1,4-Dimethyl-1,4-dihydro-1,2,4,5-tetrazine and Its *N*-Alkyl Salt. Synthesis, Structure, and Chemistry[1a]

HAROLD KOHN[1b] AND R. A. OLOFSON*

Department of Chemistry, The Pennsylvania State University, University Park, Pennsylvania 16802

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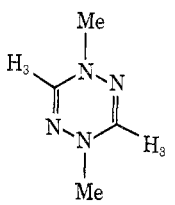
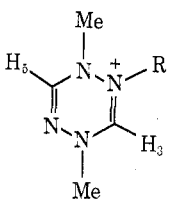
1,4-Dimethyl-1,4-dihydro-1,2,4,5-tetrazine (1) has been prepared by a convenient two-step route and shown to rearrange to a triazoline (11) in base. Attempts to differentiate between the several possible planar and boat conformations for the 8-π-available electron system (1) by nmr failed, but data pertinent to this problem were obtained from studies of the mechanism of the process, 1 → 11, and of the alkylation of 1, which occurs at nitrogen already bearing a methyl substituent (→ 12). Standard 6-π-electron model compounds (*e.g.*, polyazoles), when confronted with a similar choice, always react at an unsubstituted nitrogen. The pmr absorption for methyl attached to the positively charged nitrogen in the *N*-alkyl salts (12) is found at *higher* field than the peak attributed to methyl bonded to the formally neutral nitrogen atom, an observation which yields valuable information concerning the detailed structure of 12.

Although several substances for which a 1,4-dihydro-1,2,4,5-tetrazine structure has been proposed can be found in the literature, initial reports have usually been followed after varying time periods by retractions and structural reassignment.[2] At the time the work described here was begun, the only authenticated 1,4-dihydrotetrazines contained aryl substituents in the 1 and 4 positions.[3-5]

The goals of the present investigation were the synthesis of 1,4-dimethyl-1,4-dihydro-1,2,4,5-tetrazine (1) and its *N*-alkyl salt (2) and the comparison of the



1

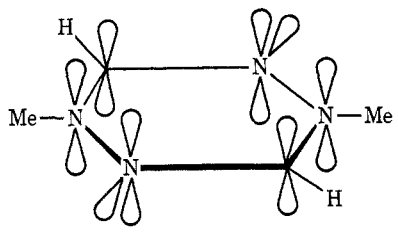


2

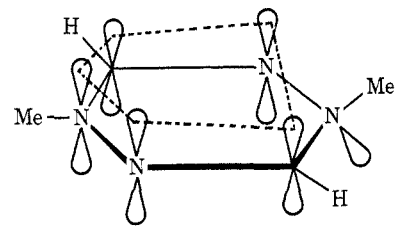
kinetic acidities (C–H_3 in 1 and C–H_3 and C–H_5 in 2) of these compounds with the values for possible tetrazole and tetrazolium cation model substrates.

The hope of differentiating between conceivable planar (**1a–d**) and boat (**1e–g**) conformations for 1, an 8-π-available electron system, provided an attractive added incentive.[6]

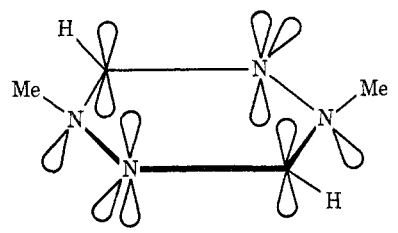
The related 1,4-dithiadiene has been shown by X-ray crystallography to possess a boat structure,[7] but nearly planar geometries are preferred for 1,4-diphenyl-, 1,4-di-*p*-chlorophenyl-, and 1,4-di-*p*-tolyl-1,4-dihydro-1,2,4,5-tetrazine because of their small dipole moments (0.8, 0.65, and 0.75 D, respectively[7]). Since conjugation



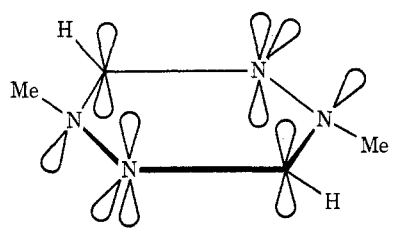
1a



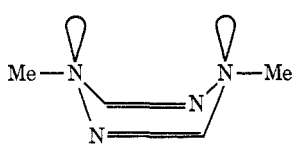
1b



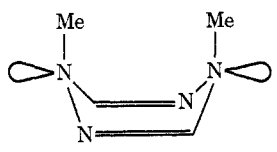
1c



1d



1e



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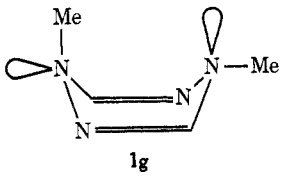


1g

(1) (a) This research has been supported in part by a grant from the U. S. Public Health Service (GM-13980). We are also indebted to Mr. F. J. Bobick and Mr. K. D. Lotts for experimental assistance. (b) NSF Predoctoral Trainee, 1966–1969; NIH Predoctoral Fellow, 1969–1970. Abstracted from Ph.D. dissertation of this author. Additional structure proof, discussion, and experimental and spectral data may be found in this reference.

(2) V. P. Wystrach in "Heterocyclic Compounds," Vol. 8, R. C. Elderfield, Ed., Wiley, New York, N. Y., 1967, p 105; P. F. Wiley in "The Chemistry of Heterocyclic Compounds," A. Weissberger, Ed., Interscience, New York, N. Y., 1956.

(3) W. Baker, W. D. Ollis, and V. D. Poole, *J. Chem. Soc.*, 3389 (1950).

(4) P. G. Edgerley and L. E. Sutton, *ibid.*, 3394 (1950).

(5) Prepared by rearrangement of *N*-arylsydnones with P_2S_5 in hot toluene or treatment of *N*-aryl-*N'*-thioformylhydrazines (from $ArNHNH_2$ + $HCS_2^-Na^+$) with NaOMe.[3]

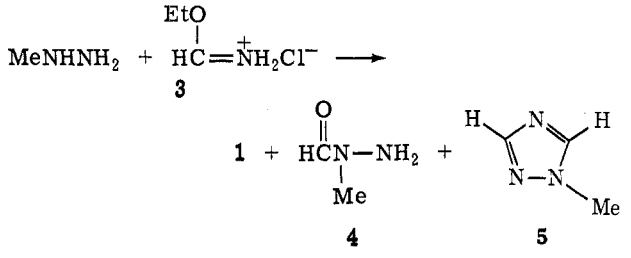
(6) The unusual potential of **1** as a ligand, which provided yet another reason to undertake its synthesis, will be examined in a future publication.

(7) W. E. Parham, H. Wynberg, W. R. Hasek, P. A. Howell, R. M. Curtis, and W. N. Lipscomb, *J. Amer. Chem. Soc.*, **76**, 4957 (1954).

of the nitrogen lone pairs with the aryl π systems is an important added complication in these latter substrates, the use of this data to predict a similar structure for **1** would not be justified. 1,4-Dialkyl-1,4-dihydropyrazines, which could also be utilized to provide answers to the geometric and electronic structure questions exemplified by **1a–g**, are not known.

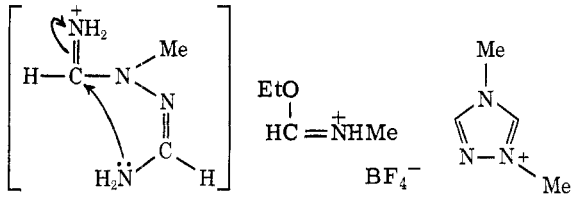
Results and Discussion

The dimethyldihydrotetrazine (**1**) was prepared in one step in 38% isolated yield by treatment of ethyl formimidate hydrochloride[8] (**3**) with methylhydrazine in ether.



3 **4** **5**

In addition to NH_4Cl, which was removed by filtration, two by-products, *N*-formyl-*N*-methylhydrazine[9] (**4**, 9%) and 1-methyl-1,2-4-triazole[10] (**5**, 27%), were also obtained. The latter compound codistilled with **1** but could be separated by selective precipitation as the oxalate salt from a solution of **1** and **5** in ether. Because **5** is probably generated by dehydrative cyclization of a diacylhydrazide intermediate such as **6**, the use of **7** in



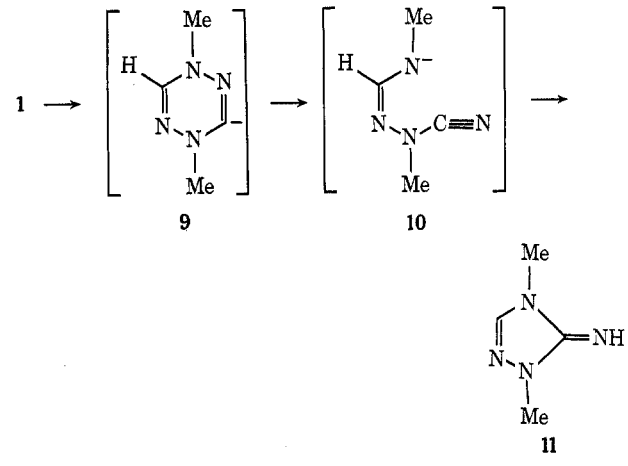
6 **7** **8**

the synthesis in place of **3** was investigated. Unfortunately, the yield of **1** from **7** and methylhydrazine was only 4%. One contaminant identified was the triazolium cation[10] (**8**).

The dihydrotetrazine **1** is a volatile, pale yellow solid, mp 45–46°, whose nmr spectrum in $CDCl_3$ contains only two singlets: δ 6.36 (area 1) and 3.01 (area 3). Other analytical and spectroscopic data are in accord with the claimed structure (see Experimental Section), and Tolles, McBride, and Thun[11] have recently isolated and identified a compound with the same properties from the mixture obtained by oxidation of (1) 1,4-dimethylhexahydro-*s*-tetrazine with HgO (14% yield before vpc purification), (2) 1,1-dimethylhydrazine with HIO_3 (trace yield), and (3) **4** with I_2 (0.1% yield). An attempt to measure the pK_B of **1** in water was unsuccessful because acid-catalyzed hydrolysis to yield a complex mixture of products occurred rapidly below pH 2.

The nmr spectrum of **1** in $CDCl_3$ did not change as the probe temperature was lowered. Even at −99°, the lowest experimentally accessible temperature, the spectrum consisted of the same unbroadened pair of singlets. Therefore, either conformational equilibration remains rapid on an nmr time scale at −99° or possible geometries for **1** are limited to the symmetrical structures, **1a,c–f**. Since the former explanation is not improbable, a choice between these alternatives based only on the negative nmr result is not justified. Further structure clues, however, can be garnered from the chemistry of **1**.

5-Imino-1,4-dimethyl-Δ^2-1,2,4-triazoline (**11**), the product expected from ring cleavage of an intermediate carbanion **9**, was obtained on treatment of **1** with



9 **10** **11**

aqueous sodium hydroxide. Baker, Ollis, and Poole[3] have reported similar base-induced isomerizations of 1,4-diaryl-1,4-dihydro-1,2,4,5-tetrazines, but formulations analogous to **11** were never considered for the products, though all published data are in accord with such structures.[12] The known triazoline **11** has previously been made by methylation of 1-methyl-5-amino-1,2,4-triazole[13] and also isolated as the HI salt from reaction of 1-amino-1,2-dimethylguanidine hydriodide with formic acid.[14]

Attempts to measure the kinetic acidity of **1** directly were unsuccessful. In Na_2CO_3–D_2O no exchange of the annular protons was observed and in NaOD–D_2O ring scission was a rapid reaction. The generation of **9** as a discrete intermediate, however, was demonstrated by reisolation of partly C_3 deuterated **1** (40–50% D) from a solution of **1** in D_2O containing 0.2 equiv of NaOD.[15] The discovery that the ring scission, **9** → **10**, is a two-step process is of special interest here. Such observations are often interpreted as an indication that the two bonds broken in the cleavage are not in the

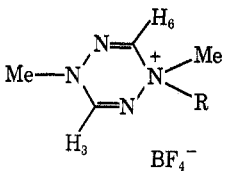
(8) R. Ohme and E. Schmitz, *Angew. Chem., Int. Ed. Engl.*, **6**, 566 (1967).
(9) C. T. Pedersen, *Acta Chem. Scand.*, **18**, 2199 (1964).
(10) R. A. Olofson and R. V. Kendall, *J. Org. Chem.*, **35**, 2246 (1970).
(11) W. M. Tolles, W. R. McBride, and W. E. Thun, *J. Amer. Chem. Soc.*, **91**, 2443 (1969). These authors made **1** in order to compare the esr spectrum of the derived cation radical with the spectra of the related verdazyl and tetrazolinyl radicals. The conformational and electronic structure questions introduced here were not considered.
(12) A 1-aryl-3-arylamino-1,2,4-triazole structure was proposed. No reaction pathway was presented.
(13) G. Cipens and V. Grensteins, *Latv. PSR Zinat. Akad. Vestis, Khim. Ser.*, 263 (1962); *Chem. Abstr.*, **59**, 12790*h* (1962). Since the melting point listed in the original article was 56–58° while that found for the product from **1** was 66–68°, the latter compound was also converted to the known HI salt, mp 225–225.5° (lit.[14] mp 226°).
(14) C.-F. Kröger, G. Schoknecht, and H. Beyer, *Chem. Ber.*, **97**, 396 (1964).
(15) Using estimates based on these experimental observations, the kinetic acidity is between that of 1- and 2-methyltetrazole: R. A. Olofson, H. Kohn, R. V. Kendall, and W. P. Piekielek, Abstracts, 160th National Meeting of the American Chemical Society, Chicago, Ill., Sept 1970, ORGN 76. The significance of this result will be discussed elsewhere.

planar trans relationship required for a concerted E2 elimination[16]—a requirement only fulfilled in **1** by one of the boat conformations, **e–g**. However, enough exceptions to this generalization are known[16] so that it cannot be used to definitely exclude structures **a–d** for **1**.

When **1** was alkylated with $Me_3O^+BF_4^-$, the product was not the cation **2**, but instead 1,1,4-trimethyl-1,4-dihydro-1,2,4,5-tetrazinium BF_4^- (**12a**) in 83% yield (Table I). A similar salt (**12b**) was isolated from reaction of **1** with $Et_3O^+BF_4^-$.

TABLE I

NMR (CD_3CN) FOR **12a** AND **12b**



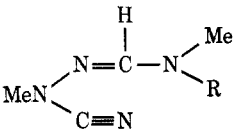
BF_4^-

12a, R = Me
b, R = Et

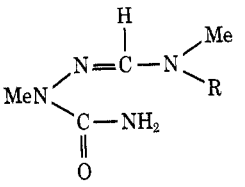
	12a	12b
Proton Spectra, δ (*J*, Hz)		
H_3 and H_6	7.78,[a] 7.06[b]	7.83, 7.04
NMe	3.50	3.48
$^+$NMe	3.35	3.28
$^+NCH_2$		3.71 (q, 7.5)
CCH_3		1.31 (t, 7.5)
^{13}C Spectra (and $J_{^{13}C-H}$), ppm from TMS (*J*, Hz)		
H_3 and H_6	150.4 (207)	150.3 (206)
	126.5 (235)	125.4 (235)
NMe	42.5 (~141)	42.3 (142)
$^+$NMe	54.0 (148)	52.3 (147)
$^+NCH_2$		63.2 (148)
CCH_3		8.80 (~138)

[a] $J_{^{13}C-H}$ = 207 Hz; also *J* = 0.1 Hz with NMe and 0.3 Hz with $^+$NMe (from decoupling); also splitting by N. [b] $J_{^{13}C-H}$ = 238 Hz; also splitting by N.

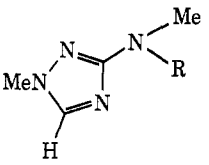
The nmr data reproduced here unambiguously eliminate structure **2** for these salts.[17] Because of the equivalence of one NMe and NR in **12a** (peak remains a singlet at −50°) and the nonequivalence of the two NMe's in **12b**, the new *N*-alkyl must be situated on one of the N atoms already bearing a methyl substituent. A small coupling (*ca.* 1.5 Hz) between H_3 and H_6 is partially masked by further coupling to nitrogen. Other analytical and spectral data consistent with structures **12** are recorded in the Experimental Section. In addition, **12a** and **12b** both underwent ready ring cleavage to the expected nitriles (**13a,b**) on short treatment with base. On longer reaction with aqueous NaOH, the ureas **14** were obtained along with the triazoles **15**. The triazole structure assignment is only tentative; some isomeric triazole structures have not been excluded. Spectral and analytical data for **13–15** are summarized in Table II. The nitriles were shown to be precursors to both the ureas and the triazoles, and the ureas were shown to be neither intermediates on the pathway from nitrile to triazole nor possible sources of triazole. Because product ratios varied dramatically



13a, R = Me
b, R = Et



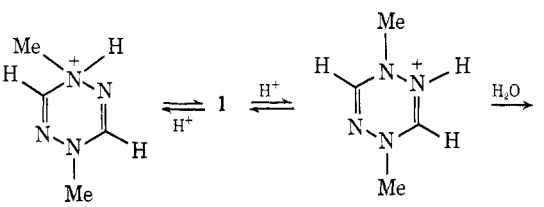
14a, R = Me
b, R = Et



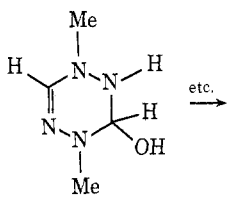
15a, R = Me
b, R = Et

with reaction conditions, this proof required the use of crossover experiments in which, for example, methyl salt **12a** was treated with NaOH in the presence of ethyl nitrile **13b** or ethyl urea **14b** (see Experimental Section).

The salt **12a** is stable in water below pH 8 (even in 0.1 *N* HCl). At higher pD in D_2O, exchange of both H_3 and H_5 seems to be competitive with ring opening to **13a**, but this conclusion is only tentative since partly deuterated **12a** could not be reisolated from the reaction solution. The stability of **12** in dilute acid might seem surprising in view of the ready hydrolysis of its precursor **1** in this medium. This apparent contradiction is easily resolved if hydrolysis of **1** does not involve protonation at N_1, but rather protonation at N_2 to give **16**, which then adds water and proceeds to prod-



stable



16

ucts. Attempts to thermally isomerize **12a** to **2** (R = Me) were unsuccessful.

The discovery that the pmr absorption of methyl attached to the positively charged nitrogen in **12a** occurs at higher field (δ 3.35) than the peak assigned to the methyl bonded to the formally neutral nitrogen atom (δ 3.50) was most unexpected and was especially fascinating, since introduction of a positive charge normally has a strong deshielding effect at adjacent positions (Me_4N^+ δ 3.2 *vs.* Me_3N δ 2.2, both in D_2O) but a much smaller effect at more distant sites.[18] This observation becomes even more significant because of the gross symmetry considerations which make the second *N*-methyl an ideal model for most of the other structure factors included in the variation of chemical

(16) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," 2nd ed, Cornell University Press, Ithaca, N. Y., 1969, Chapter 9.

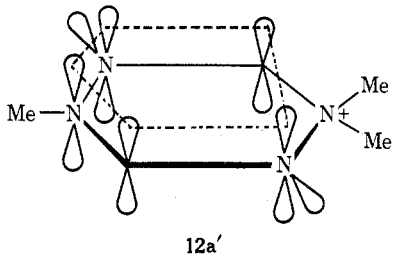
(17) The proton spectrum has been measured in several solvents (see Experimental Section). Note also the nmr and mass spectral evidence for the RNMe unit in degradation products **13–15** (Table I, including footnotes).

(18) L. M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," 2nd ed, Part 2, Pergamon Press, New York, N. Y., 1969.

TABLE II
SPECTRAL AND ANALYTICAL DATA FOR **13**, **14**, AND **15**

	13a	**13b**	**14a**	**14b**	**15a**	**15b**
Nmr, δ, in	CCl_4	CCl_4	$CDCl_3$	$CDCl_3$	CCl_4	$CDCl_3$
H—C=N[a]	7.69	7.76	7.34	7.38	7.36	7.40
MeN—	2.98	2.99	3.18	3.16	3.67	3.70
R—N—Me	2.85	2.83	2.88	2.83	2.82	2.86
R[b]	↑	3.24, 1.12	↑	3.25, 1.13	↑	3.18, 1.14
NH_2[c]			5.53	5.86		
Ir, μ,[d] in	CCl_4	CCl_4	$CHCl_3$	$CHCl_3$	CCl_4	$CHCl_3$
C≡N	4.58 (m)	4.56 (m)				
—C=N	6.09 (s)	6.14 (s)	6.08 (s), 6.47 (s)	6.09 (s), 6.44 (s)		
—C=O						
—NH_2			2.83 (w), 2.94 (w)	2.83 (w), 2.94 (w)		
Mass spectrum, *m/e*,[d] P	126	140	144	158	126	140
Analysis	$C_5H_{10}N_4$	$C_6H_{12}N_4$	$C_6H_{12}N_4O$	$C_6H_{14}N_4O$	$C_5H_{10}N_4$	$C_6H_{12}N_4$
Calcd C	47.60	51.41	41.65	45.55	47.60	51.41
Found C	47.89	51.51	41.97	45.42	47.40	51.38
Calcd H	7.99	8.63	8.39	8.92	7.99	8.63
Found H	8.21	8.36	8.62	8.99	8.02	8.81
Calcd N	44.41	39.97	38.86	35.41	44.41	39.97
Found N	43.99	40.21	39.10	35.36	44.27	39.87

[a] Not NH; not washed out with D_2O. [b] Quartet and triplet; J = 7.5 Hz for **13b** and 7Hz for **14b** and **15b**. [c] Broad singlet; exchanged with D_2O. [d] More extensive ir and mass spectral data in ref 1b. Of particular significance is the finding that the mass spectral ion $C_3H_8N^+$ (from MeNEt unit) is the base (100%) peak in **13b**, **14b**, and **15b**; see Experimental Section.



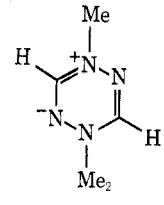
12a′

shift. An attractive rationalization of this dichotomy involves the postulation of the detailed structure **12a′** for the *N*-methyl salt of **1**.

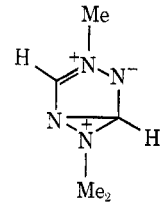
The six π electrons are assumed to constitute an aromatic Hückel sextet, at least to the extent that an appreciable ring current can be induced in a magnetic field. For such a system, as in other benzene derivatives, the methyl protons in the ring plane should be greatly deshielded while the methyl protons above and below the plane in **12a′** should be affected to a much lesser extent.[18,19] In ^{13}C magnetic resonance spectra, electron density factors are of primary importance while anisotropic (ring current) effects generally play a much smaller role in the determination of chemical shift than in proton spectra.[20] The ^{13}C resonance for $^+NMe_2$ in **12a′** should therefore be found at lower field than the absorption for NMe, the reverse of the proton order. As can be verified from an examination of the data given, this expectation is in accord with the experimental result.

If the interpretation of the nmr data elucidated here is correct, **12** qualifies as a "homoaromatic" compound.[21] In comparison with other species whose assignment to this class is based on experimental data, however, **12** is unusual in that no formal charge is associated with the π system. In earlier examples the instability inherent in such a charged system (or in an excited state) was required to bring into operation the amount of "homoaromatic stabilization" necessary for an experimentally observable effect. For example, structural and nmr evidence relating to the question of cyclic electron delocalization (monohomobenzene character) in tropylidene is ambiguous.[22] Enhanced homoaromaticity in **12** *vs.* tropylidene and related substances[22] would be readily explained in terms of the spatial distance and geometrical factors which permit maximum overlap without increased angle strain. The positive charge as well as the number and placement of the nitrogen atoms could also be important, since their combined effect is to increase the resonance contribution from the canonical structure **12a″** and as a further consequence also from **12a‴**.

Structure **12a′** as depicted is π isoelectronic with the pentadienyl anion and thus subject to the same orbital



12a″



12a‴

(19) A qualitatively similar argument can be derived just from considerations of the diamagnetic anisotropy of isolated C=N bonds. However, such effects are generally much too small in magnitude at the distances required in **12** to account for the present observations.[18]

(20) A. J. Jones, T. D. Alger, D. M. Grant, and W. M. Lichtman, *J. Amer. Chem. Soc.*, **92**, 2386 (1970), and references cited therein.

(21) S. Winstein in "Aromaticity," Special Publication No. 21, The Chemical Society, London, 1967, pp 5–45.

(22) See footnotes 52a–c and 53a–b in ref 21. Even the exaltation of its molecular diamagnetic susceptibility is not large: H. J. Dauben, J. D. Wilson, and J. L. Laity, *J. Amer. Chem. Soc.*, **91**, 1991 (1969). For a review of data on other hydrocarbons (*e.g.*, triquinacene, *cis,cis,cis*-cyclonona-1,4,7-triene), see ref 21, pp 42–43.

symmetry determined 1,5 π-bonding interactions[23] which make the planar "U" conformation of this anion experimentally more stable than the alternative "W" and "sickle" forms.[24] It is also useful to note that, in molecular orbital calculations, the insulating methylene group of the cyclohexadienyl anion mixes in to stabilize the highest occupied molecular orbital just as it does in methylallyl anion (a rationalization for the known greater stability of the cis form).[23,25] The replacement of the CH_2 in cyclohexadienyl anion by $^+NMe_2$ is expected to enhance this stabilization. Since its physical consequences are unknown, the operation of the final hypothetical "hyperconjugation" effect above could alone explain the nmr data.

The arguments above increase the attractiveness of those geometries and electronic configurations of **1** in which "homoaromatic character" can be visualized as a significant factor (*e.g.*, **1b**, **1g**). The simple fact of the isolation of **12** (instead of **2**) itself testifies to the unique nature of **1**, since, among the thousands of cases published, there is no known instance of a potentially Hückel-aromatic heterocycle in which alkylation by an electrophilic reagent occurs at an electron pair which can be contributed by ring nitrogen to the π system when a second, necessarily orthogonal sp^2 electron pair on nitrogen is also available for alkylation. For example, 1,2-dimethylpyrazolium cation, not the 1,1-dimethyl isomer, is the product from methylation of 1-methylpyrazole.[26]

Experimental Section[27]

1,4-Dimethyl-1,4-dihydro-1,2,4,5-tetrazine (1).—(Since HCN is a possible minor side reaction product, this experiment, including early isolation steps, should be performed in a hood!) Ethyl formimidate hydrochloride (from $HCONH_2$, EtOH, and $PhCOCl$[8]) (163 g, 1.5 mol) was added (45 min) in small aliquots *via* a powder funnel to a stirred mixture of $MeNHNH_2$ (69 g, 1.5 mol) and a few milliliters of anhydrous ether. The exothermic reaction was kept under control (moderate ether reflux) by adjusting the rate of formimidate addition and by cooling the mixture with an ice bath. During the reaction small amounts of ether (total 80–100 ml) were added to facilitate manipulation of the bright yellow pasty mixture. The precipitated NH_4Cl was filtered off and washed with 100 ml of ether. The total filtrate was concentrated and then vacuum distilled at 1 Torr using (a) an oil bath to prevent overheating and the possibility of detonation, (b) a large distilling flask to minimize problems caused by bumping of the very viscous liquid, (c) an inefficient condenser to avoid solidification of higher melting fractions, and (d) a Dry Ice–acetone bath to cool the collection flasks and thus effect complete condensation of each fraction. The distillation fraction, bp 45–55°, 51.9 g, contained a mixture of the desired product and 1-methyl-1,2,4-triazole. Lower boiling fractions contained only ethanol, ether, and methylhydrazine. A side product, *N*-formyl-*N*-methylhydrazine, which distilled at 65° (10.2 g, 9%), was purified by vpc and compared with an authentic sample.[9]

The ratio of **1** to **5** in the distillate fraction could be determined by nmr analysis [1.5:1.0 tetrazine (41%) to triazole (27%)] and the two compounds separated by selective precipitation of the latter as the oxalate salt from an ether solution. Oxalic acid (*18.9 g, 0.21 mol; 1 mol per assayed mol* **5**) *in 200 ml of ether* was added dropwise to a stirred solution of the distillate fraction in 100 ml of ether. During the addition a white granular solid precipitated. (If additional oxalic acid was added, the oxalate salt of **1** began to precipitate as a fluffy white solid, and this change in the character of the precipitate could also be used as an end point and as a crude assay of **5**.) After addition was complete the mixture was stirred for 30 min and filtered, and **1** was isolated from the filtrate by vacuum distillation: yield 32.0 g (38%); bp 55–60° (1.0 Torr); mp 45–46° (lit.[11] mp 44–46°); vpc retention time 31 min (10 ft × 0.25 in. 20% Carbowax 20M on 60/80 Chromosorb W, 152°, 38 cc/min); ir (CCl_4) 3.46 (s), 3.57 (m), 6.27 (s), 7.90 (s), 9.72 (s), 11.35 μ (s); uv (cyclohexane) 240 nm (ϵ 6200), (absolute ethanol) 236 (5900), (water) 230 (7500); mass spectrum *m/e* 112.0745 (P, calcd 112.0748), 97 (P − Me), 83 (P − MeN); nmr ($CDCl_3$) δ 6.36 (s, $J_{^{13}C-H}$ = 200 Hz, 1), 3.01 (s, $J_{^{13}C-H}$ = 137 Hz, 3), same at 60, 100, and 220 megacycles; at −99° in CD_2Cl_2 (*vs.* CH_2Cl_2, A-60A) two singlets were still found, δ 6.46 and 2.92); ^{13}C spectra (in CD_3CN *vs.* TMS) 40.7 (J = 137 Hz), 142.4 ppm [J = 200 (d), 5 (q) Hz].

Anal. Calcd for $C_4H_8N_4$: C, 42.84; H, 7.19; N, 49.96. Found: C, 42.48; H, 7.02; N, 50.08.

5 was regenerated from the oxalate salt (42.4 g) by treatment with aqueous KOH. The filtrate obtained after removal of the insoluble potassium oxalate was extracted with CH_2Cl_2 and **5** was isolated from this extract by distillation and compared with an authentic sample.[10]

1,4-Dimethyl-1,4-dihydro-1,2,4,5-tetrazine (*N*-Methylformimidate Method).—Ethyl *N*-methylformimidate HBF_4 salt was obtained as a colorless oil (99%) by reaction of HCONHMe with $Et_3O^+BF_4^-$. While the crude product was a mixture of geometrical isomers, it was otherwise uncontaminated by impurities: nmr (CD_3NO_2) δ 8.6–10.3 (broad, 1), 8.2–8.5 (broad asymmetrical d, 1), 4.5–5.0 (m, 2), 2.9–3.3 (asymmetrical d, 3), 1.2–1.8 (m, 3). This salt (13.0 g, 0.074 mol) was added (30 min) to a stirred, cooled (0°) solution of $MeNHNH_2$ (3.46 g, 0.075 mol) in 15 ml of ether (under N_2). The mixture was then stirred overnight at room temperature and evaporated at reduced pressure, and the multicomponent mixture was analyzed by nmr. Two species identified were **1**, which was isolated (0.16 g, 4%) by vacuum distillation, and 1,4-dimethyl-1,2,4-triazolium BF_4^- [nmr (CD_3CN) δ 9.29 (s, 1), 8.59 (s, 1), 4.07 (s, 3), 3.93 (s, 3)], which could be partially purified by selective extraction of more soluble salts into ethanol followed by fractional precipitation from nitromethane–ether. Comparison of this sample (nmr, 85% pure) with material[10] obtained by alkylation of **5** confirmed the structural assignment.

5-Imino-1,4-dimethyl-Δ^2-1,2,4-triazoline (11).—**1** (1.2 g, 0.011 mol) was dissolved in 25 ml of aqueous 4% NaOH (0.025 mol) and stirred at room temperature for 18 hr. The solution was then saturated with NaCl and extracted with 3 × 40 ml of CH_2Cl_2. The dried (Na_2SO_4) extract was evaporated, affording a white solid which was purified by vacuum sublimation: yield 0.54 g (45%); mp 66–68° (lit.[13] mp 56–58°); nmr ($CDCl_3$) δ 7.23 (s, 1), 3.94 (s, 1), 3.39 (s, 3), 3.25 (s, 3); mass spectrum *m/e* 112 (P), 111 (P − H).

Anal. Calcd for $C_4H_8N_4$: C, 42.84; H, 7.19; N, 49.96. Found: C, 42.68; H, 7.44; N, 49.84.

The known HI salt of the triazoline was made by reaction with aqueous hydriodic acid, mp 225–225.5° (lit.[14] mp 226°).

Annular Proton Exchange of 1 in NaOD–D_2O.—**1** (0.82 g, 0.0073 mol) dissolved in 10 ml of 0.135 *N* NaOD–D_2O (>99.8% D), was kept at 30 ± 1° for 4 hr. The solution was then extracted with 3 × 10 ml of $CHCl_3$ and the extracts were dried (Na_2SO_4) and evaporated at reduced pressure, yielding a semisolid residue whose nmr spectrum showed it to be a mixture (6.5:1 molar ratio) of partly deuterated **1** and N-deuterated and partly C_3-deuterated **11**. **1** (0.21 g) could be isolated pure by fractional vacuum sublimation. The extent of deuteration at the annular positions was 47% by nmr analysis and 38% from

(23) R. Hoffmann and R. A. Olofson, *J. Amer. Chem. Soc.*, **88**, 943 (1966).

(24) R. B. Bates, R. H. Carnighan, and C. E. Staples, *ibid.*, **85**, 3031 (1963). Steric effects most easily explain the dichotomy between this result and that of H. Kloosterziel and G. J. Heiszwolf, *Recl. Trav. Chim. Pays-Bas*, **89**, 413 (1970). Note incompleteness of delocalization: H. Kloosterziel and J. A. A. van Drunen, *ibid.*, **89**, 368 (1970).

(25) This is also true for cyclopropene and cycloheptatriene but not for cyclobutenyl anion, cyclohexadienyl cation, and cyclopentadiene, all of which have nodes which pass through the methylene group in the relevant orbital.[23]

(26) Similarly, 1,7a-diazaindene is alkylated at the 1 position and 1-methylpyridone-4 is alkylated on oxygen, not nitrogen.

(27) Melting points were determined in Kimax, soft glass capillary tubes using a Thomas-Hoover melting point apparatus equipped with a calibrated thermometer. Pmr spectra were run on a Varian A-60A (equipped with V-6040 variable temperature controller), HA-100, or 220 spectrometer using an internal TMS standard; ^{13}C spectra and $J_{^{13}C-H}$ values were measured on a JOEL PS100 with a JEM-PFT-100 Fourier Transform spectrometer equipped with a Nicolet Model 1080E extended memory unit. Solvents and reactants were of the best commercial grade available and were used without further purification. Mass spectral data were obtained at 70 eV on an MS-902 double-focusing spectrometer.

less accurate mass spectral data (39% H_2, 47% HD, and 14% D_2 compound).

Acid Hydrolysis of 1.—An attempt to determine the pK_B of **1** (uv) was unsuccessful because hydrolytic decomposition occurred below pH 2. When the hydrolysis was performed on a 20% by weight solution of **1** in 10% DCl–D_2O in an nmr tube, the initial yellow color almost immediately darkened to orange but after 20 min the solution was colorless. The nmr spectrum continually changed during this period and for several days thereafter and became more and more complicated. None of the products were identified.

1,1,4-Trimethyl-1,4-dihydro-1,2,4,5-tetrazinium Fluoroborate (12a).—$Me_3O^+BF_4^-$ (5.92 g, 0.04 mol) in 90 ml of CH_3NO_2 was added dropwise to a stirred solution of 4.48 g (0.04 mol) of **1** in 30 ml of CH_3NO_2. The red solution was stirred at room temperature for 5 hr and the product was isolated by precipitation with ether. Purification of the white solid was accomplished by reprecipitation with ether from a 1:1 CH_3NO_2–CH_2Cl_2 solution: yield 7.10 g (83%); mp 119.5–122°; ir (Nujol) BF_4^- at 9.3–9.7 μ (s); uv (CH_3CN) 275 nm (ϵ 1200), 208 (3700), (H_2O) 268 (1700), 205 (4400), (0.1 *N* HCl–H_2O) 269 (1700), 205 (4200); nmr (CD_3CN) δ 7.78 (broad s, 1), 7.06 (broad s, 1), 3.50 (s, 3), 3.35 (s, 6) (the peak at 3.35 remained a singlet at −50°). Spectra were also measured in DMSO-d_6, CF_3CO_2D, CF_3CO_2D–D_2O (1:1), and 0.1 *N* DCl–D_2O buffers below pD 8 (at higher pD hydrolysis occurred). Except for minor position variations and sharpening of the ring protons to doublets [in DMSO-d_6 δ 8.23 (broad, 1.3 Hz), 7.44 (distinct d, 1.5 Hz)], the spectra were unchanged. The $^+NMe_2$ peak never was found at lower field than the NMe resonance and both absorptions were always found as singlets.

Anal. Calcd for $C_5H_{11}N_4BF_4$: C, 28.07; H, 5.18; N, 26.18. Found: C, 27.94; H, 5.40; N, 26.13.

1-Ethyl-1,4-dimethyl-1,4-dihydro-1,2,4,5-tetrazinium Fluoroborate (12b).—Ethylation of **1** was achieved using the procedure described in the previous experiment with $Et_3O^+BF_4^-$ (7.60 g, 0.04 mol) as the alkylating agent and CH_2Cl_2 as the reaction solvent: yield of white solid 6.49 g (71%); mp 125–127°; ir (Nujol) BF_4^- at 9.2–9.7 μ (s); nmr (CD_3CN) δ 7.83 (broad s, width at half-height 4 Hz, 1), 7.04 (broad d, 1.5 Hz, 1), 3.71 (q, 7.5 Hz, 2), 3.48 (s, 3), 3.28 (s, 3), 1.31 (t, 7.5 Hz, 3).

Anal. Calcd for $C_6H_{13}N_4BF_4$: C, 31.61; H, 5.75; N, 24.57. Found: C, 31.86; H, 6.05; N, 24.87.

***N*-Cyano-*N*-methyl-*N'*,*N'*-dimethylformamidrazone (13a).**—A 2 *N* aqueous NaOH solution (8 ml, 0.016 mol) was added dropwise with stirring to a solution of **12a** (2.00 g, 0.00935 mol) in water (32 ml). The solution was immediately extracted with 3 × 40 ml of CH_2Cl_2, and the combined extracts were dried (Na_2SO_4) and concentrated to a yellow oil, which afforded **13a** on distillation as a colorless liquid, yield 0.79 g (67%), bp 71–72° (0.6 Torr).

***N*-Cyano-*N*-methyl-*N'*-ethyl-*N'*-methylformamidrazone (13b).**—The preceding reaction was repeated using 2.00 g (0.0088 mol) of **12b** in place of **12a**: yield 0.88 g (72%); bp 69–70° (0.6 Torr). Important peaks in the mass spectrum of **13b** besides the parent (intensity 99%) included $C_4H_7N_2^+$ [found 83.0600, calcd 83.0609 (71%)], $C_3H_5N_2^+$ [found 69.0452, calcd 69.0453 (50%)], $C_3H_8N^+$ (found 58.0660, calcd 58.0657).

***N*-Carbamyl-*N*-methyl-*N'*,*N'*-dimethylformamidrazone (14a).**—**13a** (1.00 g, 0.0079 mol) was dissolved in 10 ml (0.002 mol) of 0.2 *N* NaOH and the solution was allowed to stand at room temperature for 18 hr. The reaction mixture was then extracted with 3 × 40 ml of CH_2Cl_2, and the combined extracts were dried (Na_2SO_4) and pumped to near dryness. The nmr spectrum of this semisolid residue indicated it to be a 2.3:1 mixture of **14a** and **15a**. **14a** was isolated by several precipitations with hexane from a 1:4 CH_2Cl_2–CCl_4 solution, yield 0.41 g (36%), mp 116–118°.

***N*-Carbamyl-*N*-methyl-*N'*-ethyl-*N'*-methylformamidrazone (14b).**—The above reaction was repeated using 1.00 g (0.0071 mol) of **13b** instead of **13a**. The ratio of **14b** to **15b** determined by nmr analysis of the initial residue was 13:1. Isolation and purification of **14b** was accomplished by three recrystallizations from CCl_4–hexane, yield 0.46 g (41%), mp 72–74°. Important **14b** mass spectral peaks besides the parent mass ion (33%) included $C_5H_{13}N_3^+$ [found 115.1110, calcd 115.1109 (30%)], $C_4H_9N_2^+$ [found 85.0760, calcd 85.0766 (31%)], $C_4H_{10}N^+$ [found 72.0808, calcd 72.0813 (24%)], $C_3H_8N^+$ [found 58.0650, calcd 58.0657 (100%)].

14b could be recovered after 16 hr at room temperature in 65% yield (0.11 g) by the extraction procedure above from a solution made of 0.17 g (0.0011 mol) of substrate and 5 ml (0.0025 mol) of 0.5 *N* aqueous NaOH. There was no evidence for the presence of any **15b** in the extract.

1-Methyl-3-dimethylamino-1,2,4-triazole (15a).—A solution of **12a** (2.96 g, 0.0138 mol) in 38 ml (0.016 mol) of 0.42 *N* aqueous NaOH was kept at room temperature for 12 hr and then extracted with 3 × 40 ml of CH_2Cl_2. The extracts were dried (Na_2SO_4), concentrated, and distilled, yield 0.96 g (55%), bp 43.5° (0.5 Torr).

15a was also converted to its HI salt by reaction with aqueous HI. The salt, which turned brown after a few days, was isolated by repeated trituration of the initial product with ether: mp 133.5–136°; nmr ($CDCl_3$) δ 11.51 (s, 1), 8.13 (s, 1), 4.08 (s, 3), 3.47 (s, 6).

The pot residue remaining after distillation of **15a** contained 0.07 g of crude **14a** (nmr).

1-Methyl-3-ethylmethylamino-1,2,4-triazole (15b).—This compound, bp 45° (0.6 Torr), was prepared in 55% yield (0.92 g) from 2.70 g (0.012 mol) of **12b** in 38 ml (0.015 mol) of aqueous 0.4 *N* NaOH using the method described in the preceding experiment. An important mass spectral fragment besides P (7%), P − Me (19%), and P − Et (10%) was $C_3H_8N^+$ [found 58.0655, calcd 58.0657 (100%)].

The unstable **15b** HI salt was also made: mp 96–100°; nmr ($CDCl_3$) δ 11.48 (broad s, 1), 8.06 (s, 1), 4.05 (s, 3), 3.75 (q, 7 Hz, 2), 3.43 (s, 3), 1.39 (t, 7 Hz, 3).

Concentration of the initial distillation residue afforded 0.09 g of crude **14b**.

15b was recovered by extraction in 68% yield (0.27 g) from a solution (0.40 g, 0.0029 mol) in 4.0 ml (0.0008 mol) of 0.2 *N* aqueous NaOH after 14 hr at room temperature. No **14b** was present along with the crude **15b** in the product (nmr).

Reaction of a Mixture of 12a and 14b with Aqueous NaOH.—Only **15a** (0.2 g) and no **15b** (<1%) was found (nmr) in the crude triazole distillate obtained from reaction of a solution of 1.24 g (0.0058 mol) of **12a** and 0.92 g (0.0058 mol) of **14b** in 18.9 ml (0.0075 mol) of 0.4 *N* aqueous NaOH at room temperature for 15 hr followed by the normal extraction work-up.

Reaction of a Mixture of 12a and 13b with Aqueous NaOH.—The preceding experiment was repeated with **13b** (0.81 g, 0.0058 mol) in place of the derived urea. The crude triazole distillate (0.41 g) was shown (nmr) to be a mixture of **15a** and **15b** (1.4:1).

Registry No.—**1**, 35341-96-9; **11**, 23350-29-0; **12b**, 35541-98-1; **12b**, 35341-99-2; **13a**, 35342-00-8; **13a**, 35342-01-9; **14a**, 35342-02-0; **14b**, 35342-03-1; **15a**, 35342-04-2; **15b**, 35342-05-3.