Table II

Preparation of Compounds **1**, **2**, **4**, and **5**

Compd	Hydrazine–Ketone	Solvent		Time, hr	Yield, %
		Reaction	Recrystn		
1	8–1	EtOH	PhH	16	. . .
2	4–1	EtOH	C_5H_5N, $CHCl_3$–ligroin, $PhCH_3$	16	95 crude
4	10–1	n-PrOH–$PhCH_3$	PhH–ligroin	16	59 crude
5	10–1	n-PrOH–$PhCH_3$	Xylene	16	72 crude
					12 pure
				144	28 pure

Table III

2,3-Diazanaphthalenes and 2,3-Diazaanthracenes

Compd	Mp, °C	Calcd, %			Found, %		
		C	H	N	C	H	N
1	197.5–199.5 (lit.[a] 192)	85.1	5.0	9.9	85.4	5.2	9.8
2	338–341[b]	88.5	5.1	6.5	87.7	5.0	6.4
3	283 dec	86.7	5.6	7.8	86.8	5.4	7.8
4	277–279	89.3	5.0	5.8	88.9	4.9	5.7
5	384–386	90.6	5.0	4.4	90.6	5.1	4.2

[a] A. Guyot and J. Catel, *Compt. Rend.*, **140,** 1348 (1905). [b] A satisfactory analysis could not be obtained; characterized as a quaternary salt in the Experimental Section.

and at 1.45 and 1.30 ppm (C–Me). Integration indicated a 38/62 ratio of isomers.

Anal. Calcd for $C_{28}H_{26}O_3$: C, 82.0; H, 6.3. Found: C, 81.9; H, 6.3.

1,4-Dimethyl-9,10-diphenyl-2,3-diazaanthracene (3).—To a solution of 2.67 g of 1,3-dimethoxy-1,3-dimethyl-4,9-diphenyl-1,3-dihydronaphtho[2,3-*c*]furan in 20 ml of dioxane was added 5 ml of 5% hydrochloric acid. After 30 min, hydrazine was added to the solution until it was basic to litmus. Sufficient ethanol was added to homogenize the mixture which was then refluxed overnight. Stripping gave a yellow solid which, when recrystallized from ethanol, yielded 0.96 g (41%) of bright yellow crystals, mp 265° dec. A second recrystallization from ethanol provided an analytical sample, mp 283° dec.

Anal. Calcd for $C_{26}H_{20}N_2$: C, 86.7; H, 5.6; N, 7.8. Found: C, 86.8; H, 5.4; N, 7.8.

2-Methyl-1,4,5,8-tetraphenyl-3-aza-2-azonianaphthalene Iodide.—To a solution of 2 g of **2** in 50 ml of chloroform was added 10 ml of methyl iodide. After the solution had stood overnight, it was diluted with ether to give an orange solid. Recrystallization from ethanol and then methanol gave an orange solid which was solvated even after drying at 180°, mp 309–314° dec.

Anal. Calcd for $C_{33}H_{25}IN_2 \cdot CH_3OH$: C, 67.1; H, 4.8; I, 20.9. Found: C, 67.0; H, 4.6; I, 21.3.

Acknowledgment.—We thank Mr. R. L. Young for assistance in determining the nmr spectra.

Ten π-Electron Nitrogen Heterocyclic Compounds. IX. The Syntheses and Nuclear Magnetic Resonance Spectra of Some Methylnaphthyridines

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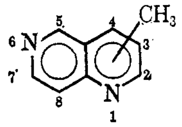
Received April 8, 1966

As part of a study of the chemistry of bicyclic heteroaromatic compounds[1] we have been interested in the chemistry of the various naphthyridines.[2] Before a systematic study of these compounds could be undertaken, it became necessary to develop reasonable synthetic methods for the preparation of some of these substances.

The syntheses of the various parent and methyl-substituted naphthyridines generally involve multistep sequences, often affording the desired compounds only in low yields.[3] These tedious methods have considerably limited the study of naphthyridines. Our recent interest in 1,6-naphthyridines prompted us to study the applicability of the Skraup reaction to 4-aminopyridine. This was done despite the numerous comments in the literature[3] that this reaction does not occur with 4-aminopyridine. Since the over-all yields leading to the parent or methyl-1,6-naphthyridines (**1**) by the conventional procedures rarely exceed 4%, even a potentially low-yield, one-step Skraup synthesis would be a considerable synthetic improvement.



1.

Methyl-1,6-naphthyridines.—Rapaport and Batcho[4] have recently reported the preparation of 2-methyl- and of 4-methyl-1,5-naphthyridine by a modified Skraup reaction on 3-aminopyridine. We decided to apply this reaction to 4-aminopyridine in the hope of obtaining the 2-methyl- and the 4-methyl-1,6-naphthyridines. Neither one of these compounds had been prepared since they are not readily available by any of the known syntheses of 1,6-naphthyridines.

Two recent papers[5] describe the Skraup synthesis as applied to 4-aminopyridine N-oxide, a reaction which affords the corresponding 1,6-naphthyridine 6-oxide. No compounds substituted in the 2, 3, or 4 position were obtained. The use of the N-oxide starting material was predicated upon the assumption that the free amines would not undergo the cyclization reaction. Where the yields are reported for the Skraup reaction on the N-oxides, they are 5% or less.

The condensation of 4-aminopyridine with methyl vinyl ketone in the presence of Sulfo-mix afforded a low-melting solid $C_9H_8N_2$. The nmr spectrum of this material is reported in Table I and is clearly in agreement with the assigned structure of this compound, 4-methyl-1,6-naphthyridine (**2**). Similarly, the condensation of

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(1) W. W. Paudler and H. L. Blewitt, *J. Org. Chem.*, **31**, 1295 (1966).

(2) W. W. Paudler and T. J. Kress, *J. Heterocyclic Chem.*, **2**, 393 (1965).

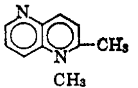
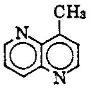
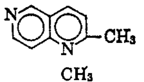
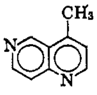
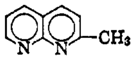
(3) R. C. Elderfield, "Heterocyclic Compounds," Vol. 7, John Wiley and Sons, Inc., New York, N. Y., 1961, pp 198–236.

(4) H. Rapaport and A. Batcho, *J. Org. Chem.*, **28**, 1753 (1963).

(5) T. Kato, F. Hamaguchi, and T. Oiwa, *Pharm. Bull.* (Tokyo), **4**, 178 (1956). S. Tamura, T. Kudo, and Y. Yanagishara, *Yakugaku Zasshi*, **80**, 562 (1960).

TABLE I

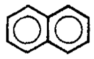
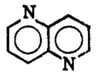
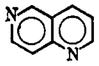
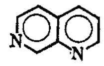
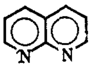
NMR SPECTRAL DATA OF VARIOUS METHYLNAPHTHYRIDINES

Compd	Chemical shift (τ)								Coupling constants (cps)									
	CH_3	H-2	H-3	H-4	H-5	H-6	H-7	H-8	$J_{H\text{-}3,\,CH_3}$	J_{23}	J_{34}	J_{48}	J_{56}	J_{57}	J_{58}	J_{67}	J_{68}	J_{78}
	7.30	...	2.52	1.77	...	1.17	2.63	1.80	...	...	8.8	0.8	...	...	...	4.2	1.6	8.4
	7.14	1.03	2.44	...	...	0.88	2.28	1.47	0.9	4.4	...	...	...	...	...	4.1	1.8	8.7
	7.24	...	2.63	1.86	0.81	...	1.26	2.17	...	...	8.2	0.9	...	...	0.9	...	...	6.0
	7.24	1.03	2.68	...	0.47	...	1.20	2.06	0.9	4.5	...	...	...	...	0.8	...	...	6.0
	7.24	...	2.69	1.99	2.65	0.97	...	...	...	...	8.4	...	8.4	2.0	...	4.4	...	...[a]

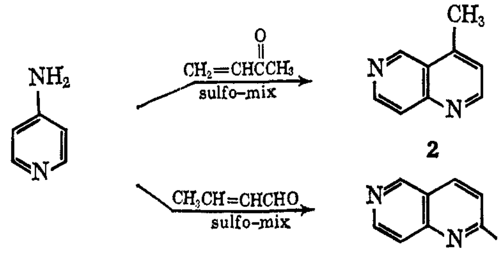
[a] Prepared by the method described by E. V. Brown, *J. Org. Chem.*, **30**, 1607 (1965).

TABLE II

TOTAL π ENERGIES AND DELOCALIZATION ENERGIES (DE) OF SOME NAPHTHYRIDINES

					
Total π energy	$10\alpha + 13.68\beta$	$10\alpha + 13.99\beta$	$10\alpha + 13.96\beta$	$10\alpha + 13.96\beta$	$10\alpha + 13.99\beta$
DE (units of β)	3.68	3.63	3.60	3.60	3.63

4-aminopyridine with crotonaldehyde afforded a solid $C_9H_8N_2$, whose nmr spectrum (Table I) is in agreement with the assigned structure, 2-methyl-1,6-naphthyridine (2).



2

3

HMO Calculations of the Naphthyridines.—It became of interest to calculate the total π energies and the delocalization energies of the various naphthyridines and to compare these data with the corresponding energies of naphthalene. Simple HMO calculations[6] employing $\alpha_0 + 0.5\beta_0$ for the coulomb integral of the nitrogen atoms and $0.8\beta_0$ for the bond integral of the C=N bond, afforded the energies recorded in Table II. It is clear from these data, that the total π energies, as well as the delocalization energies (DE) of the different naphthyridines are effectively the same. Furthermore, these energies are essentially the same as the corresponding values for naphthalene.

Nmr Spectra of Methylnaphthyridines.—The nmr data for the various 2 and 4-methylnaphthyridines are reported in Table I. As expected, the methyl protons of the 2-methyl groups are singlets, while those of the 4-methyl groups are spin–spin coupled to H-3. Similar coupling effects have been observed in the related 2-methyl- and 4-methylquinolines.

Elvidge and Jackman[7,8] have recently defined aromatic compounds as "these substances which sustain an induced ring current." This definition of aromaticity has been critized.[9] Abraham and Thomas[9] suggest that while the existence of a ring current can be used as a sensitive test for the detection of aromatic character, it is not directly related to the resonance energy or reactivity of the molecule in question. The validity of the whole concept of ring current has, in fact, been questioned.[10a]

We feel, however, that one can still semiquantitatively correlate the chemical shifts of methyl protons[10b] with aromaticity in *geometrically closely related* systems.

It has been shown that the replacement of an sp^2 carbon atom by a sp^2 nitrogen atom adjacent to an aromatic carbon atom bearing a methyl group will cause a paramagnetic shielding of 0.1 ppm of the methyl protons.[7] If the other effects which contribute to the shielding of the methyl protons in the naphthyridines are the same as those in naphthalene, we would expect that the chemical shift of the methyl groups in the 2 position should differ from that of the methyl group in 2-methylnaphthalene (τ 7.38) by the paramagnetic shielding effect of 0.1 ppm of the nitrogen atom only. That this is essentially the case, is shown by the data presented in Table I.

Since the heteroatom contribution of a nitrogen atom is only 0.1 ppm towards an *o*-methyl group, one would anticipate that the contribution to a *p*-methyl group should be exceedingly small. Consequently, we would predict that the chemical shifts of the 4-methyl protons of the different naphthyridines should be the same as the chemical shift of the methyl

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[6] T. Peacock, [*J. Chem. Soc.*, 2308 (1959)] has reported the results of SCF calculations on 1,5- and 1,8-naphthyridines and has correlated these results with the ultraviolet spectra of the compounds.

[7] J. A. Elvidge and W. A. Jackman, *ibid.*, 859 (1961).

[8] J. A. Elvidge, *Chem. Commun.*, 160 (1965).

[9] R. J. Abraham and W. A. Thomas, *J. Chem. Soc.*, 127 (1966).

[10] (a) J. I. Musher, *J. Chem. Phys.*, **43**, 4081 (1965). (b) Consideration of the chemical shifts of the ring protons in these correlations is subject to other considerations[7] and will be discussed, along with other heteroaromatic systems, in a forthcoming paper.

group protons on 1-methylnaphthalene (τ 7.25). The only discrepancy might be expected for the 4-methyl group protons in 4-methyl-1,5-naphthyridine, where the 5-nitrogen atom might influence the 4-methyl group protons by the anisotropic effect of its unshared pair of electrons and/or by its inductive effect. We do indeed observe that the chemical shifts of the various 4-methyl group protons are as predicted, except for an increased deshielding (0.1 ppm) of the methyl group protons in 4-methyl-1,5-naphthyridine.

The nmr data are therefore in agreement with the predictions of the HMO calculations and we can suggest (if there is indeed a correlation between ring current and aromaticity) that the resonance energies of the naphthyridines are essentially the same as the resonance energy of naphthalene, and that the replacement of two sp^2 carbon atoms by two sp^2 nitrogen atoms does not greatly alter the resonance stabilization of these bicyclic heteroaromatic compounds.

Experimental Section[11]

4-Methyl-1,6-naphthyridine.—To a solution of 70 ml of Sulfo-mix,[12] 25 ml of water, and 23.5 g (0.25 mole) of 4-aminopyridine, warmed to 115°, was added dropwise over 1 hr, 18.0 g (0.26 mole) of methyl vinyl ketone. The bath temperature was raised to 120° and the reaction mixture was stirred for 5 hr. The cooled solution was made basic with aqueous sodium hydroxide and steam distilled. The distillate (1 l.) was adjusted to pH 4 with phosphoric acid and extracted with five 50-ml portions of chloroform. The combined extracts were dried and on evaporation to dryness a clear oil remained which solidified after some time to form clusters. Chromatography on neutral grade 3 alumina yielded 0.36 g (1%) of 4-methyl-1,6-naphthyridine: mp 68–69°; $\lambda_{\max}^{\text{MeOH}}$ 203 mμ (log ϵ 481), 208 (4.53), 220 sh (4.44), 254 (3.48), 263 sh (3.45), 275 sh (3.28), 295 sh (3.30), 305 (3.44), 317 (3.43). The infrared out-of-plane vibrations of the free base in chloroform are 870, 850, 820 cm^{-1} as expected[4] for a 4-substituted 1,6-naphthyridine.

The sample was converted to the monopicrate for elemental analysis (picrate mp 184–185°).

Anal. Calcd. for $C_{15}H_{11}N_5O_7$: C, 48.25; H, 2.97; N,18.76. Found: C, 48.27; H, 3.20; N, 18.80.

2-Methyl-1,6-naphthyridine.—The same procedure was used as for the preparation of 4-methyl-1,6-naphthyridine, except that 50 g (0.60 mole) of crotonaldehyde was substituted for the methyl vinyl ketone. The yield of 2-methyl-1,6-naphthyridine was 0.18 g (0.5%): mp 60–61°; $\lambda_{\max}^{\text{MeOH}}$ 205 mμ (log ϵ 4.78), 225 (4.56), 230 sh (4.44), 298 (3.53), 311 (3.52). The infrared out-of-plane vibrations of the free base in chloroform are: 895, 840 cm^{-1} as expected[4] for a 2-substituted 1,6-naphthyridine. Monopicrate (mp 173–174°).

Anal. Calcd for $C_{15}H_{11}N_5O_7$: C, 48.26; H, 2.97; N, 18.76. Found: C, 48.00; H, 3.04; N, 18.90.

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[11] Melting points are corrected. Nmr spectra were obtained with a Varian A-60 spectrometer. The microanalyses were performed by Mrs. S. De Boer of this department.

[12] W. P. Utermohlen, Jr., *J. Org. Chem.*, **8**, 544 (1943).

Pyrolysis of 1-Methyl-3- isopropylidenecyclobutene

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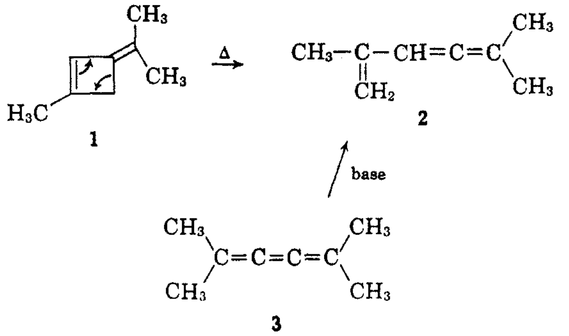
In connection with another problem,[1] we sought a convenient synthesis of the vinylallene 2, to confirm its presence as a rearrangement product from cumulene **3**. An attractive route appeared to be pyrolysis of the known cyclobutene **1**,[2] which by a cyclobutene to butadiene rearrangement would give 2 directly. A study of the rearrangement also seemed of interest in view of recent attention to such isomerizations.[3]



A sample of purified **1** was made available through the generosity of Dr. W. H. Sharkey. The compound indeed undergoes the isomerization at temperatures above 175° to give isomer **2** in reasonable yield. From a preparative point of view the pyrolysis was best carried out in the injector (340°) of a gas chromatograph with **2** being collected in 45 to 55% yield.

Isomer **2**, C_8H_{12}, exhibits infrared absorption at the expected positions, including 1941 cm^{-1} (allene) and 876 cm^{-1} (terminal methylene). The ultraviolet spectrum of **2** exhibits a $\lambda_{\max}^{\text{EtOH}}$ at 218 mμ (ϵ 22,000).[4] The nmr spectrum of **2** was quite informative showing a 6-proton singlet at δ 1.70 (allenic methyls), a broadened 3-proton singlet at δ 1.75 (vinyl methyl), a 2-proton multiplet at δ 4.78 (terminal methylene) and a one 1-proton multiplet at δ 5.67 (allenic hydrogen). Catalytic hydrogenation resulted in the uptake of 3 moles of hydrogen to give 2,5-dimethylhexane, identical with an authentic sample. The thermal rearrangement product was identical in all respects with **2** obtained from **3**.[1,5]

For the kinetic runs, small samples of **1**, dissolved in *n*-hexane (as an internal standard), were sealed, and the reactions run in a constant-temperature Woods metal bath. Unfortunately, similarity in the ultraviolet spectra of **1** and **2** required that the disappearance of **1** be followed by gas chromatography. Formation of **2** did not quite parallel disappearance of **1**, most likely due to dimerization.[6] From the rates at 200° and 220°, the activation energy shown in Table I was calculated. Also shown are the data for two related isomerizations.

It is noted from the data in Table I that the isomerization of **1** is much slower than that of the nonconju-

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[1] F. T. Bond and D. E. Bradway, *J. Am. Chem. Soc.*, **87**, 4977 (1965).

[2] J. K. Williams and W. H. Sharkey, *ibid.*, **81**, 4269 (1959).

[3] See for example: (a) M. A. Battiste and M. E. Burns, *Tetrahedron Letters*, 523 (1966); (b) R. Criegee, D. Seebach, R. E. Winter, B. Barritzu, and H. A. Brune, *Chem. Ber.*, **98**, 2339 (1965); (c) H. M. Frey, D. C. Marshall, and R. F. Skinner, *Trans. Faraday Soc.*, **61**, 861 (1965), and earlier references cited therien.

[4] *Cf.* vinylallene itself shows infrared absorption at 1940 cm^{-1} and $\lambda_{\max}^{\text{EtOH}}$ 216.5 mμ: E. R. H. Jones, H. H. Lee, and M. C. Whiting, *J. Chem. Soc.*, 341 (1960).

[5] A compound assigned structure **2** has been reported previously: A. F. Thompson and E. N. Shaw, *J. Am. Chem. Soc.*, **64** 363 (1942).

[6] H. Fischer, "The Chemistry of Alkenes," S. Patai, Ed., Interscience Publishers, Inc., New York, N. Y., 1964, p 1064.