derivative which may be convertible to other interesting C^{14}-labeled compounds. Furthermore, nonradioactive 1,2-*O*-isopropylidene-L-idofuranurono-γ-lactone appears to be an interesting starting material for the synthesis of L-idose and its derivatives.

Experimental[8]

Preparation of 1,2-*O*-Isopropylidene-D-*xylo*-dialdopentofuranose.—A solution of 22 g. of 1,2-*O*-isopropylidene-D-glucofuranose and 5 g. of sodium hydrogen carbonate in 150 ml. of water was oxidized with 22 g. of sodium metaperiodate according to Sowden.[9] The reaction mixture was then filtered and the filtrate was extracted with five 300-ml. portions of chloroform. The combined extracts were dried (sodium sulfate) and evaporated under reduced pressure to a sirup which was kept for several days in a desiccator evacuated with an oil-pump to remove the traces of formaldehyde and chloroform. The resulting sirupy 1,2-*O*-isopropylidene-D-*xylo*-dialdopentofuranose (8.4 g.) furnished a semicarbazone derivative, m.p. 202–205° dec. (recorded[9] 202–202.5°).

1,2-*O*-Isopropylidene-D-glucofuranono-γ-lactone and 1,2-*O*-Isopropylidene-L-idofuranurono-γ-lactone.—A solution of 0.8 g. of sodium cyanide in 30 ml. of water was cooled to 0° and added to an equally cold solution of approximately 4 g. of 1,2-*O*-isopropylidene-D-*xylo*-dialdopentofuranose and 1.2 g. of sodium hydrogen carbonate in 40 ml. of water containing several lumps of solid carbon dioxide. After evaporation of the carbon dioxide, the mixture was kept at 0° for 2 days, then at room temperature for 3 days, and was finally heated at 60° for 5 hr. with aeration and concentration of the solution. The concentrated solution was then evaporated under diminished pressure to dryness and the residue was boiled briefly with 50 ml. of methanol, cooled, 100 ml. of diethyl ether was added, and the precipitate of the sodium salts and sodium hydrogen carbonate filtered, washed with ether and dried. The dry precipitate was dissolved in 20 ml. of water and the solution, after adjustment to *p*H 2 with 4 *N* hydrogen chloride, was extracted 10 times with 50-ml. portions of ethyl acetate. The combined extracts, after drying (sodium sulfate) and evaporation of the solvent, furnished a partly crystalline residue which was lactonized, according to the method of Sowden,[2] by heating under reflux with 40 ml. of toluene for 3 hr. The resulting clear solution was decanted from the small amount of insoluble material, cooled and gradually diluted with petroleum ether (b.p. 35–55°). The crude mixture of the lactones which separated (1.47 g.) was dissolved in 6 ml. of ethyl acetate, 1.5 ml. of petroleum ether was added, and the solution was added to a 2 (diam.) × 25 cm. column of Florex XXX[10] and Celite[11] (4:1). The column was then developed with a mixture of the same solvents (4:1) and (using a fraction collector) the effluent was collected in 5-ml. fractions and evaporated with an infrared lamp. Fractions 10–13 contained crystalline 1,2-*O*-isopropylidene-L-iodofuranurono-γ-lactone, which was recrystallized from acetone–petroleum ether. Fraction 13 gave a mixture, and fractions 14–20 furnished crystalline 1,2-*O*-isopropylidene-D-glucofuranurono-γ-lactone, which was recrystallized from ethyl acetate and petroleum ether. Further amounts of products were obtained on rechromatography of the combined mother liquors and of fraction 13, followed by recrystallization as before; total yield 0.546 g. of 1,2-*O*-isopropylidene-D-glucofuranurono-γ-lactone, m.p. 120°, and 0.568 g. of 1,2-*O*-isopropylidene-L-idofuranurono-γ-lactone, m.p. 137–138°, $[\alpha]^{26}D$ +91° (*c* 1.82, acetone). Sowden,[2] in certain variations of his procedure, has found this compound contaminating 1,2-*O*-isopropylidene-D-glucofuranurono-γ-lactone and reports m.p. 128–130° and $[\alpha]_D$ +87.5° (water).

Anal. Calcd. for $C_9H_{12}O_6$: C, 50.00; H, 5.55. Found: C, 50.09; H, 5.72.

In a parallel experiment, condensation of the same amounts of sodium cyanide and 1,2-*O*-isopropylidene-D-*xylo*-dialdopentofuranose in the presence of 1.5 g. of sodium carbonate (in place of 1.2 g. of sodium hydrogen carbonate) furnished 0.204 g. of 1,2-*O*-isopropylidene-D-glucofuranurono-γ-lactone and 0.121 g. of 1,2-*O*-isopropylidene-L-idofuranurono-γ-lactone.

The above D-glucuronic acid derivative was converted to D-glucose according to the procedure of Roseman.[6]

1,2-*O*-Isopropylidene-L-idofuranose.—Reduction of 0.230 g. of 1,2-*O*-isopropylidene-L-idofuranurono-γ-lactone with lithium aluminum hydride according to the method employed by Roseman[6] for the corresponding derivative of D-glucose, furnished 1,2-*O*-isopropylidene-L-idofuranose (recrystallized from ethyl acetate); yield 0.178 g., m.p. 113–114°, $[\alpha]^{26}D$ −20° (*c* 2.7, methanol), recorded[7] m.p. 112–114° and $[\alpha]_D$ −29° (water).

L-Iduronic Acid.—A solution of 1 g. of 1,2-*O*-isopropylidene-L-idofuranurono-γ-lactone in 25 ml. of water containing 5 ml. of Amberlite IR-120-H[12] was heated over the steam-bath for 3 hr. The solution was then filtered and the filtrate was evaporated under reduced pressure. The residue was crystallized from methanol by the addition of ethyl acetate and was recrystallized in the same manner. The product, L-iduronic acid, gave a strong naphthoresorcinol test for uronic acids and its freshly prepared aqueous solution was acid to litmus; yield 0.3 g., m.p. 131–132°, $[\alpha]^{22}D$ +37° (3.5 min.) → +33° (28 min., 4 hr.) (*c* 3, water).

Anal. Calcd. for $C_6H_{10}O_7$: C, 37.11; H, 5.15. Found: C, 37.10; H, 5.38.

(8) The experiments described have been carried out with unlabeled materials but were later applied to the production of D-glucose-6-C^{14} through employment of sodium cyanide-C^{14}.

(9) K. Iwadare, *Bull. Chem. Soc. Japan*, **16**, 40 (1941); J. C. Sowden, THIS JOURNAL, **73**, 5496 (1951).

(10) Product of the Floridin Co., Warren, Pa.

(11) Product of Johns-Manville Co., New York, N. Y.

(12) Product of Rohm and Haas Co., Philadelphia, Pa.

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Purines. IV. The Infrared Spectrum of Purine and Certain Substituted Purine Derivatives[1]

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The biological importance of pyrimidine compounds has led to rather extensive studies of their infrared spectra[2] for information which might lead to their qualitative or quantitative determination or to their identification. This work has been helpful in elucidating several of the structural features of certain pyrimidine compounds and to the discovery of what may be characteristic absorption bands associated with the presence of the pyrimidine ring system.[3]

The infrared spectra of the quinazoline compounds have been studied in this Laboratory[4] and several structural problems of these compounds have been resolved.[5] It was observed in the course of this work that a group of frequencies (due to C=N and C=C structures) common to the quinazoline ring (1478–1517, 1566–1581 and 1612–1628 $cm.^{-1}$) systems did not appear in the quinazolone or quinazolinedione structures.

Recently Blout and Fields[6] have published the infrared spectral data of guanine, adenine, hypoxanthine and xanthine. All four of these purines were

(1) This work was supported in part by grants from the Division of Research Grants and Fellowships, National Institutes of Health, Public Health Service. Published with the approval of the Monographs Publication Committee, Oregon State College, as Research Paper No. 265, School of Science, Department of Chemistry.

(2) I. A. Brownlie, *J. Chem. Soc.*, 3062 (1950); C. L. Angyal and R. L. Werner, *ibid.*, 2911 (1952); H. W. Thompson, D. L. Nicholson and L. N. Short, *Faraday Soc. London*, **9**, 222 (1951).

(3) L. N. Short and H. W. Thompson, *J. Chem. Soc.*, 169 (1952).

(4) H. Culbertson, J. C. Decius and B. E. Christensen, THIS JOURNAL, **74**, 4834 (1952).

(5) H. Culbertson, C. Willits and B. E. Christensen, *ibid.*, **76**, 3533 (1954).

(6) E. R. Blout and M. Fields, *ibid.*, **72**, 479 (1950).

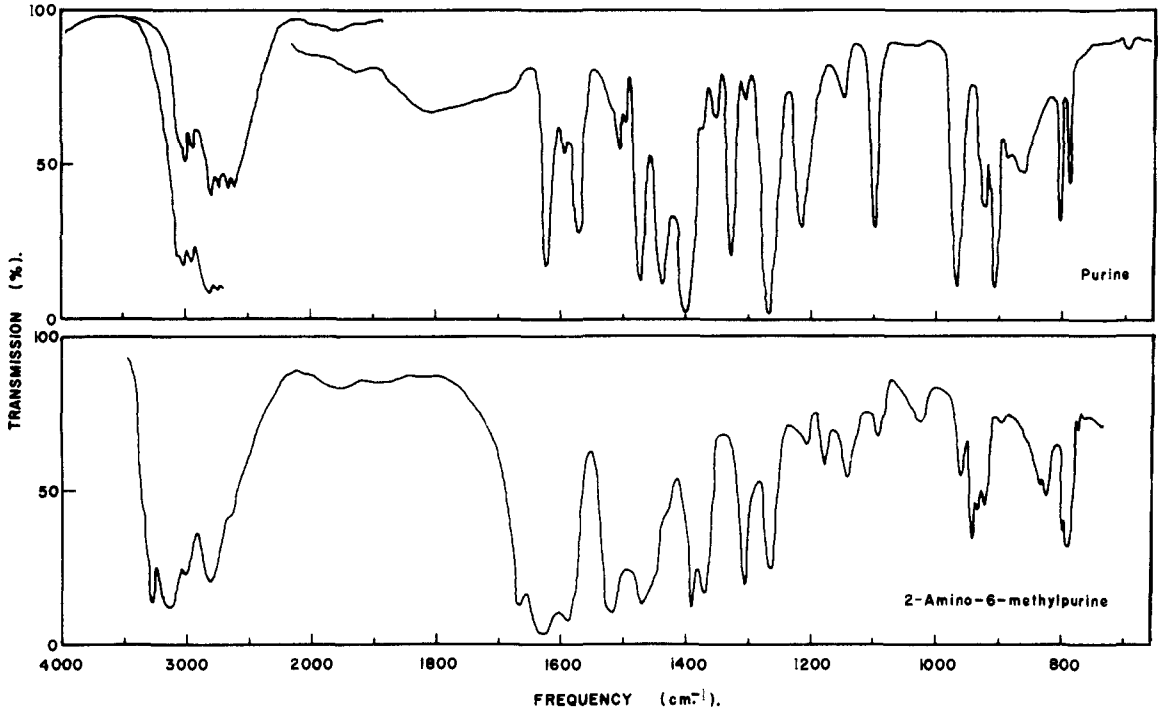


Fig. 1.

reported to have intense absorption bands in the regions 1670–1700 and 1558–1610 cm.$^{-1}$ which these investigators attributed to C=C and C=N stretching modes in the purine ring system; a third band characteristic of this type of compound was located in the region of 935–957 cm.$^{-1}$. Since this Laboratory in the course of other work had acquired a substantial number of other purine derivatives it appeared worthwhile to obtain their infrared spectra for purposes of comparison with the observations of Blout and Fields as well as with the related pyrimidine and quinazoline structures.

Discussion

Due to the absence of tautomeric effects as well as to the influence of substituents, the study of the infrared spectrum of purine free base itself should be most fruitful in the search for absorptions characteristics of this ring system. The infrared spectra are composed of vibrations due to the component parts of the molecule as well as to those of the molecule as a whole; many of the latter are to be found in the region below 1350 cm.$^{-1}$.

Examination of the data in Table II indicates several regions of intense absorption which will be designated as group I (2500–3500 cm.$^{-1}$), group II (1550–1700 cm.$^{-1}$), group III (1000–1550 cm.$^{-1}$), group IV (below 1000 cm.$^{-1}$) for purposes of discussion.

Group I (2500–3500 cm.$^{-1}$).—This region contains the hydrogen stretching vibrations along with possible overtones and combinations of the lower frequencies. The most conspicuous feature of this region is the absence of strong absorption peaks above 3000 cm.$^{-1}$ in purine itself; when an amino group is substituted in the 2- or 6-position, well-resolved peaks appear between 3100 and 3400 cm.$^{-1}$. In all the compounds (with the possible exception of 2-N-diethylaminopurine) there is a broad absorption with a peak at about 2700 cm.$^{-1}$ and a gradually weakening edge extending on the low frequency side to below 2300 cm.$^{-1}$. Since X-ray diffraction studies[7] have shown that related compounds form numerous intermolecular hydrogen bonds in the crystalline state, the infrared data are interpreted most readily by assuming the existence of hydrogen bonds of varying strength. In this connection it is interesting to note the disappearance of the long wave length tail on the band centered at about 2700 cm.$^{-1}$ observed by Blout and Fields in theobromine and caffeine. This absorption is apparently due to an exceptionally strong H bond formed by the H atom of the 7-position.

Group II (1550–1700 cm.$^{-1}$).—Unsubstituted purine exhibits very strong absorption peaks at 1571 and 1622 cm.$^{-1}$; the corresponding frequencies in 2-N-diethylaminopurine occur at 1568 and 1632. In some of the derivatives the apparently corresponding peaks are poorly resolved and lie closer to 1600 (see Fig. 1, which contrasts the spectrum of purine with 2-amino-6-methylpurine). Substitution of an amino group apparently produces a new strong band at about 1670 cm.$^{-1}$ and substitution of a hydroxyl group produces a corresponding maximum nearer 1700 cm.$^{-1}$. Thus the band falling between 5.88 and 5.98 μ observed by Blout and Fields is probably not a double bond stretch in the ring but either the deformation of the NH_2 or OH group, or more likely the interaction of such a motion with the stretching of the external double bonds in the

(7) J. M. Broomhead, *Acta Cryst.*, **1**, 324 (1948); W. Cochran, *ibid.*, **4**, 81 (1951); J. M. Broomhead, *ibid.*, **4**, 92 (1951).

TABLE I

MOLECULAR DISTILLATION OF PURINE SERIES

Compound R_1	Compound R_2	Sublimation Temp., °C.	Compound R_1	Compound R_2	Sublimation Temp., °C.
H	H	140	NH_2	NH	150
$(C_2H_5)_2N$	H	133	SH	H	220
NH_2	CH_3	170	CH_3	OH	220
CH_3	NH_2	180	OH	CH_3	220
CH_3S	NH_2	160	SH	NH_2	230
NH_2	NH_2	170			

structures whose importance is attested by the X-ray studies.[7] Considering the limited number of purine derivatives available to those workers complete confirmation could hardly be expected.

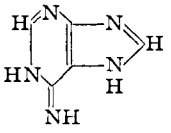
Group III (1000–1550 cm.$^{-1}$).—Although numerous strong bands occur in this region, they vary too widely upon substitution to permit definite conclusions. However, the appearance of intense absorption in the region of 1323 cm.$^{-1}$ coupled with the failure to find absorption in the region of 2500 cm.$^{-1}$ in the case of the sulfur-containing purines is indicative of a thione rather than a thiol structure.

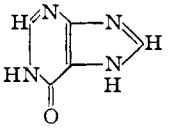
TABLE II

INFRARED ABSORPTION SPECTRA IN CM.$^{-1}$ OF PURINE SERIES

vw, very weak; w, weak; m, medium; s, strong; vs, very strong. 1, 2,N-diethylaminopurine; 2, 2,6-diaminopurine; 3, 2-aminopurine; 4, 6-amino-2-methylpurine; 5, 2-hydroxy-6-methylpurine; 6, 6-hydroxy-2-methylpurine; 7, 6-amino-2-methylmercaptopurine; 8, 2-thiopurine; 9, 6-amino-2-thiopurine.

1	2	3	4	5	6	7	8	9
3076 m	3434 m	3240 vs	3271 vs	3040 vs	3040 vs	3295 vs	2974 s	2987 vs
2953 s	3240 s	3110 vs	3120 vs	2922 vs	2885 vs	3146 vs	2905 s	
2822 m	3080 vs	2957 s	2763 s	2885 vs	2785 vs	2909 s	2822 s	
2792 m	2763 s	2881 s		2792 vs		2841 s		
2733 m		2703 vs				2763 s		
2564 m		2595 vs				2580 s		
		2534 vs						
1632 vs	1673 s	1645 vs	1671 vs	1649 vs	1693 vs	1681 vs	1649 vs	1679 vs
1568 vs	1661 s	1620 vs	1601 vs		1681 vs	1667 s	1591 vs	1595 vs
	1600 vw	1579 vs			1600 s			
1537 vs	1493 s	1516 vs	1535 m	1512 s	1535 m	1636 s	1497 s	1534 s
1532 vs	1450 s	1509 vs	1486 m	1476 s	1454 s	1605 vs	1430 s	1493 s
1493 m	1413 s	1493 vs	1432 s	1393 s	1429 s	1586 vs	1405 s	1415 s
1461 m	1408 s	1453 vs	1396 vs	1369 s	1378 s	1485 s	1323 vs	1367 m
1430 vs	1393 s	1429 vs	1374 m	1329 s	1363 s	1446 s	1295 s	1318 s
1367 vs	1359 s	1408 vs	1353 m	1291 s	1261 s	1435 s	1258 s	1237 s
1357 vs	1286 m	1395 vs	1331 s	1222 m	1212 m	1339 vs	1201 s	1179 s
1327 m	1234 m	1357 s	1266 s	1182 m	1178 m	1327 vs	1160 m	1123 s
1296 s	1163 w	1335 m	1234 m	1103 m	1141 m	1309 s	1118 vs	
1271 m	1147 w	1305 s	1160 m	1032 m	1020 w	1261 s	1016 m	
1239 s	1115 m	1280 vs	1113 m			1248 s		
1211 m	1096 m	1245 s	1052 w			1155 s		
1184 w		1204 s	1012 m			1124 m		
1165 m		1172 m				1074 m		
1130 w		1139 s				1025 m		
1088 m								
1037 m								
967 w	983 m	964 s	987 m	960 m	948 m	968 m	944 m	941 s
948 m	937 m	952 s	983 m	917 s	810 m	956 m	925 m	782 m
932 m	861 m	929 s	933 s	868 m	787 m	947 s	879 m	
880 m	846 s	871 m	848 w	827 s	666 m	935 s	794 s	
839 w	794 m	844 s	812 m	782 m		871 m	774 m	
799 m	781 m	797 s	795 m	673 m		850 s	730 m	
794 m	750 m	786 s				825 m		
785 m	711 m					788 s		
743 w						779 s		
						731 m		
						682 s		
						677 s		





Group IV (below 1000 cm.$^{-1}$).—Here again the spectra are relatively variable, but two rather similar regions of absorption seem to characterize the series. One is a band falling between 925 and 975 cm.$^{-1}$, first observed by Blout and Fields,[6] which is sometimes resolved into several components. The other is a doublet falling close to

800 cm.$^{-1}$ of which the higher frequency component is invariably the more intense. The absorptions at or near 1622 and 1571 cm.$^{-1}$ in purine accord to this interpretation are characteristic of the pyrimidine-like ring common to purine, pyrimidine, and quinazoline. In pyrimidine itself,[2] strong or very strong peaks are found at 1610 and 1569 cm.$^{-1}$; in quinazoline,[4] strong absorptions, reasonably stable against substitutions, are found at 1622 and 1566 cm.$^{-1}$. Bellamy[8] has criticized the assignment of the higher of these two frequencies as a characteristic C=C and/or C=N ring vibration on the substantial grounds that such a frequency was observed previously in pyrimidines which in many cases involved amino-substitution, an objection which does not apply here. We are, however, at a loss to explain the disappearance of this band in the work of Short and Thompson.[3]

Experimental

Preparation of Purines.—The mono- and disubstituted purines were prepared previously in this Laboratory.[9] The salts were converted to free bases for the purpose of this study. Purine was prepared by the procedure of Albert and Brown.[10] All samples were tested for homogeneity by paper chromatography according to the procedure of Vischer and Chargaff.[11]

Preparation of Samples.—The free bases of all compounds were examined as solids sublimed on rock salt crystals at 10^{-5} mm. pressure in a manner similar to that of Blout and Fields.[6] Sublimation data are included in Table I.

Instrumentation and Measurement.—The instrument used was a Perkin–Elmer model 12C spectrophotometer modified as described by Culbertson, *et al.*[5] The spectra were obtained by single beam operation of a NaCl or LiF prism followed by a point by point comparison of the spectrum of the sample with that of a blank. The single beam method was preferable to the double beam because of the higher resolution obtainable. Such resolution was desirable since several of the films, notably that of purine itself (see Fig. 1) yielded numerous very sharp absorption peaks with a width of the order of 10 cm.$^{-1}$.

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Conjugate Addition Reactions of Azoles. II. 1,2,4-Triazole, Tetrazole, Nitropyrazoles and Benzotriazole

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In a previous paper[1] we reported our observations on the conjugate addition of 1,2,3-triazole and benzotriazole to a variety of α,β-unsaturated carbonyl compounds. We have completed additional studies of this reaction in which 1,2,4-triazole, tetrazole, 4-nitropyrazole and 3,5-dimethyl-4-nitropyrazole have been added to acrylic acid, benzalacetophenone, benzalacetone, *p*-methoxybenzalacetophenone and dibenzalacetone, and in which benzotriazole has been added to *m*- and *p*-nitrobenzaldehyde. The addition reaction is carried out using an alkaline catalyst—either pyridine or Triton B—and the product is isolated from the reaction mixture in various ways dependent on the chemical properties and solubilities of the products. Some of the products are insoluble in both ether and water and can be separated from the reactants by washing with water to remove the azole and with ether to remove the unsaturated carbonyl compound. The unusual combination of water and carbon tetrachloride solubility of 1-phenyl-1-(1′-tetrazolyl)-butanone-3 is noteworthy.

The structures of the adducts obtained from the pyrazoles, from tetrazole and from 1,2,4-triazole can be assigned with reasonable certainty. Two principal problems are encountered. These involve the alternative structures which may result from 1,2- as opposed to 1,4-addition and the isomeric structures which result from reactions of the tetrazole and the triazole in tautomeric forms to give products substituted on one or the other of two nitrogen positions. Although 1,2-addition of azoles is entirely feasible, as is shown by the data recorded herewith on the 1,2-addition of benzotriazole to *m*- and *p*-nitrobenzaldehydes and as previously reported to cinnamaldehyde, the products obtained in these studies usually appear as 1,4-adducts whenever 1,4-addition is possible. The presence of the carboxylic acid group in the acrylic acid adducts from the pyrazoles, tetrazole and 1,2,4-triazole establish these as 1,4-adducts. The ultraviolet absorption data for products having a phenyl ketone structure show the customary carbonyl absorption again establishing 1,4-addition. For example, acetophenone has an absorption maximum at 245 mμ (log ϵ 4.0) and β-phenyl-β-(1′-tetrazolyl)-propiophenone has a maximum at 243 mμ (log ϵ 4.12).

There is a unique feature of structural significance in the ultraviolet absorption of the tetrazole adducts. A broad, intense absorption band in the 275–315 mμ range is shown by β-phenyl-β-(1′-tetrazolyl)-propiophenone (log ϵ 3.55 at 295–315 mμ); by 1-phenyl-1-(1′-tetrazolyl)-butanone-3 (log ϵ 3.60 at 275–295 mμ); and by 1,5-diphenyl-5-(1′-tetrazolyl)-1-pentenone-3 (log ϵ 4.4 at 285–305 mμ). Simple carbonyl compounds do not absorb in this region and even when conjugated with an aromatic ring as in acetophenone the absorption band in this range is much weaker (log ϵ 3.1 at 286 mμ) and is more narrow. It is possible that the carbonyl absorption in the two of these compounds in which the carbonyl group is thus conjugated may contribute to the absorption in this range—but the contribution cannot be very significant since the intensity of the absorption for the phenyl ketone is nearly the same as that of the methyl ketone. Furthermore, absorption in this range is strikingly absent from the spectra of the closely related 1-phenyl-1-[1′-(1,2,3-triazolyl)]-butanone-3. This absorption also may result from the phenyltetrazolylmethane structure. That such structural types might absorb in this region is suggested by the data for diphenylmethane[2] (log ϵ 2.7 at 262 mμ, with

(1) R. H. Wiley, N. R. Smith, D. M. Johnson and J. Moffat, THIS JOURNAL, **76**, 4933 (1954).

(2) W. R. Orndorff, R. C. Gibbs, S. A. McNulty and C. B. Shapiro, *ibid.*, **49**, 151 (1927).