

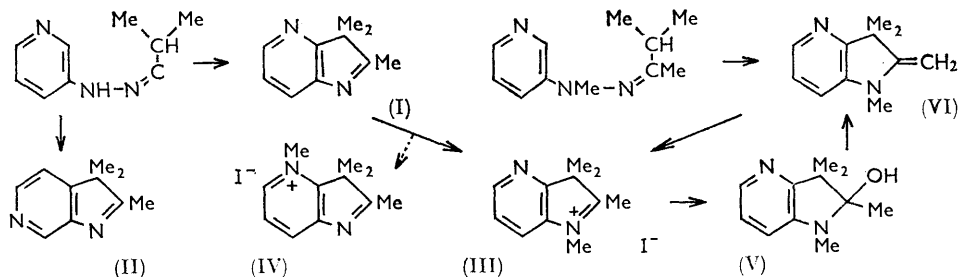
117. Diazaindenes and Their Quaternary Salts. Part II.¹ The Cyclisation of Isopropyl Methyl Ketone 3-Pyridylhydrazone.

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Isopropyl methyl ketone 3-pyridylhydrazone undergoes the Fischer indole synthesis to give a base to which the 1,4-diazaindene structure (I) is assigned. With methyl iodide it gives the 1-methiodide, which has also been synthesised by way of 1,3,3-trimethyl-2-methylene-1,4-diazaindene (VI). The methiodide yields cyanine dyes, the light absorption of which is discussed.

PART I of this series¹ described the preparation of a diazaindene by cyclisation of isopropyl methyl ketone 2-pyridylhydrazone catalysed by zinc chloride. We have now found that the isomeric 3-pyridylhydrazone also undergoes the Fischer indole synthesis to give another diazaindene. This was obtained as a hygroscopic liquid which has been characterised as its picrate and methiodide.

This base might be the 1,4- (I) or the 1,6-diazaindene (II). Evidence that it is the former is, however, provided by the infrared spectrum.



It is probably the CH out-of-plane deformation vibrations in pyridines that causes strong absorption in the 900—700 cm^{-1} region, the position of the bands depending largely on the number of adjacent hydrogen atoms in the ring, as with benzene derivatives.²



Thus, a diazaindene (I) would be expected to resemble, not only the 1,7-diazaindene (VII) and 2,3-disubstituted pyridines, but also *vic*-trisubstituted benzenes. On the other hand, a diazaindene (II) should be comparable with the 1,5-diazaindene (VIII), 3,4-disubstituted

¹ Part I, Ficken and Kendall, *J.*, 1959, 3202.

² Bellamy, "The Infra-Red Spectra of Complex Molecules," Methuen and Co. Ltd., London, 2nd edn., 1958, p. 280.

pyridines, and *as*-trisubstituted benzenes. Some relevant data are given in Table 1, including the two compounds (V) and (VI), the preparation of which is discussed below. These, and the diazaindene to which they are related, show two strong bands in the infrared region under discussion. Although it is not possible to say which of the two is the result of a CH out-of-plane vibration, both bands are in each case consistent with a 2,3-disubstituted pyridine structure; 3,4-disubstitution would appear to be excluded. The base is therefore on this evidence assigned the 1,4-diazaindene structure (I).

This conclusion is in agreement with the rather limited evidence that electrophilic attack on a pyridine possessing an *ortho,para*-directing 3-substituent leads to substitution in the 2- in preference to the 4-position.³ It is of interest that a Skraup reaction on 3-aminopyridine apparently gives only 1,5-naphthyridine (*i.e.*, 2-substitution).⁴ As regards Fischer syntheses on 3-hydrazinopyridines, Clemo and Holt⁵ have prepared a tetrahydro-carboline by this method, but here cyclisation on to C₍₄₎ was forced by the presence of a 2-methyl group. The only other reported examples involved 2-chloro-5-hydrazinopyridine, where Fischer syntheses were assumed to lead to 1,4-diazaindenes.⁶

We have shown¹ that both of the methiodides of 2,3,3-trimethyl-3*H*-1,7-diazaindene (VII) have a reactive 2-methyl group. In the present case, however, only the 1-methiodide (III) could, the reactive species being the methylene base (VI) (*cf.* Mills and Raper⁷). The 4-methiodide (IV) would not activate the 2-methyl group, owing to the impossibility of forming a methylene base possessing a *meta*-quinonoid pyridine ring. In fact the methiodide obtained by quaternisation of the base (I) possessed a very reactive methyl

TABLE 1. *Strong absorption bands in the CH deformation region (cm.⁻¹).*

<i>Benzenes</i> ^a			
1,2,3-Trisubst.	780—760	1,2,4-Trisubst.	825—805
<i>Pyridines</i>			
2,3-Dimethyl ^b	787	3,4-Dimethyl ^b	839, 821
2-Acetamido-3-methyl	803		
<i>2,3,3-Trimethyl-3H-diazaindenes</i>			
1,7-Diaza (VII)	807	1,5-Diaza ^c (VIII)	842
Diazaindene (I) 813, 786. Compound (V) 802, 783. Compound (VI) 794, 776.			

^a West, "Chemical Applications of Spectroscopy," Interscience Publ. Inc., New York, 1956, p. 391. ^b Coulson, Cox, Herington, and Martin, *J.*, 1959, 1934. ^c Unpublished work.

TABLE 2. *Light absorption of dyes [λ_{\max} (Å); and log ϵ in parentheses].*

Dye (IX).....	Obs.	Calc.	Deviation	Deviation of 1,7-diazaindene dye
Nucleus (A) in (X)	5580 (4.49)	5770	190	140
(1) 1,3,3-Trimethyl-3 <i>H</i> -indole-2 ...	5440 (5.05)	5455	15	15
(2) 3-Methyl-2-benzoxazole	5030 (4.74)	5140	110	120
(3) 3-Methyl-2-benzothiazole	5350 (4.99)	5510	160	155
(4) 1-Methyl-2-quinoline	5475 (5.00)	5745	270	305
(5) 1-Methyl-4-quinoline	5775 (4.91)	6255	480	515

group, and cyanines were readily obtained in good yield by using the usual reagents. The resulting structure (III) was proved by synthesis of the identical methiodide by addition of hydrogen iodide to the methylene base (VI), obtained by cyclisation of isopropyl methyl ketone *N*-methyl-*N*-3-pyridylhydrazone by zinc chloride.

In attempts to reconvert the methiodide (III) into the methylene base (VI) by aqueous

³ (a) Albert, "Heterocyclic Chemistry," University of London Athlone Press, 1959, p. 64; (b) Schofield, *Quart. Rev.*, 1950, **4**, 382.

⁴ Bobranski and Sucharda, *Ber.*, 1927, **60**, 1081.

⁵ Clemo and Holt, *J.*, 1953, 1313.

⁶ Deutsche Gold und Silberscheideanstalt, B.P. 259,982/1925; *cf.* Takahashi, Saikachi, Goto, and Shimamura, *J. Pharm. Soc. Japan*, 1944, **64**, No. 8A, 7; *Chem. Abs.*, 1951, **45**, 8529.

⁷ Mills and Raper, *J.*, 1925, **127**, 2466.

was refractionated, to give material, b. p. 103—107°/16 mm. (14.4 g.), from which 2,3,3-trimethyl-3H-1,4-diazaindene was obtained as a colourless hygroscopic liquid, b. p. 112°/19 mm., n_D^{15} 1.5432 (Found: N, 17.6, 17.8. $C_{10}H_{12}N_2$ requires N, 17.5%). The picrate, yellow plates from ethanol, had m. p. 160° (Found: C, 49.4; H, 4.1. $C_{16}H_{15}N_5O_7$ requires C, 49.4; H, 3.9%).

The diazaindene (2.45 g.) was refluxed in ethanol (10 ml.) with methyl iodide (2.0 ml.) for 40 min., by which time crystals had separated. These were filtered off after refrigeration and washed successively with a little ice-cold ethanol and acetone. The 1-methiodide (III) (2.59 g.) formed colourless needles, m. p. 252—253° (decomp.), from ethanol (Found: C, 44.2; H, 5.2; I, 41.95; N, 9.0. $C_{11}H_{15}IN_2$ requires C, 43.7; H, 5.0; I, 42.0; N, 9.3%).

N-Methyl-*N*-3-pyridylhydrazine.—3-(Methylnitrosoamino)pyridine¹⁰ was reduced in 85% yield with lithium aluminium hydride, as described in Part I; the b. p. was 112°/1.2 mm. to 118°/1.0 mm. Plazek *et al.*¹⁰ give b. p. 191°/11 mm.

1,3,3-Trimethyl-2-methylene-1,4-diazaindene.—*N*-Methyl-*N*-3-pyridylhydrazine (18.6 g.) and isopropyl methyl ketone (20 ml.) were warmed for 2½ hr. on the steam-bath with acetic acid (0.5 ml.). Volatile material was removed at 100°/16 mm., and the residual yellow-brown oil was heated with anhydrous zinc chloride (0.5 g.), a vigorous reaction occurring at 190°. Heating was continued for 20 min., during which the temperature was raised to 210°, and the thick brown residue was distilled. No sharp boiling fraction could be obtained, but the material (11.4 g.) boiling between 106° and 130°/19 mm. was collected and treated in propan-2-ol (110 ml.) with freshly distilled hydriodic acid (*d* 1.70; 9.6 ml.). The crystals which separated slowly were collected and washed successively with a little cold propan-2-ol and ether to give the 1-methiodide (III) (5.33 g.), m. p. 252—253° (decomp.), undepressed by the product of quaternisation of the diazaindene (I). The infrared spectra of the two samples were identical, and they yielded styryl dyes (see below) which were identical in m. p. and mixed m. p. and in their light absorption (visible and infrared). A fraction (5.2 g.), b. p. 132—160°/18 mm., from the distillation, when similarly treated with hydriodic acid, gave a further quantity (0.65 g.) of the methiodide (combined yield based on the pyridylhydrazine, 13%).

The methiodide (6.02 g.) was warmed to about 40° with *N*-sodium hydroxide (50 ml.) for a few minutes. After cooling in ice, the solid was collected, washed with a little cold water, and crystallised from ethyl acetate. 2-Hydroxy-1,2,3,3-tetramethyl-1,4-diazaindene (V) (1.97 g.) was obtained as colourless crystals, m. p. 91°, which fairly rapidly became pink and liquefied when exposed to the air (Found: N, 14.8. $C_{11}H_{16}N_2O$ requires N, 14.9%). Evaporation of an ethyl acetate solution of this compound to dryness on the steam-bath gave an oil which did not solidify when strongly cooled. An ethereal solution of this oil was dried (K_2CO_3) and distilled, 1,3,3-trimethyl-2-methylene-1,4-diazaindene (VI) being obtained as a pale yellow liquid, b. p. 125°/18 mm., n_D^{20} 1.5800, which very rapidly became red in the air (Found: C, 75.4; H, 8.0. $C_{11}H_{14}N_2$ requires C, 75.8; H, 8.1%).

Preparation of Dyes from the Methiodide (III).—(a) *Trimethincyanines.* These dyes were prepared by reaction of the quaternary salt (III) with an ω -ethylthiovinyl or ω -acetanilidovinyl heterocyclic methiodide in pyridine. The symmetrical dye (XI) was obtained by reaction of the methiodide (III) with ethyl orthoformate in pyridine. The results are summarised in Table 3, yields referring respectively to the crude and once recrystallised dyes.

TABLE 3. (A) (1,3,3-Trimethyl-3H-1,4-diazaindene-2)-trimethincyanine iodides (X).

Dye	M. p.	Yield (%) [*]	Solvent [*] (ml./g.)	Appearance	Formula	Found (%)	Reqd. (%)
(XI)	326 ^d	56; 24	E(35)	Hexagonal golden plates	$C_{23}H_{27}IN_4$	I, 26.15	26.1
1 ^b	296 ^d	78; 49	M(65)	Red plates, blue reflex	$C_{24}H_{25}ClN_3O_4$ ^c	N, 9.0	9.2
2	238	53; 36	EW	Red needles	$C_{21}H_{22}IN_3O$	I, 27.5	27.6
3	260 ^d	59; 40	M(30)	Green prisms	$C_{21}H_{22}IN_3S$	I, 26.85	26.7
4	286—287 ^d	70; 42	M(55)	Green prisms	$C_{23}H_{24}IN_3$	I, 26.8	27.0
5	299	28; 25	M(75)	Green needles	$C_{23}H_{24}IN_3 \cdot H_2O$	I, 26.1	26.0

^a E = Ethanol, M = Methanol, W = Water. ^b These numbers refer to Table 2. ^c Perchlorate. ^d With decomp. ^{*} See text.

(b) *Dimethinmerocyanines and styryl dye.* The methiodide (III) (0.71 g.) and 5-ethoxy-methylene-3-ethyl-2-thiothiazolid-4-one (0.51 g.) were refluxed together in ethanol (5.0 ml.) containing triethylamine (0.4 ml.) for 1 hr. The solid (0.42 g.) which separated on cooling

¹⁰ Plazek, Marcinikow, and Stammer, *Roczniki Chem.*, 1935, **15**, 365; *Chem. Abs.*, 1936, **30**, 1377.

crystallised from methanol (70 ml.), to give 5-(1,2-dihydro-1,3,3-trimethyl-3H-1,4-diazainden-2-ylidene)ethylidene-3-ethyl-2-thiothiazolid-4-one (0.33 g.), red prisms, m. p. 228° (Found: S, 18.3. C₁₇H₁₉N₃OS₂ requires S, 18.6%), λ_{max} . 4850 Å (log ϵ 4.86). The methiodide (III) (0.75 g.), 3-methyl-1-phenylpyrazol-5-one (0.45 g.), pyridine (5.0 ml.), and ethyl orthoformate (0.8 ml.) were refluxed together for 45 min. The solid (0.70 g.) which separated when the solution was cooled and diluted with ethanol crystallised from methanol (80 ml.), to give 4-(1,2-dihydro-1,3,3-trimethyl-3H-1,4-diazainden-2-ylidene)ethylidene-3-methyl-1-phenylpyrazol-5-one (0.60 g.), red plates with a silver reflex, m. p. 220—221° (Found: C, 71.4; H, 6.2; N, 14.7. 2C₂₂H₂₂N₄O, H₂O requires C, 71.9; H, 6.3; N, 15.2%), λ_{max} . 4630 Å (log ϵ 4.70).

The methiodide (III) (0.30 g.) and *p*-dimethylaminobenzaldehyde (0.20 g.) were refluxed for 1 hr. in ethanol (5.0 ml.) containing 1 drop of piperidine. The resulting solution was cooled and treated with a concentrated aqueous solution of potassium iodide to precipitate 3,3-dimethyl-2-*p*-dimethylaminostyryl-3H-1,4-diazaindene 1-methiodide (IX) (0.29 g.), green plates, m. p. 268°, from water (Found: C, 55.1; H, 5.6; I, 28.7. C₂₀H₂₄IN₃ requires C, 55.4; H, 5.6; I, 29.3%).

Infrared Spectra.—These were measured on an Infracord spectrophotometer, model 137, compounds (I) and (VI) as liquids, the others as Nujol mulls.

2,3,3-Trimethyl-3H-1,4-diazaindene (I): 2950m, 1605m, 1580w, 1560m, 1458m, 1428w, 1412s, 1380w, 1360w, 1292m, 1272w, 1246m, 1180s, 1152w, 1110m, 1100m, 1036w, 995w, 939w, 870w, 813s, 786s cm⁻¹.

2,3,3-Trimethyl-3H-1,5-diazaindene (VIII): 3400w, 1880w, 1635w, 1600m, 1560s, 1500w, 1410m, 1326w, 1252m, 1214m, 1160m, 1094m, 1024m, 990m, 967w, 942m, 934m, 877s, 842s, 823w, 799w, 784w.

2,3,3-Trimethyl-3H-1,7-diazaindene (VII): 1560s, 1400s, 1296w, 1266m, 1210m, 1144w, 1120w, 1082w, 1035w, 992w, 952w, 934w, 875m, 807s, 722m, 695m.

2-Hydroxy-1,2,3,3-tetramethyl-1,4-diazaindene (V): 3200s, 2640w, 2530w, 1950w, 1870w, 1780w, 1730m, 1670m, 1610s, 1595s, 1450s, 1320s, 1288m, 1244m, 1222m, 1192s, 1162m, 1124s, 1102s, 1048m, 1020w, 954w, 930s, 901m, 802s, 783s, 682m.

1,3,3-Trimethyl-2-methylene-1,4-diazaindene (VI): 3120w, 3030m, 1730m, 1670s, 1610s, 1595w, 1488m, 1462s, 1436w, 1388m, 1368w, 1336s, 1316s, 1266m, 1208w, 1196m, 1156s, 1130m, 1084w, 1044m, 952w, 940m, 892w, 794s, 776s, 689w.

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