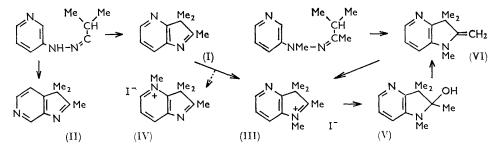
117. Diazaindenes and Their Quaternary Salts. Part II.¹ The Cyclisation of Isopropyl Methyl Ketone 3-Pyridylhydrazone.

By G. E. FICKEN and J. D. KENDALL.

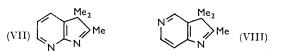
Isopropyl methyl ketone 3-pyridylhydrazone undergoes the Fischer indole synthesis to give a base to which the 1,4-diazaindene structure (I) is assigned. With methyl iodide it gives the 1-methiodide, which has also been synthesised by way of 1,3,3-trimethyl-2-methylene-1,4-diazaindane (VI). The methiodide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

PART I of this series ¹ 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 Holt ⁵ have prepared a tetrahydrocarboline 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 shown ¹ that both of the methiodides of 2,3,3-trimethyl-3H-1,7-diazaindenc (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 Raper ⁷). 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 th	e CH	deformation	region	(cm. ~1).
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	Benz	ienes ^a						
1,2,3-Trisubst.	780—760	1,2,4-Trisubst 825-805						
Pyridines								
2,3-Dimethyl ^b 2-Acetamido-3-methyl	787 80 3	3,4-Dimethyl ^b 839, 821						
2,3,3-Trimethyl-3H-diazaindenes								
1,7-Diaza (VII)	807	1,5-Diaza ^e (VIII) 842						
Diazaindene (I) 813, 786.	Compound	(V) 802, 783. Compound (VI) 794, 776.						
^a West, "Chemical Application	s of Spectro	scopy." Interscience Publ. Inc., New York, 1956.						

rk, 1956, p. 391. ^b Coulson, Cox, Herington, and Martin, J., 1959, 1934. ^c Unpublished work.

TABLE 2. Light absorption of dyes $[\lambda_{\max}]$ (A); and $\log \varepsilon$ in particular terms of the second	parentneses].	
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	Obs.	Calc.	Deviation	Deviation of 1,7-diazaindene dye
Dye (IX)	5580 (4·49)	5770	190	140
Nucleus (A) in (X)				
(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) Schofeld, Quart. Rev., 1950, **4**, 382. ⁴ Bobranski and Sucharda, Ber., 1927, **60**, 1081.

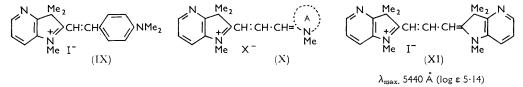
⁵ Clemo and Holt, J., 1953, 1313.
⁶ Deutsche Gold und Silberscheideanstalt, B.P. 259,982/1925; cf. Takahashi, Saikachi, Goto, and Shimamura, J. Pharm. Soc. Japan, 1944, 64, No. 8A, 7; Chem. Abs., 1951, 45, 8529.
 ⁷ Mills and Raper, J., 1925, 127, 2466.

x

alkali, the product obtained initially was the pseudobase (V), which however readily lost water on gentle heating to give the methylene base.

Although the 4-methiodide (IV) could not be isolated, some was probably formed during the quaternisation of base (I), as the yield of the 1-methiodide was at best a little over 50%. This is in sharp contrast, however, to the behaviour of the isomeric 1,7- and 1,5-diazaindene. The former has been estimated to give <10% of 1-methiodide on quaternisation,¹ and the latter also quaternises almost exclusively on the pyridine nitrogen atom. The predominant quaternisation of the 1,7-diazaindene on N₍₇₎ was ascribed to the considerably greater basicity of the pyridine than of the pyrrolenine nitrogen atom. Since a similar disparity would be expected in any diazaindene containing one nitrogen in each ring, some other factor must be at work in the case of (I). The most obvious explanation appears to be that only in (I) would there be any steric hindrance to quaternisation on the pyridine nitrogen, owing to the gem-dimethyl group at position 3. This appears to provide additional evidence for formulation of the base as a 1,4- rather than a 1,6-diazaindene.

Light Absorption of the Dyes.—The cyanines and merocyanines prepared from the methiodide (III) proved, as expected, very similar in their light absorption to the isomers obtained from the 1,7-diazaindene 1-methiodide.¹ Table 2 gives the absorption data for the styryl dye (IX) and for a series of trimethincyanines (X), arranged in order of increasing basicity of (A). The Brooker "deviations" are derived as described in Part I,¹ the requisite symmetrical dye being (XI). Some figures pertaining to the corresponding



1,7-diazaindene dyes, taken from Part I,¹ are included for comparison. For the more strongly basic nuclei (A), *viz.*, dyes (4) and (5), the deviations for dyes (X) are somewhat less than for the related 1,7-diazaindene dyes, whilst the reverse is true for dye (IX). These facts indicate that, following Brooker and Sprague's arguments,⁸ $N_{(1)}$ is slightly more basic in (I) than in the 1,7-diazaindene (VII).

EXPERIMENTAL

Isopropyl Methyl Ketone 3-Pyridylhydrazone.—3-Aminopyridine (91 g.) was diazotised and reduced with stannous chloride by Räth's method.⁹ The resulting stannichloride was stirred with isopropyl methyl ketone (200 ml.) and excess of aqueous sodium hydroxide, and the solution was continuously extracted with ether. Removal of the solvent and excess of ketone from the dried (K_2CO_3) extract left a thick brown oil (87 g.) which was used immediately for the preparation of the diazaindene. Distillation of this oil at 180—200°/20 mm. gave isopropyl methyl ketone 3-pyridylhydrazone, which formed colourless plates, m. p. 89—90° from cyclohexane (Found: C, 67.5; H, 8.2. $C_{10}H_{15}N_3$ requires C, 67.8; H, 8.5%). The crystals rapidly became brown in the air.

2,3,3-Trimethyl-3H-1,4-diazaindene (I).—The crude hydrazone (68 g.) was heated with anhydrous zinc chloride (1.0 g.), the temperature (external) being raised during $1\frac{1}{2}$ hr. from 195° to 220°. Fractionation of the thick brown residue gave a first fraction (20.3 g.), b. p. 62°/0.8 mm. to 86°/1.0 mm., followed by a fraction (7.5 g.) of b. p. 89—92°/0.8 mm. The latter solidified on cooling and consisted largely of 3-aminopyridine; the picrate, yellow needles from 2-methoxyethanol, had m. p. and mixed m. p. with 3-aminopyridine picrate 200—201° (Found: N, 21.9. Calc. for C₁₁H₉N₅O₇: N, 21.7%). The first fraction from the distillation

⁸ Brooker and Sprague, J. Amer. Chem. Soc., 1945, 67, 1869.

⁹ Räth, Annalen, 1931, **486**, 103.

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., $n_{\rm D}^{15}$ 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)pyridine ¹⁰ was reduced in 85% yield with lithium aluminium hydride, as described in Part I; the b. p. was $112^{\circ}/1.2$ mm. to $118^{\circ}/1.0$ mm. Plazek *et al.*¹⁰ give b. p. $191^{\circ}/11$ mm.

1,3,3-Trimethyl-2-methylene-1,4-diazaindane.—N-Methyl-N-3-pyridylhydrazine (18.6 g.) and isopropyl methyl ketone (20 ml.) were warmed for $2\frac{1}{2}$ 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 1methiodide (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-diazaindane (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 (K₂CO₃) and distilled, 1,3,3-trimethyl-2-methylene-1,4-diazaindane (VI) being obtained as a pale yellow liquid, b. p. 125°/18 mm., n_p^{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-Trimeth	l-3H-1,4-diazaindene-2)-trimethincyanine	iodides (X).
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Due	M n	Yield	Solvent ^a		Economicale	Found	Reqd.
Dye	М. р.	(%) *	(ml./g.)	Appearance	Formula	(%)	(%)
(XI)	326 d	56; 24	E(35)	Hexagonal golden plates	$C_{23}H_{27}IN_4$	I, 26·15	$26 \cdot 1$
1 b	296 d	78; 49	M(65)	Red plates, blue reflex	C24H28CIN3O4 C	N, 9·0	$9 \cdot 2$
2	238	53; 36	EW	Red needles	C ₂₁ H ₂₂ IN ₃ O	I, 27·5	27.6
3	260 d	59; 40	M(30)	Green prisms	C ₂₁ H ₂₂ IN ₃ S	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
$\overline{5}$	299	28; 25	M(75)	Green needles	$C_{23}H_{24}IN_3$, H_2O	I, 26·1	26.0
a	F - Ethand	M = N	Nethanol 1	W - Water & These numb	ers refer to Table	9 C Dore	hlorato

^{*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-ethoxymethylene-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, Rocznicki 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-2ylidene)ethylidene-3-ethyl-2-thiothiazolid-4-one (0·33 g.), red prisms, m. p. 228° (Found: S, 18·3. $C_{17}H_{19}N_3OS_2$ 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. $2C_{22}H_{22}N_4O,H_2O$ 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. $C_{20}H_{24}IN_3$ 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-diazaindane (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-diazaindane (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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