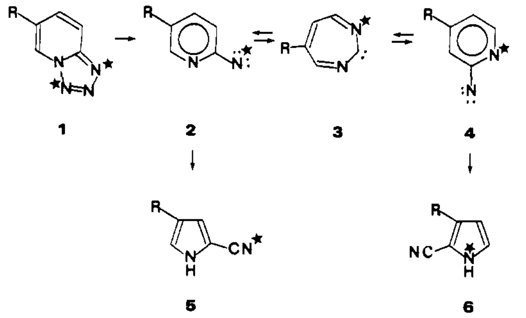
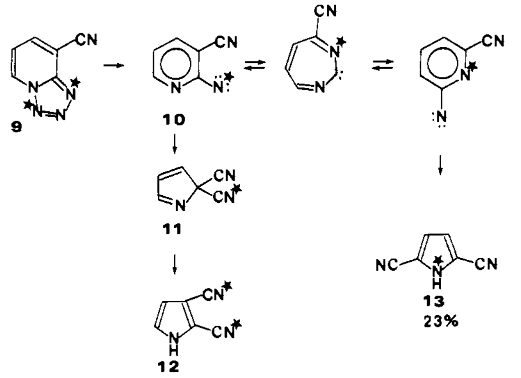
Scheme I

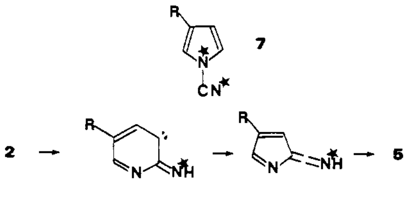


Scheme II



^{15}N-Labeled 6-methyltetrazolo[1,5-*a*]pyridine (**1**, R = CH_3) was obtained from 2-bromo-5-methylpyridine and potassium azide-*1*(*3*)-^{15}N using a known method.[6] Thermolysis of tetrazolopyridines results in tetrazole–azide tautomerism[7] and subsequent nitrene formation.[8] Gas-phase pyrolysis[9] of **1** at 365°, using 1 mm of N_2 as carrier gas, gave the ^{15}N-labeled nitrene **2**, which is in equilibrium with the isomeric nitrene **4** by means of the intermediate **3**.[8] The mixture of cyanopyrroles formed was analyzed and separated by gas chromatography (20% Carbowax 20M on Chromosorb W) and identified as **5** and **6** (R = CH_3) by comparison with known (unlabeled) samples.[10] The ratio **5**:**6** was 62:38. **5** was exclusively labeled on the cyano group, as shown by hydrolysis to 4-methylpyrrole-2-carboxylic acid which had lost all the label. Similarly, it was shown that **6** was labeled exclusively on the pyrrole nitrogen (Scheme I).[11]

The above results prove that the individual nitrenes **2** and **4** (R = CH_3) contract without any scrambling process intervening in the contraction step. The products are *not* formed via initial contraction to 1-cyanopyrroles (**7**), which would have resulted in identical labeling patterns in **5** and **6.** The absence of **7** contrasts the behavior of pyrazinylnitrenes and 2-pyrimidylnitrenes, which contract to 1-cyanoimidazoles and -pyrazoles, respectively.[2,12,13] The results do not exclude ring contraction via iminocarbenes[4] (eq 1), but such a mechanism can be excluded in the pyrolysis of the labeled tetrazole **9** (Scheme II).



(1)

9 at 365° (1 mmN_2) gave two dinitriles, **12** and **13**, which were separated by thick layer chromatography (SiO_2–$CHCl_3$), and the position of label was determined by Raman spectroscopy. **13** showed no displacement of the CN absorption, while the mass spectrum indicated that **13** carried a full label. The label must therefore be on the pyrrole-nitrogen. However, **12** showed a displacement of the two CN-absorptions by ca. 25 cm^{-1}, in agreement with ^{15}N-labeling. Since there is no way in which the initial nitrene **10** can undergo a hydrogen shift of the type depicted in eq 1, yielding the observed product, **12**, the latter must be formed by direct ring contraction to **11** (Scheme II).

There are thus at least two mechanisms of ring contraction in arylnitrenes: direct and indirect. The *direct* contraction can give either C-nitriles, as observed in **10**, or N-nitriles, as observed in pyrazinylnitrenes and 2-pyrimidylnitrenes.[2,12,13] The *indirect* contraction takes place via iminocarbenes, as observed in phenylnitrene and 2-naphthylnitrene.[4] The *rates* of the ring contractions follow the order: phenylnitrene < 2-pyridylnitrene < pyrazinylnitrene.[14] The rate increase can be ascribed to the increased electrophilicities of the hetarylnitrenes. This lowers the activation energies for ring contraction so much that the isomerization to iminocarbenes[4] cannot compete. The naphthylnitrenes contract in good yields at 480°, i.e., not quite as easily as the pyridylnitrenes, and it is possible that they constitute a borderline case, reacting by both the direct and the indirect contraction mechanism.[4]

References and Notes

(1) Part VI of the series "Hetarylnitrenes". Part V: see ref. 2. This work was supported by the Schweizerischer Nationalfonds, project No. 2.258.074. We thank S. Ruzicka for help with the Raman spectra.

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(9) The pyrolysis apparatus is described by R. Gleiter, W. Rettig, and C. Wentrup, *Helv. Chim. Acta*, **57**, 2111 (1974).

(10) We thank Dr. R. A. Jones, University of East Anglia, Norwich, for providing NMR spectra of methylcyanopyrroles.

(11) An analogous study of 6-cyanotetrazolo[1,5-a]pyridine-*1*(*3*)-^{15}N (**1**, R = CN) yielded a mixture of dinitriles **5** and **6** (R = CN) in which only 8% of the label was on the pyrrole nitrogen. The ratio **5:6** determined by NMR spectroscopy was 92:8, indicating that only **6** (R = CN) was ring labeled, whereas **5** (R = CN) was labeled on the CN group (A. Chollet, Diploma Thesis, University of Lausanne, 1974).

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(14) The evidence is that phenylnitrene requires an almost explosive reaction,[3,5] the pyridylnitrenes contract already at 365° in the gas phase, and pyrazinylnitrenes contract even in solution.[2,12,13]

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Experimental Evidence for Geometrical Variations in the Transition State of the SN2 Reaction

Sir:

The success of the transition state theory of reaction rates has led to several attempts to predict the structure of the transition state. In particular, the changes in bond lengths and bond orders of the transition state accompanying minor structural changes in the reactants have been the subject of theoretical interest. Among these predictions the Hammond postulate,[1] the Thornton rules,[2] and the rules of Harris and Kurz[3] are perhaps the best known.

Rather few unambiguous experimental measures of tran-

Table I. Relative Rate Constants for N-Methylation of 2-Substituted Thiazoles by Methyl Iodide and Methyl Tosylate in Nitrobenzene at 30 °C

Substituent	Log k/k_0 X = I	Log k/k_0 X = Tos
Methyl	0	0
Ethyl	−0.108	−0.116
Isopropyl	−0.44	−0.47
tert-Butyl	−1.61	−1.66
n-Propyl	−0.112	−0.122
Isobutyl	−0.141	−0.137
Neopentyl	−0.29	−0.27

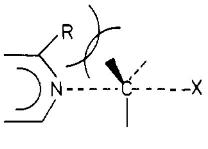
Table II. Relative Rate Constants for N-Methylation of 2-Substituted Pyridines by Methyl Iodide and Methyl Fluorosulfonate at 30 °C

Substituent	Log k/k_0 X = I (in acetone)	Log k/k_0 X = SO_3F (in benzene)
H	0	0
Methyl	−0.42	−0.29
Amino	−0.08	−0.15
Ethyl	−0.62	−0.51
Isopropyl	−1.30	−0.94
Phenyl	−2.00	−1.38
Chloro	−2.37	−1.62
Cyano	−3.09	−2.17
tert-Butyl	−3.58	−2.58

sition state structure have been reported. Such data include chlorine kinetic isotope effects in nucleophilic displacements on R–Cl[4] and substituent effects on solvent sensitivity[5] and on leaving group sensitivity[6] in the SN2 reaction. We recently proposed[7] to use a quantitative equation correlating rate constants to steric parameters as a tool for such an aim.

We wish to report experimental evidence for geometrical variations in the transition state of the Menshutkin reaction with a change of the leaving group.

Consider the SN2 reaction with a 2-substituted pyridine or 2-substituted thiazole as the nucleophile and a substrate of the type CH_3X. The rate of this reaction has been shown to be strongly dependent upon the steric requirements of the 2-substituent.[8] Thus the rate will also be expected to be sensitive to the length of the bond being formed in the transition state (the C–N bond), since the steric strain varies with this distance. The shorter the C–N length the more important will be the steric interaction between the substituent R and the central methyl.



Thornton,[2] as well as Harris and Kurz,[3] predict that an increase in the basicity of the leaving group moves the transition state closer to the products, which implies a shortening of the C–N bond. If these theoretical predictions are safe, we can expect that the sensitivity to steric effects will decrease with the nature of the leaving groups in the order TsO > I > SO_3F. These theoretical approaches, however, do not tell us what variation in the leaving group is needed in order to make this effect experimentally observable.

In the first series, 2-alkylthiazoles were methylated by methyl iodide or methyl tosylate. The rate constants were determined in nitrobenzene by a conductometric technique previously described,[9] and the results are shown in Table I and Figure 1.

In a second series, ortho-substituted pyridines were methylated by methyl iodide or methyl fluorosulfonate. The kinetics with methyl iodide was followed by the conductometric method in acetone. The high reactivity of methyl fluorosulfonate made it impossible to run the kinetics in acetone or any other solvent suitable for the conductometric method. This reaction series was instead studied by a competitive technique[8d,10] with benzene as solvent. Several investigations indicate that such competition reactions are almost solvent independent in aprotic media.[11] The results are presented in Table II and Figure 2.

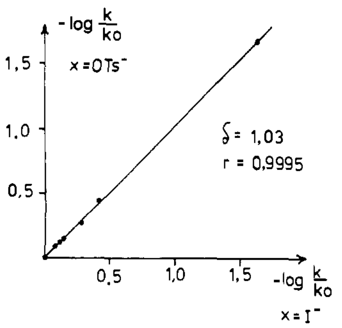


Figure 1. Plot of relative rates for methylation of 2-substituted thiazoles with methyl iodide or methyl tosylate (δ = slope; r = correlation coefficient).

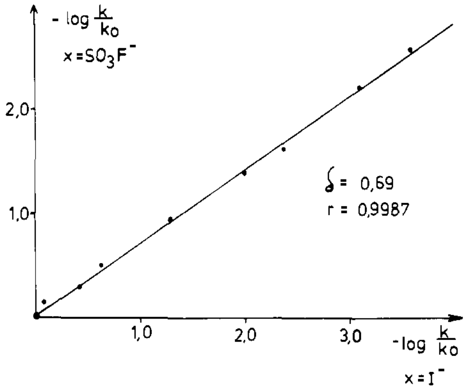


Figure 2. Plot of relative rates for methylation of 2-substituted pyridines with methyl iodide or methyl fluorosulfonate (δ = slope; r = correlation coefficient).

In both plots excellent linear correlations are obtained. The slope of a plot, log $(k/k_0)_X = \delta \log (k/k_0)_I$, should be expected to deviate from unity if the basicity of the two leaving groups is different enough to change the position of the transition state on the reaction coordinate axis. This is obviously the case in the pyridine series.[12] A value lower than unity should be expected in view of the reactivity of the leaving groups. Alkyl fluorosulfonates alkylate tertiary amine 10^4 times faster than do alkyl iodides.[13]

In the thiazole series no significant deviation of the slope from unity was obtained. This is probably due to a combination of two important differences between the systems studied. Firstly, the difference in reactivity between tosylate and iodide is much lower than between fluorosulfonate and iodide (a factor of 3 in the former case and a factor of 10^4 in the latter[13]). Secondly, methylation of ortho-substituted pyridines is twice as sensitive to the steric effect of the ortho substituent as methylation of 2-substituted thiazoles because of the smaller distance between the substituent and the reaction center in the pyridine case.[7]

In conclusion the present results experimentally establish the theoretical prediction stating that an increase of the basicity of the leaving group moves the transition state of an SN2 reaction closer to the products. Nevertheless the variation of structure in the transition state brings significant modifications to the sensitivity to steric effects only for important changes in leaving group ability.

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(12) According to theoretical predictions,[2,3] the introduction of an electron-withdrawing substituent in the nucleophile of an SN2 transition state will shorten the reacting bond which is nearer the substituent (the C–N bond). In the pyridine series with substituents of very different electronic character (alkyl, NH$_2$, CN), all compounds fall on one straight line (Figure 2) within the limits of experimental error. Thus these effects cancel out even when leaving groups as different as iodide and fluorosulfonate are compared.
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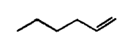
Thermal Decomposition of *cis*- and *trans*-3,4- and -3,6-Dimethyl-3,4,5,6-tetrahydropyridazines. Evidence against the Hot Diradical Postulate for Azo Decompositions

Sir:

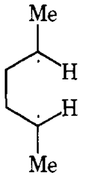
Tetramethylene diradicals are the hypothetical reactive intermediates postulated to intervene in the dimerization of olefins and the thermal cleavage of cyclobutanes.[1] Experimental efforts using stereochemical probes have been directed toward generating these reactive intermediates from different appropriately substituted precursors (olefins,[2] cyclobutanes,[3] azo compounds,[4] diazenes,[5] ketones,[6] and sulfolanes[7]) in order to characterize their behavior. Unfortunately differences in substitution, temperature, and reaction conditions have made direct comparisons of product distributions difficult.

An important 1,4-diradical with secondary radical centers is 2,5-hexanediyl (**1**),[3,6b,c,8,9] the hypothetical reactive intermediate formed by thermal cleavage of the most substituted bond in *cis*- and *trans*-1,2-dimethylcyclobutanes (studied in the gas phase at 425 ± 25° by Gerberich and Walters in 1961[3a]). Although *cis*-3,6-dimethyl-3,4,5,6-tetrahydropyridazine (**2**) has been in the literature for over a decade,[10] no successful decomposition of this pivotal azo compound for the study of **1** has been reported, nor has a synthesis of the corresponding trans isomer **3** appeared, apparently frustrated by the notoriously facile irreversible azo to hydrazone tautomerization associated with azo compounds that have enolizable hydrogens.[4b,10,11]

Table I. Percent Yields^a

Reactant	Conditions	2 			
cis-**2**	*b*	74.7	8.5	16.3	0.5
	c	72.9	9.7	16.3	1.1
trans-**3**	*b*	80.5	12.7	5.7	1.1
	c	74.4	14.9	8.9	1.8

^{a}Percent yield based on total hydrocarbon product. Typical absolute yields of hydrocarbon products from **2** and **3** were 50 and 80% at 306° and 439°, respectively. VPC analysis using 20 ft. × 1/8 in. 10% dibutyl tetrachlorophthalate; flame ionization detector. ^{b}Chamber pyrolysis (30 s at 306 ± 2°, est pressure >25 mm). ^{c}Chamber pyrolysis (5 s at 439 ± 2°, est pressure >31 mm).



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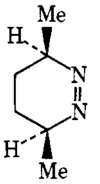
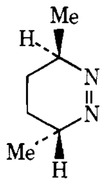


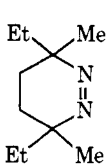
2



3

We now wish to report the successful stereospecific synthesis[12] and thermal decomposition in the gas phase (306–439°) of both *cis*- and *trans*-3,6-dimethyl-3,4,5,6-tetrahydropyridazines (**2** and **3**, respectively). Conditions and results of the pyrolyses are listed in Table I.[18]

Examination of the 1,2-dimethylcyclobutane product ratios from the cis- and trans azo decompositions (**2** and **3**, respectively) reveals that, although overall retention is preserved, the loss of stereochemistry in the closure products is relatively high (at 306°, retention/inversion (r/i) ratios are 1.9 and 2.2 from **2** and **3**, respectively) compared to the more highly substituted cyclic azo system with tertiary radical centers reported by Bartlett and Porter (at 148°, r/i ratios are ≥49 from both *meso*-, and *dl*-azo-**4**).[4a] If 1,4-diradicals with secondary centers intervene in the decomposition of **2** and **3**, the data indicate that carbon–carbon bond rotation is *competitive* with cleavage and closure. Thus, the intermediates formed from azo compounds **2** and **3** are similar in behavior to those from the thermal decomposition of *cis*- and *trans*-1,2-dimethylcyclobutanes.[3a]



4

Stephenson and Brauman[8] attempted to explain the high stereospecificity observed in the cyclic azo-**4** decomposition (as compared to the less stereospecific thermal reactions of 1,2-dimethylcyclobutanes) by directing attention to the *mode of generation* of the intermediates in the two cases. They explained the higher stereospecificites observed from **4** by suggesting that vibrationally "hot" 1,4-diradicals are