	16	3
B	256·2	protons of benzyl-CH_2 group	11	2
C (2*)	438·4	protons of benzyl-phenyl group		
D (complex)	>438·4	protons of quinazolone aromatic group	50	9

The nuclear magnetic resonance spectrum of arborine in dueterochloroform, with tetramethylsilane as an internal standard is presented in Fig. 28. The integrated area (P.U. = planimetric area units) was directly determined planimetrically from the experimental curve. Such areas are not highly accurate on the scale used. The number of protons corresponding to a particular peak is proportional to the peak area. The area of the N—CH_3 proton peak was chosen as an area of reference standard, giving 5·33 planimetric area units per proton. The results obtained are presented in Table 8. It is clear from this Table that the fourteen protons of arborine have all been well accounted for.

The complex structure embracing the regions C and D may be interpreted as follows:

C—This signal is due to the five benzyl-aromatic protons.

D (Complex)—This is due to the four aromatic quinazolone protons.

As regards the possibility for the tautomeric form VI for arborine, it may be pointed out that the N—H proton, if present, might be difficult to locate (region F of Fig. 28) as a result of confusion with the C—D complex. There should not, however, be any

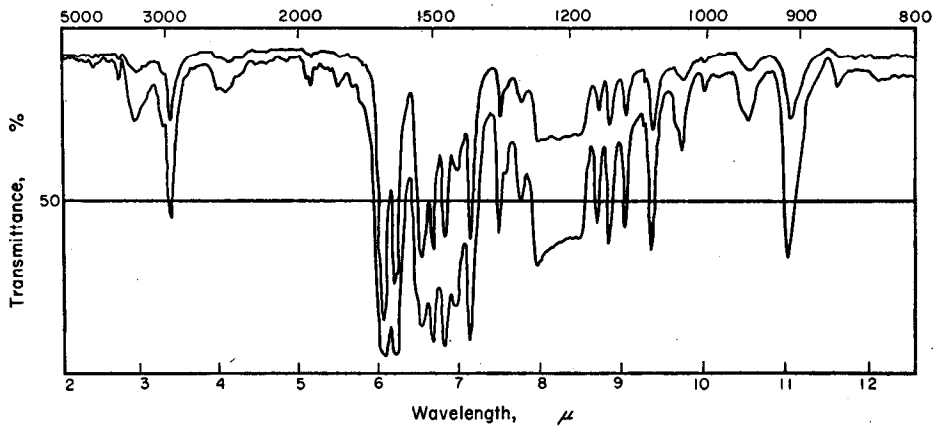


FIG. 29. I.R. curve of arborine in $CHCl_3$ using the specimen recovered by removal of deuterochloroform after the N.M.R. spectra determination.

doubt as to the absence of the vinyl proton in view of the absence of vinyl absorption in the appropriate region (region E of Fig. 28). Thus the integrated area count for the protons gives strong support to the 2-benzyl-1-methylquinazol-4-one structure (I) for arborine.

As a further check, after determination of the N.M.R. spectrum the arborine used for the purpose was recovered by evaporation of the deuterochloroform. The recovered arborine was then used for the infra-red determination. This I.R. absorption curve (Fig. 29) for arborine was found to be the same as that of arborine as obtained previously (Fig. 12), practically in all detail except for an intensity difference and small wavelength shift for the absorption in the region of 900 cm^{-1}. This difference is most probably due to traces of deuterochloroform remaining in the product after evaporation of the solution for recovery of arborine, as no special precautions were taken to remove the last traces of the solvent and as deuterochloroform has a characteristic absorption in the region 900 cm^{-1}.

It is interesting to note that the dissolution of arborine in deuterochloroform did not change the character of the spectrum in the region 2·5 to 3·0 μ. If an active proton were present, as is the case with structure VI, the broad absorptions of low intensity in the region of 2·5 to 3·0 μ would be expected to be shifted towards higher wavelength. That this does not occur in this instance lends support to the proposition that no proton is present which easily exchanges with deuterium in deuterochloroform under the conditions of simple mixing. In other words, this finding is also in line with the view that arborine exists in the form I and not in the form VI.

Considering all the results stated above it may be concluded that arborine exists as 2-benzyl-1-methylquinazol-4-one (I) both in the solid state and in solution and that

this is the stable form even in moderately acidic or alkaline solutions. As regards the oxidative degradation of arborine leading to the formation of benzaldehyde, it is quite possible that this reaction takes place through the intermediate formation of a small proportion of the tautomeric form VI which is highly reactive towards the oxidizing agent and is continuously produced; there are many well-known analogies.

EXPERIMENTAL

Arborine required for the work was obtained from the leaves of *Glycosmis arborea* Correa by the method of Chakravarti *et al.*[1] It has a marked tendency to form crystals with solvent of crystallization. On crystallization from benzene containing a little ethanol it is obtained as $C_{16}H_{14}ON_2$, C_6H_6. Also when crystallized from a large volume of water it yields crystals having the composition $C_{16}H_{14}ON_2$, $2H_2O$. For the present work, arborine was purified by repeated crystallization from benzene–ethanol; the solvent of the crystals was removed at 100°.

Dihydroarborine was obtained by hydrogenation of arborine in alcoholic solution in presence of a platinum catalyst as described previously.[1] It was purified by repeated crystallization from a mixture of chloroform and ethanol, m.p. 199–200°.

Periodic acid oxidation of arborine. The oxidation of arborine with periodic acid was carried out following the conditions used by Chatterjee and Ghosh Majumdar.[25] Benzaldehyde obtained on steam distillation of the product was converted into the 2,4-dinitrophenylhydrazone. On crystallization from aqueous ethanol it had m.p. 236° (mixed m.p. compared with an authentic specimen). The yield was, however, quite low. In the detailed publication by Chatterjee and Ghosh Majumdar[25] there is no mention about the yield.

Ozonolysis of arborine. Arborine (200 mg) was dissolved in anhydrous chloroform (20 ml) and cooled in a mixture of ice and salt, and ozonized oxygen was passed till no more absorption of ozone occurred. After removal of excess of ozone in a current of dry nitrogen and then the solvent under reduced pressure, the residue was decomposed with water and steam-distilled. Although the odour of benzaldehyde in the distillate was quite strong, it afforded the 2,4-dinitrophenylhydrazone of benzaldehyde in very poor yield. Ozonolysis of arborine was also carried out in acetic acid solution following the same procedure, but in this case also the yield of benzaldehyde was very poor. Chatterjee and Ghosh Majumdar did not mention anything about the yield obtained by their method.[25]

Action of hydrogen peroxide on arborine. Arborine (2·0 g) was heated with hydrogen peroxide (30 ml of 6%) on the steam-bath in a current of nitrogen, water being added from time to time to keep the volume of solution constant. The nitrogen gas, as it passed out of the flask, was bubbled through a solution of 2,4-dinitrophenylhydrazine in aqueous hydrochloric acid. Within a short time an orange yellow precipitate separated. On crystallization from ethanol it had m.p. 235–236° and was found to be identical with the 2,4-dinitrophenylhydrazone of benzaldehyde by comparison of mixed m.p. In this case also, although the nitrogen gas coming out of the reaction flask had quite a prominent odour of benzaldehyde, the yield of benzaldehyde was extremely poor.

1,2-*Dimethylquinazol*-4-*one.* A mixture of N^2-methylanthranilamide (1·2 g) and acetic anhydride (1·1 ml) was heated in an oil-bath at about 150° for 2 hr under partial reflux. The temp of the bath was then gradually raised from 160° to 190° during 20 min, and kept at 190° for about 10 min. The product was treated with sufficient ethanol and evaporated to dryness on the steam-bath, and this process of evaporation with ethanol repeated once more. It was then dissolved in a large excess of hot ethyl acetate, filtered while hot, and the solution concentrated, when 1,2-dimethylquinazol-4-one was obtained in yellow needles, m.p. 203–204° (Weddige[21], m.p. 199°), yield 0·94 g. As noted by Weddige, it has a strong tendency to retain moisture as water of crystallization and is hygroscopic; it is readily soluble in ethanol.

2,3-*Dihydro*-1,2-*dimethylquinazol*-4-*one.* 1,2-Dimethylquinazol-4-one (0·8 g) was dissolved in ethanol (20 ml) and shaken with Adams' platinum oxide catalyst (80 mg) under pure hydrogen. About 120 ml of the gas was absorbed, representing approximately one mole of hydrogen after taking into consideration the amount absorbed by the catalyst. The deep yellow colour of the original solution changed to light yellow at this stage and the solution acquired a strong violet fluorescence. It was filtered from the catalyst and the filtrate concentrated to a small volume and cooled in ice, when faint yellow (almost colourless) prisms of 2,3-*dihydro*-1,2-*dimethylquinazol*-4-*one* were obtained, yield 0·62 g. It was further purified by crystallization from ethyl acetate, m.p. 151–152°. (Found: C,

67·8; H, 6·7; N, 16·3; M.Wt. 177. $C_{10}H_{12}ON_2$ requires: C, 68·1; H, 6·8; N, 15·9%; M.Wt. 176). Unlike dihydroarborine, this dimethyldihydroquinazolone is readily soluble in ethanol.

2-Ethyl-1-methylquinazol-4-one. A mixture of N^2-methylanthranilamide (1·0 g) and propionic anhydride (1·2 ml) was heated in an oil-bath at 150–160° for 2 hr under partial reflux. The temp was then gradually raised to 190° during 20 min, and kept at 190° for about 10 min. The product was worked up as in the case of preparation of 1,2-dimethylquinazol-4-one and crystallized from ethyl acetate when *2-ethyl-1-methylquinazol-4-one* was obtained in light yellow prisms, yield 0·62 g, m.p. 148–149°. Like 1,2-dimethylquinazol-4-one, it is hygroscopic and is readily soluble in ethanol (Found: C, 70·5; H, 6·2; N, 15·2. $C_{11}H_{12}ON_2$ requires: C, 70·2; H, 6·4; N, 14·9%).

2,3-Dihydro-2-ethyl-1-methylquinazol-4-one. 2-Ethyl-1-methylquinazol-4-one (0·7 g) was dissolved in ethanol (20 ml) and shaken with platinum oxide (70 mg) under hydrogen. About 97 ml of the gas was absorbed representing about one mole of hydrogen (excluding absorption by the catalyst). At this stage the original yellow colour of the solution was practically completely discharged and the solution had a strong violet fluorescence. The product was isolated as in the case of the corresponding dimethyl compound, yield 0·4 g. *2,3-Dihydro-2-ethyl-1-methylquinazol-4-one* crystallizes from ethyl acetate in colourless prisms, m.p. 134–135° (Found: C, 69·3; H, 7·5; N, 14·5; M.Wt. 200. $C_{11}H_{14}ON_2$ requires: C, 69·4; H, 7·4; N, 14·7%. M.Wt.190).

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