The Synergic Nucleophilic and Electrophilic Properties of Carbenes. Synthesis of Carbazoles, Azafluorenes, δ-Carbolines, and Pyrido- and Pyrimido[2,1-*a*]isoindoles by Carbene Rearrangement. Tracer Studies of the Mechanisms and an Analysis of the ^{13}C Nuclear Magnetic Resonance Spectra of Azafluorenes[1]

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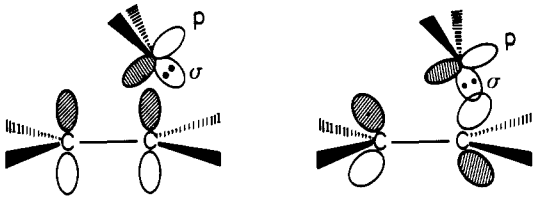
Abstract: Arylhetarylcarbenes were generated by gas-phase thermolysis of triazoles and diazo compounds. Thermolysis of 3-phenyl-*v*-triazolo[1,5-*a*]pyridine and derivatives substituted by Me, MeO, Cl, NO_2, or CN (**8a–h**) gave carbazoles (**22a–h**) in yields up to 100%. 3-(2-Naphthyl)-*v*-triazolo[1,5-*a*]pyridine (**8i**) gave a benzo[*a*]carbazole (**22i**; 30%), a benzopyrido[2,1-*a*]isoindole (**23i**; 48%), and a 5*H*-benzindeno[1,2-*b*]pyridine (**24i**; 16%). Phenyl-3-pyridyldiazomethane yielded a 56:44 mixture of 1- and 3-azafluorene (9*H*-indeno[2,1-*b*]pyridine and 5*H*-indeno[1,2-*c*]pyridine) (42%). Phenyl-3-pyridyldiazomethane-^{13}C (**11**) was synthesized, and thermolysis gave 1- and 3-azafluorene (**29**, **30**) labeled ≥93% in position 4b (benzene ring). Phenyl-4-pyridyldiazomethane yielded 2-azafluorene (9*H*-indeno[2,1-*c*]pyridine) (70%). Phenyl-4-pyridyldiazomethane-^{14}C (**14**) was synthesized, and thermolysis gave 2-azafluorene (**15**), which was degraded to 4-aminonicotinic acid (~92% ^{14}C) and barium carbonate (~8% ^{14}C). 5,7-Dimethyl-3-phenyl-*v*-triazolo[1,5-*a*]pyrimidine (**33**) yielded 2,4-dimethylpyrimido[2,1-*a*]isoindole (**36**; 72%) and 2,4-dimethyl-5*H*-pyrido[3,2-*b*]indole (**35**; 14%), also synthesized by photolysis of 2,4-dimethyl-5-anilinopyridine (**37**). Simplified syntheses of nicotinic acid-^{13}C and isonicotinic acid-^{14}C are described. The ^{13}C NMR spectra of 1-, 3-, and 4-azafluorene were analyzed in detail by means of $Eu(dpm)_3$ and $Pr(dpm)_3$ induced shifts, and by measurement of relaxation times in the presence of $Gd(dpm)_3$. The thermolysis results are in disagreement with any hypothesis that the arylhetarylcarbenes behave purely as electrophiles *or* nucleophiles in the rearrangement reactions. It is postulated that the ring expansion in arylcarbenes and -nitrenes is the result of a synergic electrophilic and nucleophilic interaction between the carbene or nitrene center and the ring: a p–π and a σ–π* interaction. The relative rates of all known nitrene rearrangements appear to correlate qualitatively with the ring-LUMO coefficients in the positions to which the nitrenes are attached.

It is generally accepted that carbenes and nitrenes react as typically electrophilic species, for example, in their addition to double bonds.[2] Exceptions are cycloheptatrienylidene[3,4] and cyclopropenylidene[5] where the vacant carbene p orbital is part of an aromatic $(4n + 2)$ π system; these carbenes undergo nucleophilic addition to double bonds. It has further been suggested that difluorocarbene undergoes nucleophilic 1,4-addition to norbornadiene.[6]

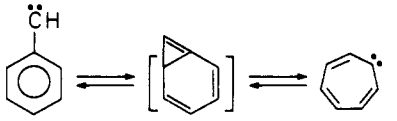
We have previously expressed the view that carbenes and nitrenes might be able to show both nucleophilic and electrophilic properties.[7–9] If the line of approach of a singlet carbene to a double bond is represented by **1**[10] (a p–π interaction), the energy of the transition state would be lowered if a simultaneous delocalization of the carbene sp^2 electrons



1 (p–π) **2** (σ–π*)

into the LUMO of the alkene could occur (a σ–π* interaction) (**2**). Such an interaction would be favored by a low-lying LUMO possessing a large coefficient in the position where carbene attack occurs.

We now report evidence that arylcarbenes can show both electrophilic and nucleophilic properties in their intramolecular ring expansions (eq 1). The ring expansions may take



3 **4** **5** (1)

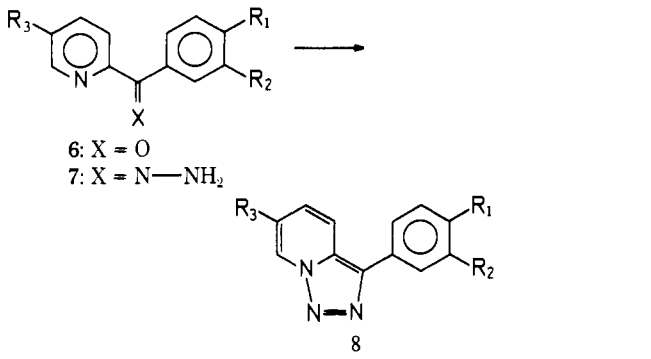
place via bicycloheptatriene intermediates (**4**), which have been trapped in cases where they are stabilized by annelation,[11] but the formation of **4** as a discrete intermediate is not a prerequisite for reactions of the type shown in eq 1.[9] Examples of rearrangements are known in which the existence of intermediates like **4** are highly unlikely.[12] However, CNDO/2 and Extended Hückel calculations indicate that the carbene carbon in **3** (and the N atom in analogous nitrenes) must move out of the plane of the benzene ring on the path of minimum energy leading to **5**.[9] The transition state must then structurally resemble **4**. The following arguments are independent of the possible existence of intermediates like **4**, and such structures are usually omitted.

Many examples of rearrangements analogous to eq 1 are known.[12,13] In the context of the present paper, it is particularly important to note that the rearrangement of diphenylcarbene to fluorene has been shown[13,14] to proceed by an expansion–contraction mechanism.

Results

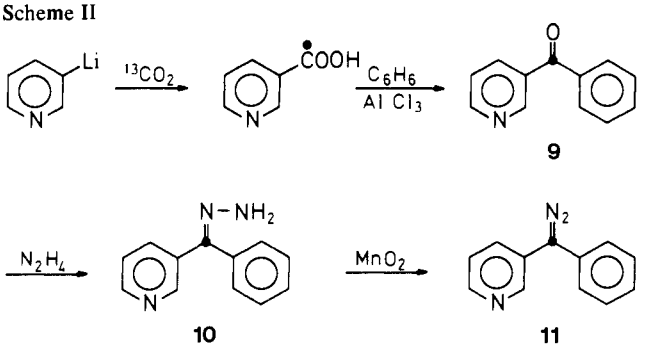
A. Syntheses. *v*-Triazolo[1,5-*a*]pyridines (**8**) were generally prepared by oxidation of the hydrazones (**7**) of the corresponding ketones (**6**)[15] (Scheme I). The ketones **6a–c** and **6g–i** were prepared by reaction of the corresponding benzo-

Scheme I

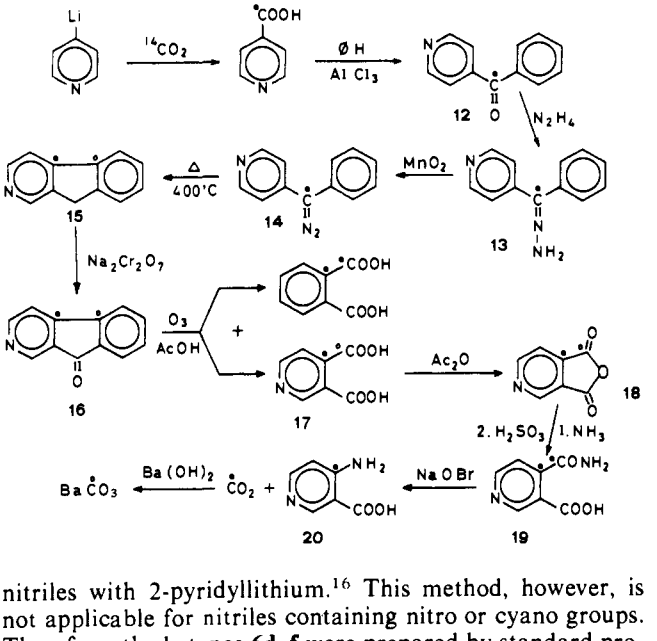


6-8	a	b	c	d	e	f	g	h	i
R_1	H	OMe	Cl	NO_2	CN	H	H	H	C_4H_4
R_2	H	H	H	H	H	NO_2	OMe	H	
R_3	H	H	H	H	H	H	H	CH_3	H

Scheme II



Scheme III



nitriles with 2-pyridyllithium.[16] This method, however, is not applicable for nitriles containing nitro or cyano groups. Therefore, the ketones **6d–f** were prepared by standard procedures, outlined in the Experimental Section.

Phenyl-3-pyridyldiazomethane-^{13}C (**11**) was prepared from $Ba^{13}CO_3$ (90% ^{13}C) by the procedure indicated in Scheme II. The carboxylation with $^{13}CO_2$ has been reported previously by Murray et al.[17] A modified, simpler apparatus is described in the Experimental Section.

Phenyl-4-pyridyldiazomethane-^{14}C (**14**) was prepared in a similar way from 4-pyridyllithium and $Ba^{14}CO_3$ (Scheme III). Gas-phase thermolysis of **14** yielded 2-azafluorene (**15**), which was degraded as follows. Dichromate oxidation of **15** followed by ozonolysis yielded a mixture of phthalic

Table I. Products of Thermolysis of *v*-Triazolo[1,5-*a*]pyridines (8)

Starting compd 8	Conditions[a]	Yields of products, % 22	23	24
a	500 (0.02)	99.74		
	900 (0.05)	99.25	*j*	*j*
b	380 (0.001)	95[b]	*j*	*j*
c	380 (0.001)	26[c]	*j*	*j*
d	400 (0.001)	88[d]	*j*	*j*
e	400 (0.001)	49[e]	*j*	*j*
f	380 (0.001)	67.5[f]	*j*	*j*
g	500 (0.005)	90[g]	*j*	*j*
h	500 (0.02)	94[h]		
i	380 (0.001)	30[i]	48	16

[a] Thermolysis conditions expressed as temperature (°C) [pressure (mm)]. [b] 2-Methoxycarbazole, mp 237° [lit. 236° (H.-J. Teuber and D. Cornelius, *Justus Liebigs Ann. Chem.*, 671, 127 (1964))]. [c] 2-Chlorocarbazole, mp 243° (subl) [lit. 244° (F. Ullmann, *Justus Liebigs Ann. Chem.*, 332, 82 (1904))]. [d] 2-Nitrocarbazole; see Experimental Section. [e] 2-Cyanocarbazole; see Experimental Section. [f] Ca. 1:3 mixture of 1- and 3-nitrocarbazole, separated by TLC [silica gel–chloroform; R_f = 0.45 and 0.64, identical with a synthetic mixture (G. T. Morgan and J. G. Mitchell, *J. Chem. Soc.*, 3283 (1931))]. [g] Mixture of 1- and 3-methoxycarbazole. [h] 2-Methylcarbazole; see Experimental Section. [i] Benzo[*a*]carbazole; see Experimental Section. [j] Not detectable by NMR of crude pyrolysate in CF_3COOH.

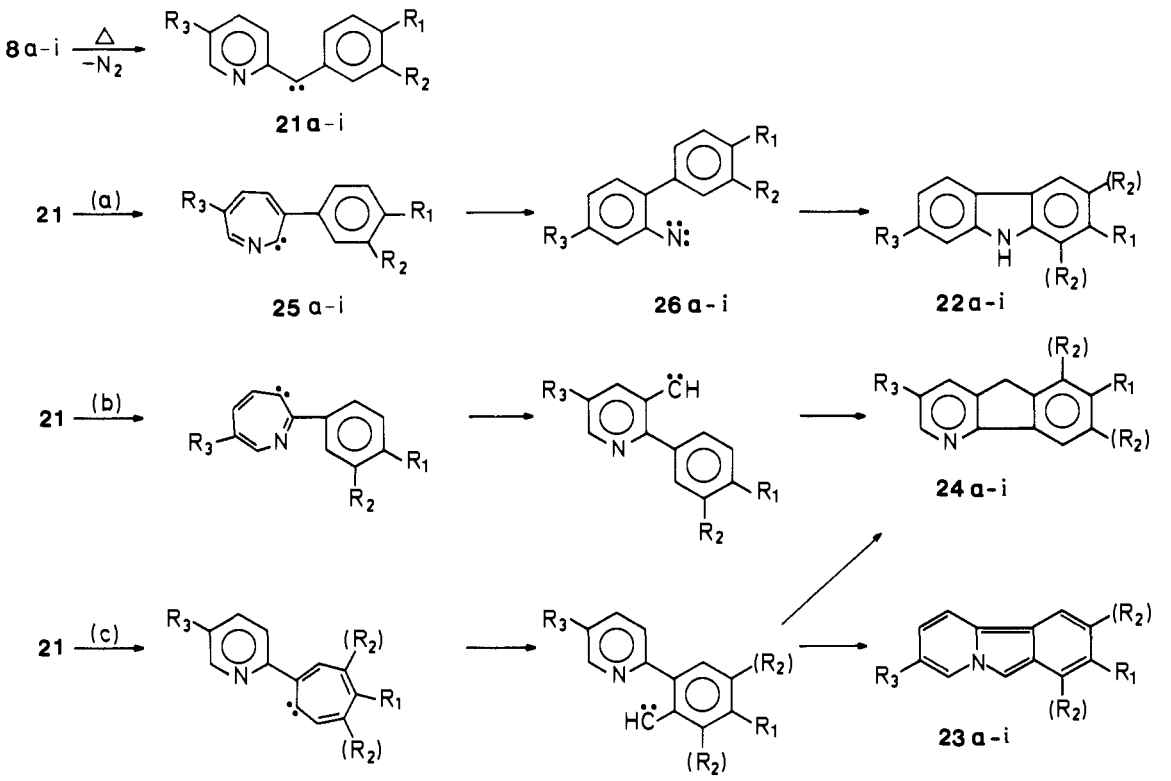
acid and pyridine-3,4-dicarboxylic acid (**17**). The latter was converted to its anhydride **18** and selectively opened[18] to 4-carboxamidonicotinic acid (**19**) by consecutive treatment with acetic anhydride, ammonia, and sulfur dioxide. A Hofmann's rearrangement of **19** afforded 4-aminonicotinic acid (**20**) and CO_2, the latter being isolated as $BaCO_3$ (Scheme III). The results of radiochemical assays are indicated in Table VII.

B. 2-Pyridylphenylcarbenes. Triazolo[1,5-*a*]pyridine undergoes valence tautomerism to 2-diazomethylpyridine in solution.[19] It is well known that diazomethanes yield carbenes on thermolysis.[20] It is therefore reasonable to assume that the 2-pyridylphenylcarbenes **21a–i** are formed by gas-phase thermolysis of **8**. The carbenes **21a–i** can a priori rearrange in three different ways, leading to three different product types, **22–24** (Scheme IV, paths a–c).

Gas-phase thermolysis of **8a–h** at temperatures between 380 and 900° (10^{-3}–10^{-2} mm) yielded carbazoles **22a–h** as the exclusive products in yields up to 100% (Table I). The specific formation of 2-methylcarbazole (**22h**) from **8h** demonstrates that the reaction (path a) must take place via an intermediate in which the atoms are disposed as in the azepinylidene **25**, that is, by carbene insertion into the 2,3-bond in pyridine. Further evidence for reaction pathway a is found in the rearrangement of 2-pyridylcarbene itself to phenylnitrene[21] which has been confirmed by ^{13}C-labeling.[12,22] The cyclization of 2-biphenylylnitrenes (**26**) to carbazoles is well documented.[23]

A search for 4-azafluorene (**24a**) by gas chromatography of the pyrolysate of **8a** was negative. Path b (Scheme IV) can therefore be excluded. It is known that pyridoisoindoles (**23**) would result from pathway c (vide infra), and their presence was carefully examined in the pyrolysates of **8a–h**. Protonation of pyridoisoindoles with trifluoroacetic or mineral acids yields the stable salts **27**[24] in which the CH_2 group is distinctly observable by NMR at $\delta \sim 5.5$. Basification of an aqueous solution of **27** with solid KOH results in

Scheme IV



the immediate precipitation of strongly colored **23,** usually yellow or red. Both the direct observation by NMR and the color test were negative for the pyrolysis products of **8a–h.** Reaction path c (Scheme IV) can therefore be excluded in these cases.

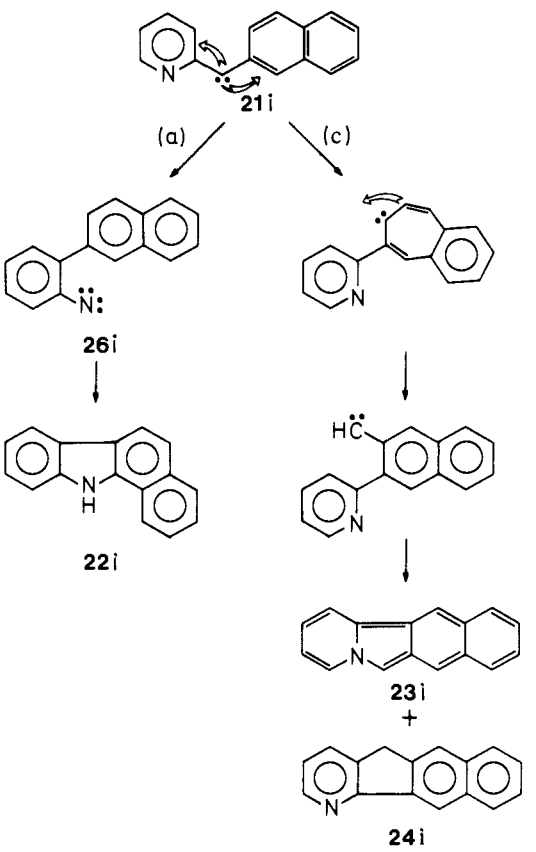
By contrast, 3-(2-naphthyl)-*v*-triazolo[1,5-*a*]pyridine (**8i**) yielded all three products, **22–24i** (Table I). **23i** and **24i** probably have linear arrangements of the rings since 2-naphthylcarbenes undergo expansion exclusively by insertion into the 1,2-bond, and not the 2,3-bond in naphthalene[13] (Scheme V). The carbazole **22i** was exclusively benzo[*a*]carbazole, which has also been obtained directly from 2-(2-naphthyl)phenylnitrene (**26i**).[25,26] The simultaneous formation of **22i** and **23i** demonstrates that both pathways a and c are now occurring. **24i** could in principle arise from either pathway b or c, with c being the more probable one.

C. **Phenyl-3-pyridylcarbene.** Gas-phase thermolysis of phenyl-3-pyridyldiazomethane (**11**) at 400° (10^{-3} mm) gave a 56:44 mixture of 1- and 3-azafluorene (9*H*-indeno-[2,1-*b*]pyridine (**29**) and 5*H*-indeno[1,2-*c*]pyridine (**30**)). As shown in Scheme VI, these products may arise by expansion of either the benzene or pyridine rings, and the reaction paths can only be distinguished by carbon labeling. In order to use ^{13}C-labeling as a mechanistic tool, it is necessary to analyze the carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra of the azafluorenes in detail. This is described in section F.

Phenyl-3-pyridyldiazomethane-^{13}C (**11**; 89% ^{13}C) was thermolyzed at 400° (10^{-3} mm) and the product mixture analyzed by ^{13}C NMR. Afterward, **29** and **30** were separated by gas chromatography, and the spectrum of pure **29** was re-recorded. 3-Azafluorene (**30**) is a surprisingly unstable compound which decomposed partly by GLC so that its ^{13}C NMR spectrum could not be used.

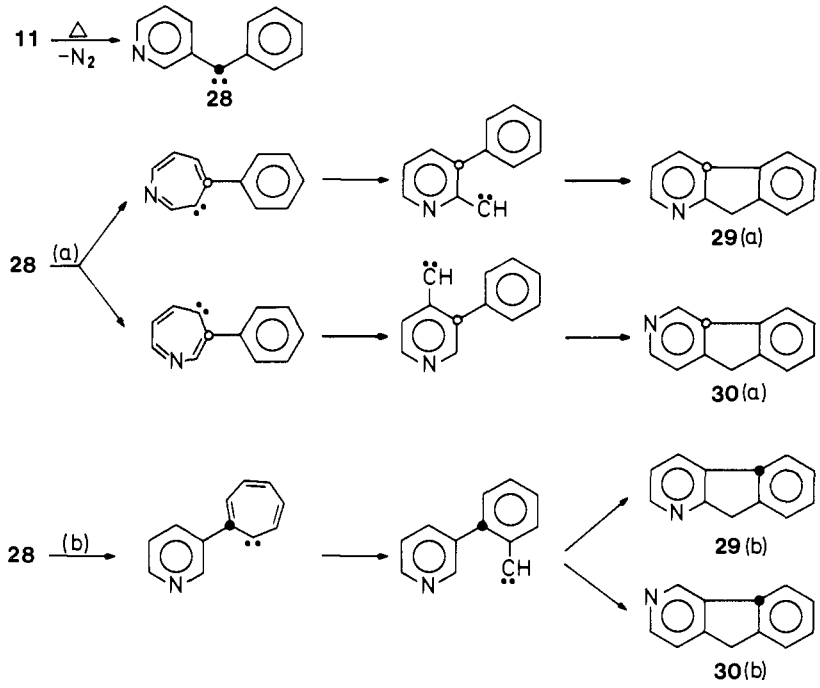
The spectra of the mixture and of pure isolated **29** showed that **29** was labeled 100% on C-4b. (For numbering, see Figure 2.) From the spectrum of the mixture, it was evident that 3-azafluorene (**30**) was labeled at least 84% on

Scheme V

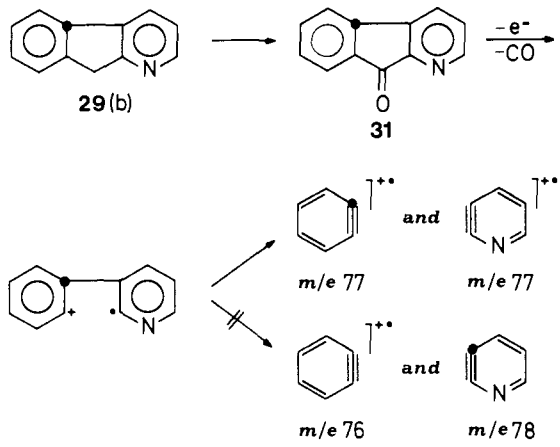


C-4b. A small peak (~16%) near the chemical shift of C-4a could be due either to labeling of C-4a or, more likely, to one of the several decomposition products of **30.** In any case, these results demonstrate that at least 93% of the label in the combined product is present in position 4b, and thus

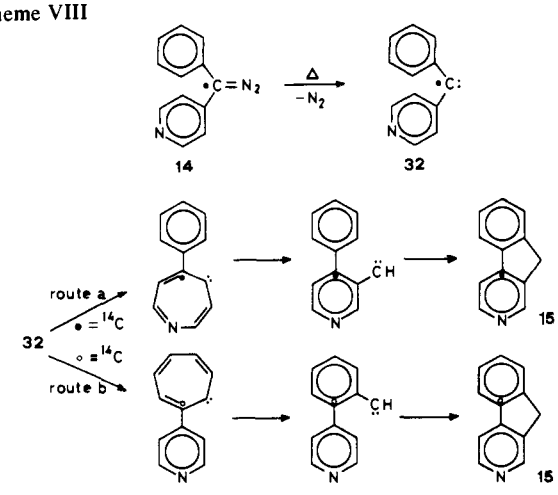
Scheme VI



Scheme VII



Scheme VIII



that *the rearrangement in Scheme VI takes place overwhelmingly by expansion of the benzene ring* (route b).

In order to verify this conclusion, the isolated 1-azafluorene-*4b*-^{13}C (**29b**) was oxidized to the fluorenone **31** and its mass spectrum recorded. Fluorenone itself is known to eliminate CO in the mass spectrometer and then fragment to two benzynes.[27] Similar fragmentations are observed in the mass spectra of the azafluorenones, as indicated in Scheme VII for **31**. The spectra are listed in the Experimental Section and support the conclusion that ^{13}C is located in the benzene ring, causing an increase in the ion current at *m/e* 77, rather than at *m/e* 76 and 78.

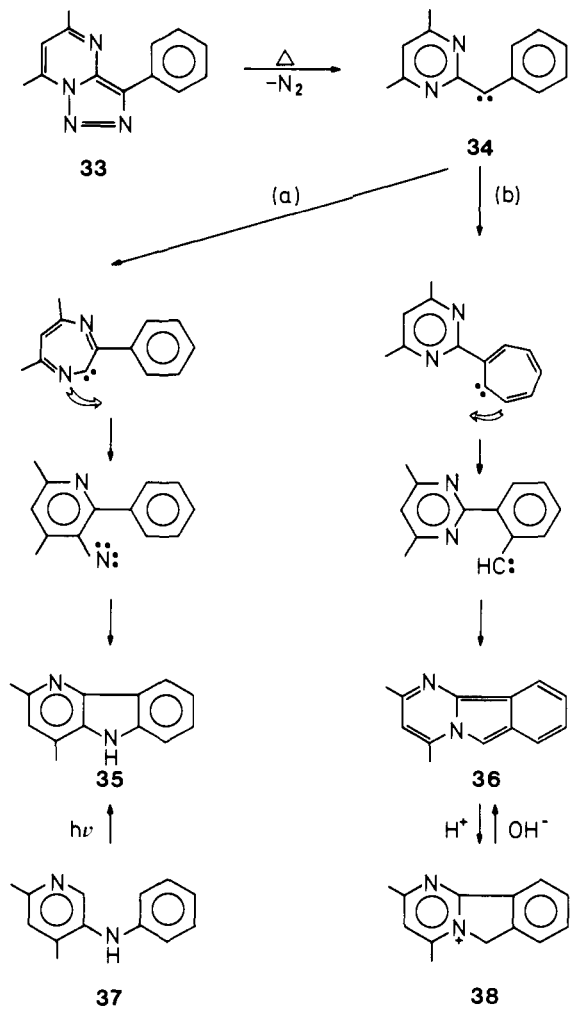
D. Phenyl-4-pyridylcarbene. Thermolysis of phenyl-4-pyridyldiazomethane at 500° (10^{-3} mm) gave 2-azafluorene (9*H*-indeno[2,1-*c*]pyridine) (**15**) in yields up to 70%. The pyrolysis product needs no further purification, thus making this the simplest preparation of 2-azafluorene available. As shown in Scheme VIII, 2-azafluorene can arise from phenyl-4-pyridylcarbene in two ways, which can only be distinguished by carbon labeling: expansion of the pyridine ring (route a), or of the benzene ring (route b). ^{14}C labeling, thermolysis, and degradation according to Scheme III resulted in 4-aminonicotinic acid (**20**) containing 91.4% of the label, and $BaCO_3$ containing 8.6% of the label (cf. Table VII). Thus, *carbene* **32** *is shown to rearrange preferentially by pyridine ring expansion* (route a, Scheme VIII).

E. Phenyl-2-pyrimidylcarbene. Gas-phase thermolysis of 5,7-dimethyl-*v*-triazolo[1,5-*a*]pyrimidine (**33**) (Scheme IX) resulted in two products, 2,4-dimethyl-5*H*-pyrido[3,2-*b*]indole (**35**; 14%) and 2,4-dimethylpyrimido[2,1-*a*]isoindole (**36**; 72%). **35** was identified by analysis and by independent synthesis by photocyclization of 2,4-dimethyl-5-anilinopyridine (**37**). **36** was identified by exact mass measurement, spectroscopy, and the characteristic reversible formation of a salt **38** exhibiting a CH_2 signal at δ 5.55 in the NMR spectrum (Figure 1). **36** is easily separated from other thermolysis products by dissolution in aqueous acid and filtration; on basification of the filtrate, yellow crystalline **36** precipitates. Although highly reactive, **36** can be stored indefinitely in an inert atmosphere in the cold.

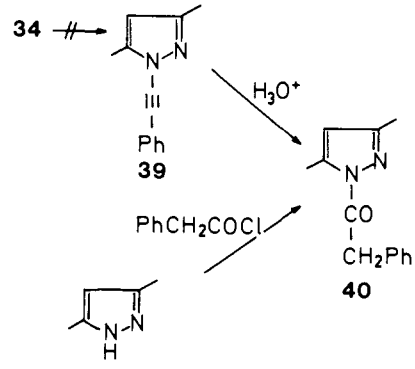
The formation of **35** and **36** in the above thermolysis demonstrates that **34** can undergo expansion of both the pyrimidine and benzene rings. The latter (route b) is favored by a factor of ca. 5.

Originally we believed that carbene **34** could undergo ring contraction to 3,5-dimethyl-1-phenylethynylpyrazole (**39**). The crude thermolysis product of **33** did in fact exhibit a medium to weak band in the ir spectrum near 2200

Scheme IX



cm^{-1}, which is not incompatible with an ethynylamine.[28] However, a search for **39** by acid hydration[29] to **40** followed



by gas chromatography was negative. **40** was independently synthesized from 2,4-dimethylpyrazole and phenacetyl chloride. Pyrolysis of **36** at 400° (10^{-3} mm) resulted in quantitative recovery, and no ir band at 2200 cm^{-1} was observable. The band at 2200 cm^{-1} in the pyrolysate of **33** is probably due to a small nitrile impurity.

F. Analysis of the ^{13}C NMR Spectra of Azafluorenes. A detailed analysis of the ^{13}C NMR spectra of 1- and 3-azafluorene was essential in order to elucidate the reaction pathways of phenyl-3-pyridylcarbene (**28**). In particular, it was of paramount importance to distinguish carbon atoms 4a and 4b (for numbering, see Figure 2). For this purpose, commercially available 4-azafluorene was first studied. Four criteria for the assignment of chemical shifts were used: (1) correlation with known ^{13}C shifts in related compounds; (2) shifts induced by Eu(dpm)$_3$; (3) shifts induced by Pr(dmp)$_3$; and (4) measurement of relaxation times (T_1) in the presence of Gd(dpm)$_3$. The results for 4- and 1-azafluorene are reported in Tables II and III, respectively.

Table II. ^{13}C NMR Data for 4-Azafluorene[a]

Peak No.	Attribution carbon No.	$\delta_{^{13}C}$, ppm	Expected shift,[b] ppm	$\Delta\delta$ Eu (dpm)$_3$[c]	T_1 Gd msec[d]	r,[e] Å
a	4a	158.9	159	4.64	350	3.9
b	3	146.9	146.4	10.6	236	3.9
c	8a	142.5	143	1.55	1500	5.6
d	4b	139.9	138–141	2.0	550	4.1
e	9a	135.7	136	−0.44	1100	5.3
f	1	130.8	131–133	2.4	2200	
g	6/7	127.5	126–128	0.7	2500	
h	6/7	125.9	126–128	0.7	2500	
i	8 (2)	124.0	124.8	0.7	4300	
j	5	119.8	119.7	4.0		
k	2 (8)	119.8	119–121	2.0		
l	9	33.6	37	1.3$_3$		

[a] ^{13}C chemical shifts relative to Me_4Si; downfield shifts are counted positive; solvent $CDCl_3$ (dried and distilled); quaternary carbons were identified from the off-resonance proton decoupled spectra; for numbering, see Figure 2. [b] By comparison with known shifts of pyridines, benzenes, fluorenes, and other condensed aromatics.[30] [c] Shift induced by 300 mg of Eu (dpm)$_3$, added to a saturated solution of 4-azafluorene in $CDCl_3$. [d] T_1 relaxation time with (subscript Gd) or without (subscript dipole–dipole) Gd(dpm)$_3$. T_1Gd calculated from $(1/T_{1\text{measd}})_{Gd} = (1/T_{1Gd}) + (1/T_{1\text{dipole-dipole}})$.[31] Measurements were on $CDCl_3$ solutions, 3 M in 4-azafluorene and 0.01 M in Gd(dmp)$_3$. [e] Gd–C distances calculated from fluorene geometry[32] using r_{Gd-N} = 3.0 Å[31] with Gd on the C_4–N axis.

It is known that the pseudo-contact isotropic shift model is not applicable to pyridine bases with shift reagents such as Eu(dpm)$_3$.[33-35] In particular, the carbons meta to the pyridine nitrogen show near-zero or negative shifts with Eu(dpm)$_3$.[33-35] This fact allows us to assign unambiguously the meta carbon 9a in 4-azafluorene (Table II), and the meta carbons 4a and 3 in 1-azafluorene (Table III). It is further known that the deviation from the pseudo-contact shifts is less pronounced with Pr(dpm)$_3$.[34,36] The shifts induced by this reagent follow qualitatively the inverse distance dependency. Thus, from the shifts induced by Eu(dpm)$_3$ and Pr(dpm)$_3$, it was possible to assign all carbon signals in 1-azafluorene, except C_6/C_7, by comparison with the known shifts induced in pyridine, quinoline, and isoquinoline[33-35] (Table III). It is seen that the assignments all agree with the values expected from correlation with known compounds.

Finally, the relaxation times (T_1) induced by Gd(dpm)$_3$ are proportional to r^6, where r is the distance between Gd and the carbon nucleus in question.[31] For two nuclei i and j, eq 2 is valid.

$$(T_i)^{1/6}/(T_j)^{1/6} = r_i/r_j \quad (2)$$

Equation 2 has been tested with 4-picoline.[31] The results for 4- and 1-azafluorene (Tables II and III) satisfy eq 2 with the same precision as obtained with 4-picoline.

Thus, four independent assignments of ^{13}C chemical shifts gave identical results. The spectrum of 3-azafluorene was then interpreted by comparison with the known shifts in 1- and 3-azafluorene (Table IV).

G. Synthetic Utility of the Pyrolysis Reactions. The carbazoles **22** obtained by carbene rearrangement (Table I) are also available from thermolysis of 2-biphenylyl azides.[25] The carbene route has the advantage that the precursors (**8**)

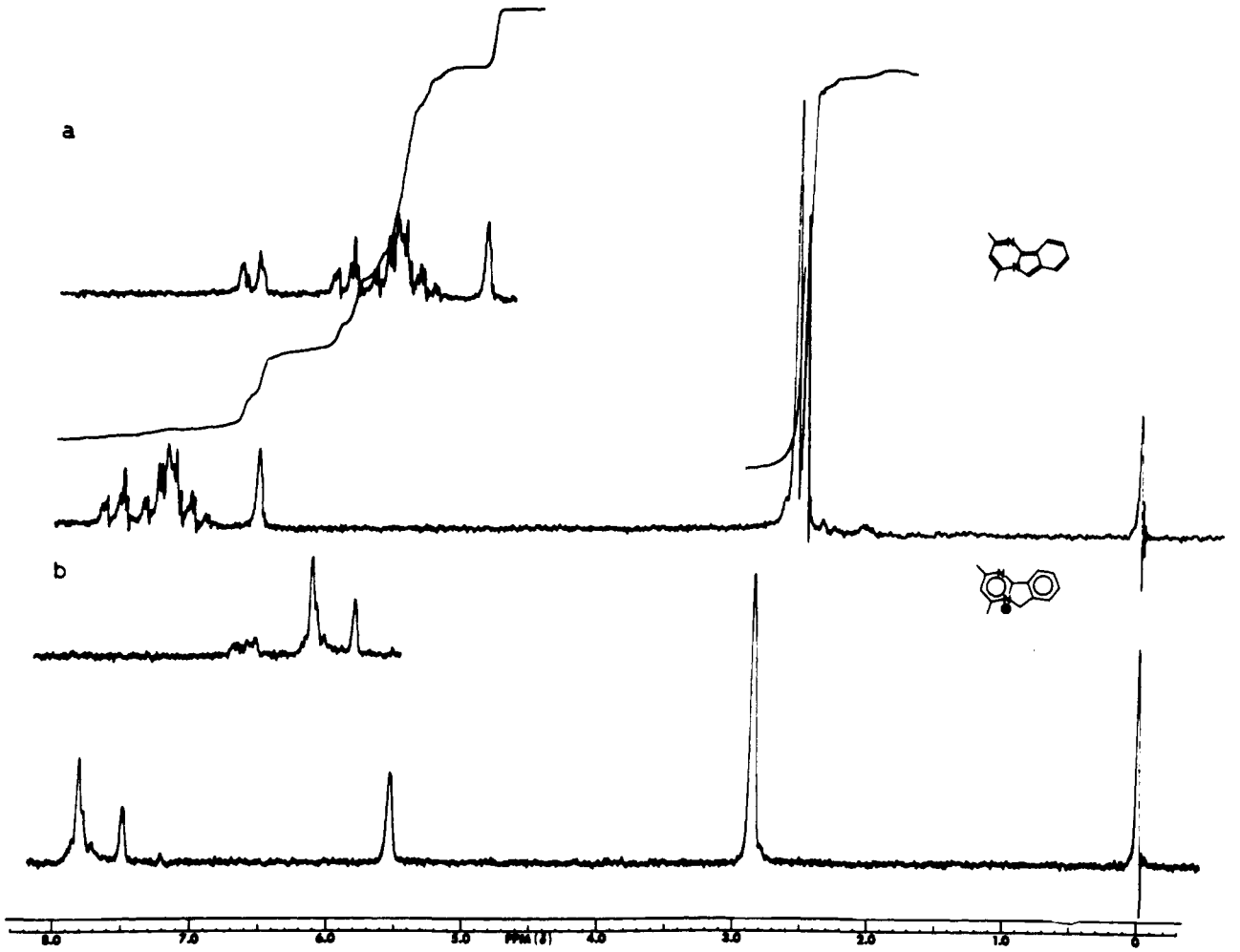


Figure 1. NMR spectrum of 2,4-dimethylpyrimido[2,1-*a*]isoindole (**36**): (a) in $CDCl_3$; (b) after addition of CF_3COOH to the $CDCl_3$ solution.

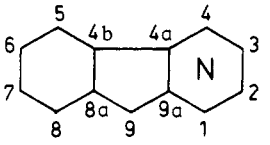


Figure 2. Numbering of azafluorenes used in ^{13}C NMR analysis.

are stable. Whether azides or triazoles are used as starting materials, gas-phase thermolysis leads to pure, crystalline products which usually need no further purification.

Gas-phase thermolysis of **8i** and **33** offers easy access to the interesting pyrido- and pyrimido[2,1-*a*]isoindoles, **23i** and **36**. **36** is very unstable in solution, and this ring system was previously unknown. Only a few examples of pyrido[2,1-*a*]isoindoles have been reported.[24,37]

1- and 3-azafluorenones were previously available only from lengthy low-yield syntheses. Doebner et al. obtained 1-azafluorenone in unspecified yield by decarboxylation of indeno[2,1-*b*]pyridine-9-one-2,4-dicarboxylic acid.[38] A more convenient synthesis is via the oxidation of benzo[*f*]quinoline (see Experimental Section), yield 12%. 1-Azafluorene appears to be a previously unknown compound. We prepared it from the ketone in 77% yield. 3-Azafluorene was prepared in 1.5% overall yield by Chatterjea et al.[39] by oxidation of benzo[*h*]isoquinoline to 3-phenylpyridine-4,2′-dicarboxylic acid followed by decarboxylation to 3-azafluorenone and Wolff-Kishner reduction. We have improved this yield to 12% overall, isolating the 3-azafluorenone after a one-step alkaline oxidation of benzo[*h*]isoquinoline, and reducing it with hydrazine. The benzo[*h*]isoquinoline itself requires a four-step synthesis,[40] the yield of which we have improved by 26%. Still, the overall yield of 3-azafluorene from commercially available precursors is only 5.6%!

By contrast, the combined yield of 1- and 3-azafluorene by pyrolysis of phenyl-3-pyridyldiazomethane (**11**) is 42% and can probably be improved. The products can be separated by chromatography.

2-Azafluorene has been prepared by Mills[41] in 1% overall yield from 2,6-dimethyl-4-phenylpyridine-3,5-dicarboxylic acid in four steps. Preparation of 2-azafluorene from nicotinic acid via 3-mesitoyl-4-phenylpyridine[42] followed by Clemmensen reduction gave 2-azafluorene in the improved yield of 9% overall (see Experimental Section), which still falls far short of the pyrolysis yield from **14** (70%). The overall yield of 2-azafluorene from phenyl 4-pyridyl ketone via pyrolysis of **14** was 51%.

Discussion

The predominant regioselectivities of ring expansion in the diarylcarbenes studied here are shown (**21a,i**, **28**, **32**, **34**). From these selectivities, it is evident that the carbene ring expansion cannot be regarded as an electrophilic substitution or addition, as it is well known that benzene is much more prone to electrophilic substitution than pyridine. Bond orders cannot be the determining factor either, because the bond orders in pyridine and benzene appear to be identical.[43] Furthermore, carbenes **32** and **28** show opposite selectivities, even though they both have the opportuni-

Table III. ^{13}C NMR Data for 1-Azafluorene[a]

Peak No.	Attribution carbon No.	$\delta_{^{13}C}$, ppm	Expected shift,[b] ppm	$-\Delta\delta$ Pr(dpm)$_3$[c]	$\Delta\delta$ Eu(dpm)$_3$[d]	T_{1Gd}, msec[e]	r,[f] Å
a	9a	163.5	157	20.8	15.7	525	3.9
b	2	146.6	146.4	21.6	16.9	540	3.9
c	8a	140.4	143	2.6	3.0	2160	5.9
d	4b	138.3	138–141	4.1	2.6	1550	5.6
e	4a	134.1	131–135	5.2	−0.4	1275	5.3
f	6/7	126.8	126–128	0.9	0.5		
g	4	126.2	126–129	6.1	5.3		
h	6/7	126.0	126–128	1.1	0.9		
i	8	124.4	124.8	1.5	1.0		
j	3	120.7	121–123	6.2	0		
k	5	119.8	119.7	1.9	1.2		
l	9	38.5	37	11.5	7.8		

[a,b] See Table II. [c] Shift induced after adding (portionwise) 0.4409 g of Pr (dpm)$_3$ to a solution of 0.5429 g of 1-azafluorene in 1.3579 g of $CDCl_3$. [d] Shift induced after adding (portionwise) 0.3959 g of Eu(dpm)$_3$ to 0.605 g of 1-azafluorene in 1.50 g of $CDCl_3$. [e] See footnote *d* in Table II. The solution was 2 *M* in 1-azafluorene and 0.01 *M* in Gd(dpm)$_3$. [f] See footnote *e* in Table II.

Table IV. ^{13}C NMR Data for 3-Azafluorene[a]

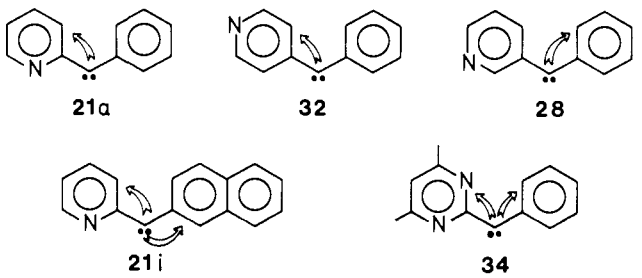
Peak No.	Attribution[b] carbon No.	$\delta_{^{13}C}$, ppm	Type of C[c]
a	9a	151.2	q
b	2	146.4	t
c	8a	141.4	q
d	4	141.1	t
e	4b	138.1	q
f	4a	137.3	q
g	6/7	127.3	t
h	6/7	126.6	t
i	8 (1)	124.6	t
j	1 (8)	120.0	t
k	5	120.0	t
l	9	36.9	s

[a] See footnote *a*, Table II. [b] On the basis of 1- and 4-azafluorene and related compounds (cf. Tables II–III). [c] From proton undecoupled spectra: q, quaternary; t, tertiary; s, secondary carbon.

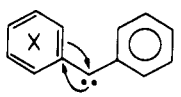
Table V. Hyperfine Splitting Constants (a_H) in Radical Anions and Reduction Potentials ($E_{1/2}$) of Parent Aromatics

Compd (position)	a_H,[a] mT	$-E_{1/2}$,[b] (V vs. Hg pool)
Benzene (1)	0.375	(≥2.6)
Pyridine (4)	0.970	2.20
Pyridine (2)	0.355	2.20
Pyridine (3)	0.082	2.20
Naphthalene (1)	0.495	1.982
Naphthalene (2)	0.183	1.982
Biphenyl (4)	0.546	2.032
Pyrimidine (4)	0.978	1.822
Pyrazine (2)	0.263	1.569
Pyrimidine (2)	0.072	1.822
Pyridazine (3)	0.0	1.657

[a] Data from F. Gerson, "Hochauflösende Esr-Spektroskopie", Verlag Chemie, Weinheim/Bergstr., 1967, and B. C. Gilbert and M. Trenwith, *Phys. Methods Heterocycl. Chem.*, 6, 96 (1974). [b] Data from K. B. Wiberg and T. P. Lewis, *J. Am. Chem. Soc.*, 92, 7154 (1970).



ty of adding to a 3,4-pyridine double bond. The selectivities of these and other carbenes and nitrenes[12] can be understood in terms of a synergic electrophilic and nucleophilic attack by the carbene on an aromatic ring (cf. the introductory section). This is symbolized in formula **41**. the carbene



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σ electrons interact with the lowest unoccupied molecular orbital (LUMO) of the most electrophilic ring (σ-LUMO interaction). The vacant carbene p orbital undergoes an electrophilic substitution onto the ortho position of the same ring (p-HOMO interaction). The ring expansion will then be favored by a low-lying LUMO possessing a large coefficient in the carbene position, and a high-lying HOMO with a large electron density in the position ortho to the carbene.

The two interactions are synergic; the donor property of the carbene makes it more electrophilic, the ring becomes more electron rich, and electrophilic substitution becomes faster. Conversely, the electrophilic substitution makes the ring more electrophilic and strengthens the σ-LUMO donation. A guide to the LUMO energies and coefficients can be obtained from the reduction potentials of the parent aromatics (ease of formation of radical anions) and the hyperfine splitting constants in the radical anions (Table V). The lower the reduction potential and the larger the splitting constant in the carbene position, the faster will be carbene ring expansion due to σ-LUMO interaction.[44]

Carbenes **21a** and **32** are situated in the very electrophilic 2- and 4-positions of pyridine. The electron density in the 3-position in pyridine is low, but electrophilic substitution is known to occur. In **28**, the carbene is not in an electrophilic position and, furthermore, expansion into the pyridine ring would mean attacking the 2- or 4-positions where the HOMO-electron densities are very low. Thus, since both nucleophilic and electrophilic interactions with the pyridine ring are unfavorable in **28**, expansion occurs in the benzene ring.

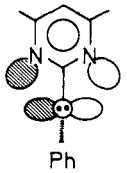
In **21i**, the LUMO level of the benzenoid part has been lowered by transforming it into naphthalene. σ-LUMO interaction is now possible with both rings, and the electrophilic p-HOMO interaction is much more favorable in the 1-position of naphthalene than in the 3-position of pyridine.

Both rings expand, and naphthalene predominates by a factor of ca. 2.

In the carbenes **21b,c** and **21g** the electron repelling substituents do not favor the σ-LUMO interaction with the benzene rings, and expansion always takes place into pyridine. The fact that **21g** expanded exclusively into the pyridine ring, despite the fact that the benzenoid positions ortho to the carbene are activated by the methoxy group, again demonstrates that the carbene does not behave as an electrophile.

It was expected that the electron-withdrawing substituents in **21d–f** might have lowered the LUMO levels of the benzenoid rings sufficiently that ring expansion would take place there. However, these LUMO's are localized essentially on the substituents,[45] and the cyano and nitro groups strongly deactivate the rings toward electrophilic substitution. Furthermore, since the yields of carbazoles **22d–f** were less than quantitative, the formation of thermally unstable isoindoles cannot be excluded.

As for carbene **34,** Table V indicates that, although the LUMO energy of pyrimidine is certainly lower than that in benzene, the LUMO coefficient in the 2-position is very low, even lower than in the pyridine 3-position. Thus **34** behaves like **28,** expanding preferentially into the benzene ring. In addition to this, carbene **34** may be stabilized in the singlet state by a four-electron three-center bonding (**42**) in which the carbene carbon is fixed in the plane of the pyrimidine ring, thus preventing rearrangement.[9] Finally, the antiaromaticity of the azirine intermediate or transition state **43** may contribute in rendering expansion of the pyrimidine



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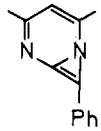

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ring unfavorable. It should be noted here that the factor 5 of benzene vs. pyrimidine ring expansion in **34** corresponds to a difference in activation energies of only 2.2 kcal/mol at 700 K or, if equilibrium is attained, to a free energy difference of 2.2 kcal/mol between the intermediates. A negative resonance energy in 1*H*-azirine of 6.7 kcal/mol has been calculated.[48] The obstacle to pyrimidine ring expansion is evidently not very high and, indeed, unsubstituted 2-pyrimidylcarbene does rearrange efficiently to 3-pyridylnitrene.[12,47]

In the nitrene series, all known nitrene ring expansions correlate with the LUMO coefficients in the corresponding azine radical anions. Thus, the relative rates of expansion in the nitrenoazines appear to be: 4-pyrimidyl > 2-pyridyl > 2-pyrazinyl > 2-pyrimidyl ≥ 3-pyridazinyl.[12]

Quantum-chemical (extended Hückel and CNDO/2) calculations fully corroborate the contention that arylcarbenes and -nitrenes can function as nucleophiles (σ-LUMO interaction) during ring expansion.[9] Both methods predict that the carbene or nitrene will move out of the ring plane during expansion. A molecular model shows that an attempt to perform a ring expansion in phenylcarbene, by means of an overlap between the vacant carbene p orbital and a ring p orbital in an out-of-plane movement of the carbene, will necessarily lead to interaction between the carbene σ orbital and the ring.

The theoretical treatment given above is nothing but a simple perturbation molecular orbital treatment.[77] The nucleophilic part of the addition of a carbene to a double bond could also be called addition with "inverse electron demand", electrophilic addition being the "normal" one. It can be no surprise that the "inverse electron demand" should manifest itself since the same phenomenon occurs in 1,3-dipolar cycloadditions[78] and Diels–Alder reactions.[79]

It should be understood, however, that this treatment is not the only possible one. If it were possible to calculate the heats of formation of the transition states corresponding to the different carbene reaction pathways, a purely thermodynamic explanation would obtain. It was shown previously[19] that thermochemistry alone suffices to explain why in **21i** the naphthyl group competes with the pyridyl group much better than does the phenyl group in **21a.** If the transition state for ring expansion resembles **4** (eq 1), naphthalene will lose less resonance energy than benzene when going to the transition state.[12] However, consideration of resonance energies and thermochemistry does not suffice to make meaningful interpretations of the other selectivities observed.[1,80] Estimates of the resonance energy of pyridine vary from ca. 4 kcal/mol lower than that of benzene[81] to equal to or higher than that of benzene.[48,82] Group additivity[83] indicates that the transformation of a pyridine to a 2,3-dihydropyridine (simulating a transition state or intermediate like **4**) is 0–3 kcal/mol less endoergic than the transformation of benzene to 1,3-cyclohexadiene. This is insufficient and too unreliable to explain the 100% selectivity of the carbene **21a** toward insertion into pyridine. In the case of the selective rearrangements of 4-pyrimidylnitrenes to pyrazinylnitrenes,[12] simply thermochemistry and resonance energies are unable to provide an explanation since the heats of formation[83] and resonance energies[81b,84] of pyrimidine and pyrazine appear to be identical.[85]

Outlook

We have shown that the regioselectivities of carbene ring expansions can be predicted from a consideration of formal σ-LUMO and p-HOMO interactions. The σ-LUMO interaction should not be restricted to intramolecular reactions of arylcarbenes but should be observable also in intermolecular addition of carbenes and nitrenes to olefins with relatively low-lying LUMO levels. Also, 1,4-addition of carbenes might be observed if LUMO energies are sufficiently low. Not surprisingly, 1,4-addition to five-membered heterocycles is unknown;[20] the LUMO energies are too high. Similarly, 2-furfurylidene and 2- and 3-thenylidene undergo ring opening instead of ring expansion.[49] The σ-LUMO interactions would be disfavored in these electron-rich heterocycles.

Experimental Section

General. Melting points are corrected when so indicated. Elemental analyses were performed by Dr. K. Eder (Université de Genève) or E. Thommen (Universität Basel). Exact mass measurements were determined on an AEI MS 902 mass spectrometer (Nestlé, S.A., Vevey). Low resolution mass spectra were recorded on a CEC 21-490 instrument at 70 eV using direct inlet, source temperature 200°. Mass spectra are reported as *m/e* value followed by relative abundance (percent base peak) in parenthesis. ^{1}H nuclear magnetic resonance (NMR) spectra were recorded on Varian A-60A or Bruker HX-90 instruments. ^{13}C nuclear magnetic resonance (^{13}C NMR) spectra were recorded at 22.63 MHz on the Bruker HX-90 Fourier transform instrument. All chemical shifts are expressed on the δ scale relative to tetramethylsilane. Infrared (ir) and ultraviolet (uv) spectra were recorded on Beckmann IR-20A and Beckmann DB-G or Carl Zeiss RPQ 20A instruments, respectively. Analytical and semipreparative gas–liquid chromatography (GLC) was performed on a Hewlett-Packard 5750 instrument using H_2 carrier gas and thermal conductivity detector. Thin layer chromatography (TLC) used silica gel GF_{254} (Merck) or aluminum oxide GF_{254} (Fluka) as indicated. Measurements of radioactivity were carried out on a Tri-Carb Packard liquid scintillation Model 3380 in the Institut d'Electrochimie & Ra-

Table VI. Aryl 2-Pyridyl Ketones (6), Hydrazones (7), and 3-Aryl-v-triazolo[1,5-a]pyridines (8)

	Ketones 6[a]		Hydrazones (7)[b]		Triazoles (8)[b]					
	Yield, %	Mp, °C	Yield, %	Mp, °C	Reagent/ solvent	Reaction time, hr	Solvent for recryst.	Yield, %	Mp, °C	Anal.
b	54	96[c]	53	Oil	Ag_2O/Et_2O	48	Et_2O	47	133–134	*j, l*
c	50	65–66[d]	79	110	Ag_2O/Et_2O	50	Et_2O	90	156–157	*j, m*
d			78	113–114	MnO_2/THF	48	Subl[f]	12	229–230	*k*
e			87	Oil	$MnO_2/CHCl_3$	48	Subl[g]	84	219–220	*k*
f			92	192	Ag_2O/DMF	94	Acetone	65	249[i]	*j, l*
g	45	69.5–70.5[j]	80	Oil	$Ag_2O/CHCl_3$	72	Subl[h]	50	95	*j, n*
h	82	Oil	37	120.5–121	Ag_2O/Et_2O	48	Et_2O	95.5	109–110	*k*
i	73	Oil	*e*	Oil	Ag_2O/Et_2O	62	Et_2O	37[e]	141–143	*j, l*

[a] Prepared according to French and Sears.[16] The crude ketones may be used directly for preparing the hydrazones. [b] Prepared according to Boyer et al.[15] at reflux temp. The hydrazones were usually used directly for preparing the triazoles, without purification. [c] Literature[53] 93–95°. [d] Literature[54] 64° lit.[55] 79°. [e] The crude hydrazone was used directly; the yield of triazole is based on the ketone **6i**. [f] Sublimed at 210° (0.01 mm). [g] Sublimed at 170° (0.01 mm). [h] Sublimed at 70–80° (0.01 mm). [i] Subl. 200°. [j] Satisfactory elemental analysis (C, H, N) was obtained. [k] Satisfactory high resolution mass spectrometric analysis was obtained. [l] Preparation by Mrs. Ingrid Noppel-Fuss. [m] Preparation by Miss Jasmine Buclin. [n] Preparation by Mr. Nguyen Mong Lan.

diochimie de l'Ecole Polytechnique Fédérale, Lausanne. The scintillation liquids used are indicated in Table VII. Each sample was measured twice. The pyrolysis apparatus was as previously described.[9]

***p*-Nitrophenyl 2-Pyridyl Ketone (6d).** To a solution of 10 g (46.7 mmol) of 2-(*p*-nitrobenzyl)pyridine[52] in 19 ml of glacial acetic acid was added dropwise a solution of 2.77 g of $Na_2Cr_2O_7 \cdot 2H_2O$ in 50 ml of acetic acid and 10 ml of H_2O. The mixture was refluxed for 3 hr with vigorous stirring, after which time a solution of 18.5 g of tartaric acid in 31 ml of acetic acid was added (this in order to form a soluble complex with Cr(III)). The resulting solution was made alkaline with 3 *N* NaOH and extracted five times with 20 ml of chloroform, the extracts were dried over $MgSO_4$, and the solvent was evaporated to yield a yellow mass which was recrystallized from ethanol: 8.5 g (80%); mp 98–99° (lit.[52] 99–100°).

***p*-Aminophenyl 2-Pyridyl Ketone.** A mixture of 10 g (43.9 mmol) of *p*-nitrophenyl 2-pyridyl ketone and 11.25 g of iron powder in 80 ml of acetic acid was heated at 100° for 4 hr with vigorous stirring. The reaction product was poured into 40 ml of water and made alkaline with 3 *N* NaOH. The precipitate of iron hydroxide was filtered, dried, and then extracted with chloroform. The alkaline filtrate above was likewise extracted with chloroform. The combined extracts were dried over $MgSO_4$, and the solvent was evaporated to give a yellow oil which slowly crystallized. Recrystallization from CH_2Cl_2 gave 6 g (69%): mp 139–140°; mass spectrum *m/e* 198 (M^+, 36.4), 170 (38.6), 120 (100), 92 (43.2). Anal. Calcd for $C_{12}H_{10}N_2O$: C, 72.73; H, 5.05; N, 14.14. Found: C, 71.92; H, 4.93; N, 14.05.

***p*-Cyanophenyl 2-Pyridyl Ketone (6e).** A cold solution of 5 g (25.3 mmol) of *p*-aminophenyl 2-pyridyl ketone in 4 g of concentrated H_2SO_4 and 30 ml of H_2O was diazotized at 0–5° with 2.8 g of $NaNO_2$ in 5.5 ml of H_2O. The resulting solution was slowly added to a vigorously stirred solution of 7.25 g of $CuSO_4 \cdot 5H_2O$ and 7.75 g of KCN in 42 ml of H_2O. During the addition, the temperature was maintained at 95°. When the addition was completed, the mixture was refluxed for 15 min, cooled, basified with 3 *N* NaOH, and filtered, and the filtrate was extracted three times with 20 ml of chloroform. After drying and evaporation of the solvent, the yellow-brown crystals were recrystallized from CH_2Cl_2 with active carbon: yield 2.5 g (48%); mp 106–107°; mass spectrum *m/e* 208 (M^+, 21.4), 207 (40.7), 182 (7.4), 181 (15.8), 180 (100), 179 (26), 130 (44.5), 102 (50), 78 (23).

Ketones Using the Method of French and Sears.[16] Ketones **6b–c** and **6g–i** were prepared from the corresponding 2-pyridyllithiums and benzonitriles according to French and Sears.[16] Yields are given in Table VI.

3-Aryl-v-triazolo[1,5-*a*]pyridines (8). The ketones **6** were converted to the hydrazones **7** which were then oxidized with Ag_2O or active MnO_2[62] by Boyer's method.[15] Reaction conditions, yields, and analytical data are reported in Table VI.

Phenyl-3-pyridyldiazomethane. Active MnO_2[62] (7.5 g) was added to a solution of 5.0 g (25.4 mmol) of 3-benzoylpyridinehydrazone[56] in 75 ml of chloroform. The mixture was stirred for 1 hr at 20–25°. Filtration and evaporation of the solvent gave a red oil which crystallized at 0°. Molecular distillation occurred without decomposition at room temperature (10^{-3} mm): yield 3.5 g (71%); mp 25–27° dec; mass spectrum *m/e* 195 (M^+, 22.9), 167 (100), 140 (21), 139 (41), 78 (11.4), 77 (18).

Decomposition of the compound at 55–60° under vacuum gave the azine of phenyl 3-pyridyl ketone, purified by chromatography on silica gel–ethyl acetate. Recrystallization from ethanol gave yellow crystals, mp 130–131°. Anal. Calcd for $C_{24}H_{18}N_2$: C, 79.56; H, 4.97; N, 15.47. Found: C, 79.26; H, 4.98; N, 15.68.

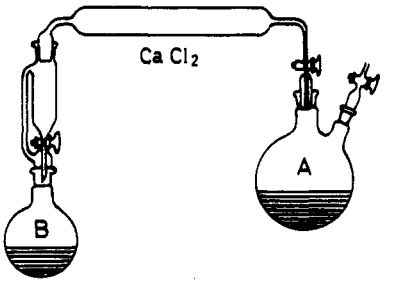

Figure 3. Carboxylation apparatus.

Nicotinic Acid-^{13}C. Essentially the preparation followed the procedure described by Murray et al.,[17] but using a highly simplified apparatus (Figure 3). Freshly distilled 3-bromopyridine (3.1 ml, 31.8 mmol) was dissolved in 180 ml of anhydrous ether in a two-necked flask (A) and cooled to −70°. Butyllithium (38 mmol as a 2 *M* solution in hexane) was added dropwise at −70° and the resulting mixture allowed to react for a further 10 min. Flask A was then attached to the apparatus as shown in Figure 3. In flask B was placed 5 g of $Ba^{13}CO_3$ (25.22 mmol, 90 atoms %; Bio-Rad Labs., Calif.) and in the addition funnel 100 ml of degassed concentrated H_2SO_4. The contents of flask A was cooled to −180°, the whole system evacuated to 10^{-2} mm, and degassed several times by intermittant heating to −50°. The system was then closed to the outside. While flask A was maintained at −50°, carboxylation occurred by the dropwise addition of the sulfuric acid to flask B while rapidly stirring magnetically. After 1 hr, the reaction mixture was hydrolyzed with 95 ml of 2.5 *N* HNO_3 and continuously extracted with ether for 4 hr. The remaining solution was then basified with 3 *N* NaOH and extraction continued for 12 hr. The extracts were discarded. The alkaline solution was acidified to pH 3.4 ± 0.3 (isoelectric point of nicotinic acid[57]) and extracted with ether for 72 hr. Evaporation to dryness of the extract left a product which was sublimed twice at 185° (10^{-2} mm): yield 2.0 g (64%) (lit.[17] 62.4%); mp 227–228° (lit.[17] 228–229°); mass spectrum *m/e* 124 (M^+, 100), 123 (9.8), 107 (26.4), 106 (45.6), 95 (11.4), 78 (49.7); mass spectrum of the unlabeled compound *m/e* 123 (100), 122 (0), 106 (32.7), 105 (52.3), 95 (6.2), 78 (53).

Phenyl 3-Pyridyl Ketone-^{13}C (9). Nicotinic acid-^{13}C (2.0 g, 16 mmol) was refluxed for 1 hr with 8.15 ml of freshly distilled $SOCl_2$. The excess $SOCl_2$ was distilled off, the last traces being re-

Table VII. Radiochemical Measurements

Compd[a]	Assay No.	Sample weight,[e] mg	Efficiency[f]	Activity, dpm	Specific activity,[g] nC/mmol
12[b]	1	10	0.946	7807031	6364
	2	10	0.950	7789266	6350
	Av				6357 ± 3%
15[b]	1	7.5	0.941	63349	635.2
	2	7.5	0.942	63293	634.6
	Av				634.9 ± 2%
19[c]	1	10	0.815	84531.7	632.1
	2	10	0.824	84909.2	634.7
	Av				633.4 ± 4%
20[c]	1	7.8	0.842	73407.4	582.0
	2	7.8	0.837	72608	575.6
	Av				578.8 ± 4%
$BaCO_3$[d]	1	100	0.940	61861	54.9
	2	100	0.938	61084	54.1
	Av				54.5 ± 3%

[a] Cf. Scheme III. Scintillator liquid: [b] 20 ml of a solution of 5 g of 2,5-diphenyloxazole (PPO) and 50 mg of 1,4-bis[2-(5-phenyloxazolyl)] benzene (POPOP) in 1 l. of toluene; [c] 5 ml of 2 *N* HCl and 15 ml of a solution of 3.5 g of PPO and 1.75 g of POPOP in 300 ml of toluene and 150 ml of Triton. [d] Moulded and suspended in a liquid composed of 5 g of PPO and 100 mg of POPOP in 1 l. of toluene and converted to gel by addition of 4% "Cab-O-Sil". [e] Estimated weighing error, 0.1 mg. [f] By external standard method.[50] [g] The statistical error was calculated according to Beers.[51]

moved in vacuo after addition of 3.5 ml of benzene. The residue was mixed with 8.2 ml of anhydrous benzene, cooled to 0°, and 5.36 g of anhydrous aluminum chloride was added in small portions with stirring. The mixture was allowed to warm to room temperature and then refluxed for 6 hr. The resulting brown oil was poured onto 35 g of ice and 3.25 ml of concentrated HCl. The solution was extracted with ether and then basified with NaOH until the precipitated aluminum hydroxide dissolved. The alkaline solution was extracted five times with 15 ml of chloroform, and the extract was washed with water, dried over $MgSO_4$, and evaporated to yield a brown oil which was distilled in vacuo [78–79° (10^{-2} mm)]. The distillate crystallized to white prisms at −10°: 2.2 g (74%); mp 36–37° (lit. for unlabeled compound[58] 36–38°); mass spectrum *m/e* 184 (M^+, 83.6), 183 (29.8), 107 (26.9), 106 (100), 105 (11.9), 78 (38.8), 77 (91); mass spectrum of unlabeled compound *m/e* 183 (M^+, 60), 182 (16.6), 106 (26.6), 105 (100), 104 (1.6), 77 (83.5).

Hydrazone of Phenyl 3-Pyridyl Ketone-^{13}C (10). A mixture of phenyl 3-pyridyl ketone-^{13}C (2.2 g, 12 mmol) and hydrazine hydrate (1.2 g, 24 mmol) in 15 ml of ethanol was refluxed for 24 hr under a Soxhlet extractor containing 2.5 g of CaO. Concentration of the solution and cooling in ice gave the hydrazone: 1.2 g (51%); mp 129–130° from ethanol (lit. for unlabeled compound[56] 130–131°); mass spectrum *m/e* 198 (M^+, 100), 197 (44.1), 182 (39), 181 (25.4), 168 (32.2), 167 (23.8), 78 (28), 77 (37).

Phenyl-3-pyridyldiazomethane-^{13}C (11). This compound was obtained in the same way as the unlabeled compound (vide supra): yield 76%; mp 26–29°.

Isonicotinic Acid-^{14}C. The procedure and apparatus was as described for nicotinic acid above (Figure 3). 4-Bromopyridine was freshly prepared by treating its hydrochloride (Fluka) with 5% NaOH and extracting with ether. 4-Bromopyridine (7.68 mmol) and 2.53 mmol of $Ba^{14}CO_3$ (100 μC; The Radiochemical Centre, Amersham, GB) gave 284.4 mg (91.4%) of isonicotinic acid-^{14}C after sublimation at 190–210° (10^{-2} mm): mp 301–302° (lit.[59] 301–304°). The 284.4 mg of product was diluted with inactive isonicotinic acid to give 2.0 g of mixed product.

Phenyl 4-Pyridyl Ketone-^{14}C (12). This was prepared in the same way as 9 (vide supra). Recrystallization from hexane gave 2.35 g (79%): specific activity 6.35 μC/mmol (see Table VII); mp 71–72° (lit.[58] 72–73°). The hydrazone (**13**) was prepared according to the procedure in ref 56.

Phenyl-4-pyridyldiazomethane-^{14}C (14) was prepared as described for the inactive compound in ref 60: mp 63–64° dec; mass spectrum *m/e* 195 (M^+, 6.25), 167 (100), 140 (28.3), 139 (53.3).

1-Azafluorenone (9*H*-Indeno[2,1-*b*]pyridin-9-one). To a refluxing suspension of benzo[*f*]quinoline (10 g, 55.9 mmol) in 800 ml of water and 4 g of NaOH was added dropwise a 10% solution of $KMnO_4$ (ca. 300 ml) with stirring until a persistent red color. The excess $KMnO_4$ was destroyed with a few drops of methanol, and the mixture was filtered while hot. The filtrate was concentrated and extracted three times with chloroform, and the extracts were dried over $MgSO_4$ and evaporated to dryness. Sublimation at 100–110° (10^{-2} mm) gave: 1.2 g (12%); mp 126–127° (lit.[38] 128–129°); mass spectrum *m/e* 182 ($(M + 1)^+$, 14.5), 181 (M^+, 100), 154 (10), 153 (72.2), 127 (77.8), 126 (31.1), 76 (21.1); ir (KBr) ν 850 (s), 910 (m), 1030 (s), 1295 (s), 1605 (m), 1730 (s) cm^{-1}.

1-Azafluorene (9*H*-Indeno[2,1-*b*]pyridine) (29). 1-Azafluorenone (0.7 g, 3.9 mmol) and hydrazine hydrate (1 g, 20 mmol) were heated for 24 hr at 180–200° in a sealed tube under Ar. The resulting mixture was taken up in chloroform, the two phases were separated, and the organic layer was dried over $MgSO_4$. Evaporation of the solvent and recrystallization from petroleum ether gave white crystals: 0.5 g (77.4%); mp 84–85°; mass spectrum *m/e* 168 ($(M + 1)^+$, 14.9), 167 (M^+, 100), 166 (19.6), 140 (12.5), 139 (19.6); NMR (CCl_4) δ 3.68 (s, 2 H), 6.6–6.7 (m, 6 H), 8.01 (d (J = 1 Hz) of d (J = 5 Hz), 1 H); ^{13}C NMR, see Table III. Anal. Calcd for $C_{12}H_9N$: C, 86.23; H, 5.39; N, 8.38. Found: C, 85.97; H, 5.47; N, 8.22.

Benzo[*h*]isoquinoline. The following series of transformations starting from 2-naphthaldehyde was carried out according to the literature—product, yield, melting point: β-(2-naphthyl)acrylic acid,[39] 95%, 202–203°; 1,2-dihydrobenzo[*h*]isoquinoline-1-one,[40] 63%, 204–205°; 1-chlorobenzo[*h*]isoquinoline,[40] 80.4%, 97–98°.

A mixture of 1-chlorobenzo[*h*]isoquinoline (10 g, 46.8 mmol) in 350 ml of ethanol, 5 g of KOH, and 4 g of Pd/C (5%) was hydrogenated at atmospheric pressure and room temperature (ca. 15 hr). After filtration of the catalyst and evaporation to dryness, an oil was obtained which crystallized spontaneously. Recrystallization from chloroform gave 7.8 g (93%), mp 46–47° (lit.[40] 47°); mass spectrum *m/e* 180 ($(M + 1)^+$, 16.6), 179 (M^+, 100), 178 (17.7), 152 (15.3), 151 (15.9).

3-Azafluorenone (5*H*-Indeno[1,2-*c*]pyridin-5-one). Benzo[*h*]isoquinoline was oxidized as described for the synthesis of 1-azafluorenone. The filtrate from oxidation of 7 g of benzo[*h*]isoquinoline was concentrated to 200 ml and, on cooling, the product crystallized as yellow needles, purified by sublimation at 210° (10^{-2} mm): 1.0 g (14%); mp 132–133° (lit.[39] 129°); mass spectrum *m/e* 182 ($(M + 1)^+$, 15.5), 181 (M^+, 100), 154 (12.7), 153 (32.4), 127 (12.7), 126 (35.2), 76 (7.8); NMR (acetone-d_6) δ 6.4–7.2 (m, 5 H), 7.6–8.7 (m, 3 H).

3-Azafluorene (5*H*-Indeno[1,2-*c*]pyridine) (30). 3-Azafluorene (1 g, 5.5 mmol) was reduced with hydrazine hydrate (1.2 g) in a sealed tube under Ar at 180–200° for 24 hr. The resulting product was taken up in chloroform and chromatographed on silica gel–chloroform. Collection of the yellow band gave an oil which transformed slowly into 3-azafluorenone in the air (analyzed by GLC), yield 829 mg (90%) [mp of picrate 185–186° (lit.[61] 187°)]; mass spectrum *m/e* 168 ($(M + 1)^+$, 16), 167 (M^+, 100), 166 (17.3), 140 (17.3), 139 (29.2); NMR (CCl_4) δ 3.55 (s, 2 H), 6.8–7.5 (m, 5 H), 8.21 (d, J = 5 Hz, 1 H), 8.49 (s, 1 H); ^{13}C NMR, see Table IV.

2-Azafluorenone (9*H*-Indeno[2,1-*c*]pyridin-9-one). 3-Mesitoyl-4-phenylpyridine[42] (2 g, 6.6 mmol) was heated with an excess of polyphosphoric acid in a Hickman distillation flask with rapid magnetic stirring, the product distilling at 195–200° (25 mm) as a brown oil. The distillate was poured into 25 ml of water and the resulting orange solution basified with 5% NaOH. The precipitated 2-azafluorenone was filtered and sublimed at 90° (0.05 mm): 0.9 g (74.8%); mp 156–157° (lit.[42] 155.5–156.5°); ir ($CHCl_3$) ν 915 (m), 1610 (s), 1725 (s) cm^{-1}; mass spectrum *m/e* 182 ($(M + 1)^+$, 16.1), 181 (M^+, 100), 154 (14.6), 153 (58.4), 127 (15.3), 126 (71.5), 76 (20.5); NMR ($CDCl_3$) δ 7.2–7.7 (m, 5 H), 8.59 (d, J = 5 Hz, 1 H), 8.71 (s, 1 H).

2-Azafluorene (9*H*-Indeno[2,1-*c*]pyridine) (15). 2-Azafluorene (0.6 g, 3.3 mmol) was refluxed for 48 hr with 2 g of Zn–$HgCl_2$ amalgam,[63] 4 ml of concentrated HCl, and 1.5 ml of water. One additional milliliter of concentrated HCl was added every 8 hr. The resulting solution was brought to pH 8 with 1 *N* NaOH and the precipitated $Zn(OH)_2$ filtered. The filtrate, as well as the dried precipitate, was extracted with methylene chloride, and the extracts were dried and condensed to give white prisms, sublimed at 60° (0.1 mm): 270 mg (48.8%); mp 78–79° (lit.[41] 78°); ir (KBr) ν

735 (vs), 1415 (s), 1450 (s), 1560 (s), 1600 (s) cm^{-1}; mass spectrum *m/e* 168 ($(M + 1)^+$, 12.7), 167 (M^+, 100), 166 (18.6), 140 (24.1), 139 (6.6); NMR (CCl_4) δ 3.77 (s, 2 H), 7.1–7.7 (m, 5 H), 8.33 (d, J = 5 Hz, 1 H), 8.49 (s, 1 H).

5-Amino-4-phenyl-1*H*-1,2,3-triazole. The original synthesis[64] was modified as follows. 5-Amino-1-benzyl-4-phenyl-1,2,3-triazole[65] (16 g, 64 mmol) was dissolved with stirring in 130 ml of liquid NH_3. Sodium (2.94 g, 128 mmol) was added in small pieces. The solution was stirred for another 30 min until disappearance of the blue color. After adding 6.83 g of NH_4Cl, the ammonia was allowed to evaporate at room temperature, and the toluene formed was then removed in vacuo. The yellow residue was taken up in ether and filtered, the precipitate was washed with ether, and the combined ethereal phases were evaporated to give the crude product. Two recrystallizations from chloroform yielded 7 g (68%) (lit.[64] 48%): mp 124–125° (lit.[64] 124°); mass spectrum *m/e* 161 ($(M + 1)^+$, 9.9), 160 (M^+, 100), 132 (1.2), 131 (3.7), 104 (61.7), 77 (16.1); NMR (Me_2SO-d_6) δ 5.13 (s, 3 H), 7.2–7.9 (m, 5 H).

5,7-Dimethyl-3-phenyl-*v*-triazolo[1,5-*a*]pyrimidine (33). This was prepared according to Sutherland and Tennant:[64] yield 93%; mp 160–161°; mass spectrum *m/e* 224 (M^+, 16.5), 197 (20.3), 196 (100), 195 (39.5), 181 (10), 155 (9.4), 128 (4.1), 115 (26.4), 104 (40.8), 66 (43.5); NMR ($CDCl_3$) δ 2.57 (s, 3 H), 2.80 (s, 3 H), 6.57 (s, 1 H), 7.2–7.7 (m, 3 H), 8.3–8.6 (m, 2 H).

5-Amino-2,4-dimethylpyridine. A solution of 2,4-lutidine (10 g, 93.5 mmol) in 8 ml of fuming HNO_3 (d = 1.52) was added dropwise with stirring during 1 hr to 50 g of 25% oleum, heated at 125–130°. The reaction mixture was kept at this temperature for 20 min, cooled to 25°, and poured onto 300 g of ice. Basification with concentrated NH_4OH, extraction with ether, and drying and evaporation of the solvent left a brown residue which was fractionally distilled. 2,4-Dimethyl-3-nitropyridine [1.85 g, 13%; bp 107–110° (12 mm)] and 2,4-dimethyl-5-nitropyridine [2.95 g; 21%; bp 118–122° (12 mm)] were collected.

2,4-Dimethyl-5-nitropyridine (2 g, 13.15 mmol) was treated with 10.8 g of $SnCl_2 \cdot 2H_2O$ in 11 ml of concentrated HCl. After the initial exothermic reaction had subsided, the mixture was refluxed for 2 hr with stirring, cooled, neutralized with 3 *N* NaOH, and filtered, the filtrate as well as the precipitate extracted with ether, and the extract dried over $MgSO_4$ and evaporated to dryness. The resulting yellow oil crystallized slowly and was recrystallized from methylene chloride: 1.2 g (75%); mp 70–71° (lit.[66] 68–71°); mass spectrum *m/e* 123 ($(M + 1)^+$, 9.7), 122 (M^+, 100), 121 (29.3), 107 (25.6), 95 (16), 94 (47.5), 80 (29.4).

2,4-Dimethyl-5*H*-pyrido[3,2-*b*]indole (35). A mixture of 5-amino-2,4-dimethylpyridine (0.7 g, 5.7 mmol), 0.51 g of K_2CO_3, 0.014 g of Cu powder, and 1.53 g (7.5 mmol) of iodobenzene was heated in a sealed tube under Ar for 18 hr at 200°. After cooling, the reaction mixture was treated with 10% NaOH and extracted with ether. The ether extract was washed several times with 3 *N* HCl and the acid layer separated, made alkaline with NaOH, and then re-extracted with ether. Drying and evaporation of the second ether extract gave a mixture of oil and crystals, which was chromatographed on silica gel (benzene–methanol 9:1). The first fraction was 2,4-dimethyl-5-diphenylaminopyridine (258 mg, 16.5%). The second fraction was 2,4-dimethyl-5-anilinopyridine, which was sublimed at 130° (0.01 mm) [520 mg, 46%; mp 157–158°; mass spectrum *m/e* 198 (M^+, 100), 197 (23.8), 183 (6.3), 182 (4.2), 120 (2.7), 77 (9.2)].

The latter compound (250 mg) was dissolved in 250 ml of dry tetrahydrofuran and irradiated in a water-cooled quartz apparatus with a 125-W Philips high-pressure mercury lamp. The reaction was followed by TLC on silica gel ($CHCl_3$–ethanol 9:1) and was terminated after ca. 35 hr. The solvent was evaporated and the product purified by two sublimations at 200° (0.01 mm): yield 163.8 mg (66.2%); mp 222–223°; ir (KBr) ν 760 (m), 935 (w), 1330 (w), 3420 (m) cm^{-1}; mass spectrum *m/e* 196 (M^+, 100), 195 (26), 181 (10), 168 (3.2); NMR (Me_2SO-d_6; 90 MHz) δ 2.77 (s, 3 H), 2.85 (s, 3 H), 7.2–7.8 (m, 4 H), 8.73 (d, J = 8 Hz, 1 H), 12.73 (s, 1 H); uv λ_{max} (ethanol) 326 nm (ϵ 3568), 303 (9850), 258 (13250), 219 (19950); exact mass (calcd for $C_{13}H_{12}N_2$, 196.1000) 196.0981.

3,5-Dimethyl-1-phenacetylpyrazole (40). 3,5-Dimethylpyrazole (2 g, 20.8 mmol) was dissolved in a large volume of ether containing 1.93 g of anhydrous pyridine. The solution was heated to reflux with stirring, and phenacetyl chloride (3.8 g; 24.6 mmol) was added dropwise. After addition was completed, the mixture was refluxed for an additional 2 hr, cooled, and filtered, and the filtrate was evaporated. The resulting yellow oil crystallized at 0° and was recrystallized from ether: 3 g (67%); mp 56–57°; ir ($CHCl_3$) ν 960 (s), 1580 (s), 1715 (vs) cm^{-1}; mass spectrum *m/e* 214 (M^+, 15.7), 182 (2), 172 (5.3), 171 (3.4), 120 (100), 91 (3.9); NMR (CCl_4) δ 2.20 (s, 3 H), 2.49 (s, 3 H), 4.32 (s, 2 H), 4.93 (s, 1 H), 7.27 (s, 5 H). Anal. Calcd for $C_{13}H_{14}N_2O$: C, 72.89; H, 6.54; N, 13.08. Found: C, 72.65; H, 6.60; N, 12.88.

Thermolyses and Degradations. Thermolysis of 2-Aryl-*v*-triazolo[1,5-*a*]pyridines (8). Thermolysis conditions and yields are given in Table I. The following examples are typical.

Thermolysis of 3-Phenyl-*v*-triazolo[1,5-*a*]pyridine (8a). (a) **8a** (0.240 g) was thermolyzed at 500° (0.02 mm), being sublimed in at 160° during 45 min. The product (205 mg, 99.74%) crystallized outside the furnace and had spectra, melting point, and mixture melting point identical with those of authentic carbazole. (b) **8a** (500 mg) was thermolyzed at 900° (0.05 mm), being sublimed in at 90° during 15 hr. Carbazole (425 mg, 99.25%) deposited as yellowish plates, mp 244–245°; mixture melting point with authentic carbazole, 245°, TLC on silica gel (benzene–2-butanone–chloroform 35:30:35; R_f 0.48) and GLC (2% Carbowax 20M on Celite 545; 260°; R_t 10.9 min) indicated the presence of a single product, identical with carbazole. The NMR spectrum of the thermolysate in CF_3COOH indicated the absence of pyrido[2,1-*a*]isoindole by the absence of a peak at δ 5–6.

Thermolysis of 3-(*p*-Cyanophenyl)-*v*-triazolo[1,5-*a*]pyridine (8e). **8e** (500 mg) was thermolyzed at 400° (10^{-3} mm), being sublimed in at 180–185° during 20 hr. 2-Cyanocarbazole deposited as yellow-orange stars: yield 214.7 mg (49.2%); mp 134–136°. TLC (as above) indicated a single product, R_f 0.51. The NMR spectrum of a solution in CF_3COOH did not allow the detection of 8-cyanopyrido[2,1-*a*]isoindole. The CF_3COOH solution was poured into water, the precipitated 2-cyanocarbazole filtered, and the filtrate basified with NaOH. No colored product precipitated. 2-Cyanocarbazole had the following properties: ir (KBr) ν 735 (s), 760 (s), 830 (s), 1250 (s), 1330 (s), 1450 (s), 1615 (s), 2230 (s), 3420 (s) cm^{-1}; mass spectrum *m/e* 193 ($(M + 1)^+$, 16), 192 (M^+, 100), 191 (11.3), 166 (1.7), 165 (8.7), 164 (12.5), 140 (3), 139 (3), 138 (4.2), 96 ((M^{2+}) 8.8); NMR (CF_3COOH) δ 6.8–7.6 (m, 7 H), 9.12 (s, 1 H); exact mass (calcd for $C_{13}H_8N_2$, 192.0687) 192.0670.

Thermolysis of 6-Methyl-3-phenyl-*v*-triazolo[1,5-*a*]pyridine (8h). Thermolysis of **8h** as described for **8a** above gave 2-methylcarbazole [(94%), mp 261–262° (corr) from ethanol (lit.[67] 259°, 261–262°)] and picrate [mp 167–168° (corr) from benzene (lit.[67] 167°)]. For comparison: 1-methylcarbazole (mp 120.5°; picrate, mp 143.5° [68]), 3-methylcarbazole (mp 206.5–207.5°; picrate, mp 180° [69]), and 4-methylcarbazole (mp 129.5–130°; picrate, mp 160.5° [70]). The ir, uv, and mass spectra were identical with those of authentic 2-methylcarbazole.

Thermolysis of 3-(2-Naphthyl)-*v*-triazolo[1,5-*a*]pyridine (8i). 8i (0.45 g) was thermolyzed at 380° (10^{-3} mm), being sublimed in at 133° during 10 hr. The burgundy red product (0.40 g, ~100% total yield) had mp 100–135° dec. The product was partitioned between aqueous CF_3COOH and $CHCl_3$. The $CHCl_3$ layer was kept for further work (see below). The pale yellow acid layer was basified with NaOH, regenerating the red precipitate which was filtered and dried in a desiccator (54.1 mg). This compound (**23i**) did not move by TLC on alumina–$CHCl_3$ but gave a slowly moving yellow spot on alumina–CF_3COOH. Evaporation of a CF_3COOH solution gave a yellow solid; basification regenerated the red solid. The red compound blackened on heating to 150°, without melting. A $CHCl_3$ solution of the red compound turned brown within 1 hr at room temperature; evaporation left a brown oil from which the red compound could not be regenerated by acid–base treatment. TLC of the brown oil showed a visible continuum. **23i** had the following properties: NMR ($CDCl_3$) δ 7–9 (complex m); NMR (CF_3COOH) δ 5.56 (s, 2 H), 7–9 (m, 10 H); ir (KBr) ν 450 (m), 630 (m), 710 (s), 725 (s), 850 (s), 1430 (m), 1580 (m), 3000 (w); uv, λ_{max} (95% ethanol) 256, 280, 330, 412, 432 nm; λ_{max} (CF_3COOH) 335, 380 (sh) nm; λ_{max} (20% $HClO_4$) 327 nm; mass spectrum *m/e* 218 ($(M + 1)^+$, 20), 217 (M^+, 100), 216 (15), 189 (6.6), 188 (14), 163 (4.4), 150 (1), 139 (2.4), 108.5 (M^{2+}, 5.5); exact mass (calcd for $C_{16}H_{11}N$, 217.0891) 217.0893.

The chloroform extract of the thermolysis product (see above)

was washed with water and dried (0.0715 g of colorless product). TLC showed two major spots (alumina-$CHCl_3$; R_f 0.41 and 0.10), the latter corresponding to the starting material. Column chromatography (alumina-$CHCl_3$) gave a mixture of benzindeno[1,2-*b*]pyridine and benzo[*a*]carbazole, and starting material (15.5 mg). Re-chromatography of the mixture gave benzindeno[1,2-*b*]pyridine (**24i**) (16% isolated yield) and benzo[*a*]carbazole (**22i**) (30% isolated yield). **24i** had the following properties: NMR ($CDCl_3$) δ 3.97 (s, 2 H), 7.02-8.62 (m, 9 H); in CF_3COOH, the singlet appeared at δ 4.1; mass spectrum almost identical with that of **23i**; exact mass (calcd for $C_{16}H_{11}N$, 217.0891) 217.0893. **22i** had the following properties: mp 225-228° subl (corr) (lit.[71,72] 227°, 227-228°); NMR ($CDCl_3$) δ 7.15-8.2 (m, 10 H), 8.7 (broad s, 1 H), identical with the published spectrum;[71] ir (KBr) ν_{max} 3215 cm^{-1}; exact mass (calcd for $C_{16}H_{11}N$, 217.0891) 217.0896.

The yields of **22i**, **23i**, and **24i** were determined by NMR integration and isolation: 30, 48, and 16%, respectively. The ratio **23i**:**24i** was ca. 1:3 when the thermolysis was carried out at 660° (0.01-0.1 mm).

Thermolysis of Phenyl-3-pyridyldiazomethane. Five hundred milligrams was thermolyzed at 400° (10^{-3} mm) during 20 hr. The starting material was distilled in very slowly (20-50°) in order to avoid too extensive azine formation. The thermolysate, a mixture of white crystals and a yellowish oil, was washed out with $CHCl_3$, giving 180 mg (42%) of a mixture of 1- and 3-azafluorene. These were separated by TLC (silica gel/benzene-2-butanone-$CHCl_3$ 35:30:35; R_f 0.20 and 0.15, respectively) and GLC (20% SE 30 on Chromosorb W; 180°; R_t 9.2 and 11.3 min, respectively). The relative yields of 1- and 3-azafluorene were 56.3:43.7 by GLC and 55.7:44.3 by NMR. The NMR and mass spectra of the products were identical with those of the synthetic samples (vide supra). 1-Azafluorene had mp 83-84° (synthetic sample 84-85°). 3-Azafluorene was partly oxidized to 3-azafluorenone during chromatography, as evidence by GLC (R_t 10.2 min). The remainder of the starting material had transformed into the azine of phenyl 3-pyridyl ketone in the sample introduction flask (cf. preparation of phenyl-3-pyridyldiazomethane).

Thermolysis of Phenyl-3-pyridyldiazomethane-^{13}C (11). The labeled compound (500 mg) was thermolyzed as described in the preceding entry. The ^{13}C NMR spectrum of the product mixture in $CDCl_3$ was recorded: δ (rel intensity %) 137.13 (11), 138.1 (56), 138.3 (100) ppm. The relative yields of 1- and 3-azafluorene-^{13}C were 56:44 by GLC. 1-Azafluorene-^{13}C was isolated by semipreparative GLC. Its ^{13}C NMR spectrum showed a single peak at δ 138.32. 3-Azafluorene-^{13}C partly decomposed on the column, the collected sample showing four new ^{13}C NMR signals.

Mass spectrum of isolated 1-azafluorene-*4b*-^{13}C, *m/e* 168 (M^+, 100), 167 (30.4), 141 (14.9), 140 (23.2).

1-Azafluorene-*4b*-^{13}C (22 mg) was oxidized to 1-azafluoren-9-one-*4b*-^{13}C by dissolving it in 2 ml of glacial acetic acid and adding 0.2 g of $Na_2Cr_2O_7$. The mixture was refluxed for 1 hr, cooled, mixed with 2 ml 5% NaOH, and extracted with chloroform, and the extract was dried and evaporated to give 11 mg of the ketone: mass spectrum *m/e* 182 (M^+, 100), 154 (63.2), 128 (58), 78 (8.4), 77 (36.7), 76 (28.3); mass spectrum of unlabeled 1-azafluoren-9-one under identical conditions *m/e* 181 (M^+, 100), 153 (72.2), 127 (77.8), 78 (5.3), 77 (20), 76 (21.1), 75 (24.4).

Thermolysis of Phenyl-4-pyridyldiazomethane. Five hundred milligrams were thermolyzed at 500° (10^{-3} mm) during 10 hr, being sublimed in at 60°. There was isolated 292 mg (68.2%) of 2-azafluorene as white plates, mp 78-79°, undepressed by admixture of the synthetic sample (vide supra). TLC (silica gel/benzene-methanol 95:5) indicated a single product (R_f 0.29). The ir, mass, and NMR spectra were identical with those of the synthetic sample and the uv spectrum with that described in the literature.[73]

Thermolysis of Phenyl-4-pyridyldiazomethane-^{14}C (14). The active compound (500 mg) was thermolyzed as described in the preceding entry to yield 300 mg (70%) of 2-azafluorene-^{14}C, mp 78-79°. This product was diluted with inactive material to give 3.0 g of 2-azafluorene [specific activity 634.9 nC/mmol (Table VII)].

Degradation of 2-Azafluorene-^{14}C (15). (a) Oxidation to 2-Azafluoren-9-one (16). The labeled 2-azafluorene (**15**) (3 g, 17.96 mmol) was dissolved in 2.5 g of glacial acetic acid. A solution of 9.0 g (28.6 mmol) of $Na_2Cr_2O_7$ in 5.0 g of acetic acid was added dropwise with stirring. The resulting mixture was refluxed for 3 hr and poured while hot into 10 ml of H_2O. After basification with 10% NaOH, extraction with $CHCl_3$, drying over $MgSO_4$, and evaporation of the solvent, the product was sublimed at 90° (0.05 mm) to yield 1.95 g (60%) of 2-azafluorenone: mp 155-156°, undepressed by admixture with a synthetic sample (vide supra).

(b) Ozonolysis to Phthalic Acid and Pyridine-3,4-dicarboxylic Acid (17). The product obtained in a (1.95 g, 10.8 mmol) was dissolved in 90% aqueous acetic acid and ozonolyzed at 20-25° with an O_2/O_3 stream furnishing 2.0 g of O_3 per hr (Welsbach T-23 apparatus). After 10 hr of ozonolysis, 60 ml of 30% H_2O_2 was added, the mixture refluxed for 2 hr, evaporated to dryness, and the residue treated with 25 ml of concentrated HCl. Continuous extraction with ether (15 hr) gave phthalic acid (436 mg, 25%), mp 204-205°. The pure compound melts at 206-208°.

The residue from the extraction was adjusted to pH 3.2 ± 0.3 and extracted anew with ether for 48 hr. After removing the solvent in vacuo, sublimation at 200° (10^{-3} mm) gave pyridine-3,4-dicarboxylic acid (895 mg, 50%): mp 249-250° dec (lit.[74] 255°); mass spectrum *m/e* 167 (M^+, 1), 149 (11.3), 123 (2.4), 105 (100), 78 (22.6), 77 (51.7).

The subsequent degradation followed the method of Bachman and Barker.[18]

(c) Pyridine-3,4-dicarboxylic Anhydride (18). The diacid **17** was dissolved in 3.5 g of acetic anhydride and refluxed for 30 min. The excess acetic anhydride was distilled, the product dried in a desiccator over KOH and sublimed at 85° (0.01 mm) giving 798 mg (99.9%): mp 76-77° (lit.[75] 77-78°); mass spectrum *m/e* 149 (M^+, 12.2), 106 (5.6), 105 (100), 78 (18), 77 (37).

(d) 4-Carboxamidonicotinic Acid (19). The anhydride **18** was dissolved in 60 ml of warm benzene and treated with a stream of ammonia for 15 min. Evaporation of the solvent gave the ammonium salt of **19**, mp 227-228° (lit.[75] 228-229°). The salt was dissolved in 2 ml of water and saturated with SO_2. Cooling to 4-5° caused precipitation of **19** (541 mg, 61%): specific activity 633.4 nC/mmol (Table VII); ir (KBr) 740 (s), 840 (s), 980 (m), 1245 (s), 1295 (m), 1360 (s), 1640 (s), 3060 (s) cm^{-1}; mass spectrum *m/e* 166 (M^+, 1), 149 (28), 148 (74.4), 105 (100), 78 (21), 77 (51.2); NMR (CF_3COOH) δ 7.74 (broad s, ~2 H), 8.32 (d, J = 6 Hz, 1 H), 9.20 (d, J = 6 Hz, 1 H), 9.57 (s, 1 H).

(e) Hofmann's Degradation to 4-Aminonicotinic Acid (20) and CO_2. The amide **19** was dissolved in 10 ml of 5% NaOH in a three-necked round-bottomed flask equipped with a nitrogen inlet tube, pressure-equalized dropping funnel, and an outlet tube connected to two consecutive wash bottles, each containing 50 ml of saturated $Ba(OH)_2$. In the dropping funnel was placed 80 ml of a solution of NaOH (15 g/l.) and Br_2 (8.5 g/l.). The system was purged with 99.99% N_2 for 5 min before connecting it to the wash bottles and again for 5 min afterward. The bromine solution was added dropwise with magnetic stirring while maintaining a slight N_2 stream. The reaction was terminated by heating for 30 min at 100°. The precipitated $BaCO_3$ was filtered (G-4 sintered glass), washed consecutively with water, methanol, and ether, and dried at 140° to give 560 mg (87%): specific activity 54.5 nC/mmol (Table VII).

The remaining reaction mixture was concentrated to ca. 15 ml and saturated with SO_2. The sulfite of **20** separated as white needles, which were recrystallized from 1 *N* H_2SO_4. The sulfite was dissolved in 15 ml of concentrated NH_4OH. Evaporation to dryness and recrystallization from water gave 392 mg (87%) of 4-aminonicotinic acid: mp 335-337° (lit.[18,76] 338-341°; ca. 330°); specific activity 578.8 nC/mmol (Table VII). The purity of the product was controlled by TLC (silica gel/ethanol-water-concentrated NH_4OH 90:5:5; R_f 0.36): ir (KBr) ν 820 (s), 860 (s), 1180 (m), 1275 (s), 1340 (s), 1380 (s), 1550 (s), 1660 (vs), 3250 (m) cm^{-1}; mass spectrum *m/e* 138 (M^+, 94), 121 (14), 120 (96), 94 (15), 93 (100), 92 (13); NMR (CF_3COOD) 7.14 (d, J = 7 Hz, 1 H), 8.08 (d (J = 7 Hz) of d (J = 1 Hz), 1 H), 8.91 (d, J = 1 Hz, 1 H). The spectrum was clearly distinguishable from that of the isomeric 3-aminoisonicotinic acid which had: NMR (CF_3COOD) 7.96 (d, J = 6 Hz, 1 H), 8.44 (d, J = 6 Hz, 1 H), 8.48 (s, 1 H).

Thermolysis of 5,7-Dimethyl-3-phenyl-*v*-triazolo[1,5-*a*]pyrimidine (33). (a) **33** (500 mg) was thermolyzed at 450° (10^{-3} mm) during 20 hr, being sublimed in at 110-115°. The yellow, crystalline product (420 mg, 96%) had: mp 83-89° dec; ir ($CHCl_3$) ν 840 (s), 1100 (vs), 1270 (s), 1350 (s), 1370 (s), 1420 (s), 1450 (s), 1610 (s), 1630 (s), 2200 (m), 3450 (w) cm^{-1}; mass spectrum *m/e* 196 (M^+, 100). The yellow solid dissolved in CF_3COOH with red color; the NMR spectrum showed a singlet at δ 5.55, correspond-

ing to the solution containing 75% of a compound possessing a CH_2 group. The CF_3COOH solution was poured into water, and the precipitated 2,4-dimethyl-5*H*-pyrido[3,2-*b*]indole (**35**) was filtered and washed with water: yield 14%; mp 221-222°; ir, NMR, and mass spectra, and TLC (silica gel/chloroform-methanol 9:1; R_f 0.32) were identical with those of the synthetic sample (vide supra). The acid filtrate from above was basified with solid NaOH, causing regeneration of a yellow precipitate. This was filtered, dissolved again in aqueous HCl, and basified with NaOH, giving yellow needles of 2,4-dimethylpyrimido[2,1-*a*]isoindole (**36**) (315 mg, 72%): mp 105–107°; ir (KBr) ν 750 (vs), 840 (s), 1100 (s), 1220 (s), 1280 (s), 1355 (s), 1375 (s), 1435 (s), 1450 (s), 1610 (s), 1635 (s) cm^{-1}; uv, λ_{max} (ethanol) 240 nm (ϵ 26010), 259.2 (15930), 280 (14270), 289.5 (13480), 334.5 (4400), 348.5 (8530), 364.0 (10190); λ_{max} (1 *N* HCl) 259, 293 nm; NMR ($CDCl_3$) δ 2.50 (s, 3 H), 2.58, (s, 3 H), 6.55 (s, 1 H), 6.9–7.7 (m, 5 H); NMR (CF_3COOH) δ 2.95 (s, 6 H), 5.55 (s, 2 H), 7.2–8.4 (m, 5 H); exact mass (calcd for $C_{13}H_{12}N_2$, 196.1000) 196.0987.

The yellow **36** was unstable in air and could not be chromatographed without decomposition. It gave a single fluorescent spot by TLC on silica gel/CF_3COOH (R_f 0.24). This spot was stable in daylight and turned yellow again on addition of 1 drop of triethylamine.

(b) After a thermolysis similar to a, the crude thermolysate was analyzed for 3,5-dimethyl-1-phenylethynylpyrazole (**39**) as follows. The thermolysate was dissolved in $CHCl_3$, cooled to −10°, and extracted with 2 *N* HCl. The organic phase was separated and analyzed by GLC. The aqueous phase was made alkaline and re-extracted with $CHCl_3$, and the extract was analyzed by GLC. 3,5-Dimethyl-1-phenacetylpyrazole (**40**) was not detectable in the extracts.

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Mechanism of [2 + 2] Cycloaddition and Related Reactions between Electron Donors and Electron Acceptors. Perepoxide Quasi-Intermediate and Its Roles in the Reactions of $^1\Delta_g$ Molecular Oxygen with Olefins

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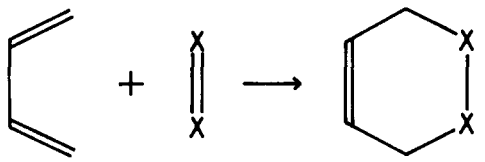
Abstract: An attempt has been made by means of the semiempirical SCF CNDO/2 method and the CI-perturbation procedure to elucidate the mechanism of stereoselective thermal [2 + 2] cycloaddition reactions between electron donors and electron acceptors. An ambiguous intervention of a perepoxide structure to be termed "quasi"-intermediate manifested itself on the CNDO/2 potential energy surface for the addition of $^1\Delta_g$ molecular oxygen to ethylene. The role of the quasi-intermediate has been discussed. In the light of the [2 + 2] cycloaddition mechanism, "ene" and [6 + 2] cycloaddition mechanisms have been discussed also.

An application of the frontier electron theory to Diels–Alder reactions was an indispensable prologue to progress in the theory of cycloaddition reactions.[1] The symmetry properties of frontier orbitals, the highest occupied (HO) molecular orbital (MO) of an electron-donating partner and the lowest unoccupied (LU) MO of an electron-accepting partner, were pointed out to be important. The symmetry rule was found afterward by Woodward and Hoffmann[2] to cover other sorts of chemical reactions and has been elevated to a brilliant and elegant stereoselection rule. A simple symmetry argument predicts that a thermal [2 + 2] cycloaddition reaction (eq 1) is the opposite to a thermal [4 +


(1)

2] cycloaddition reaction (eq 2) in the stereochemical


(2)

course. Nevertheless, we know, some chemical species, e.g., $^1\Delta_g$ molecular oxygen,[3] benzyne,[4] tetracyanoethylene,[5] azodicarboxylic ester,[6] ketene,[7] ketenimmonium cation,[8] and chlorosulfonyl isocyanate,[9] undergo both [2 + 2] and [4 + 2] cycloaddition reactions with high stereospecificity.[10-15]

In our previous paper, we pointed out the possibility of a novel [2 + 2] cycloaddition mechanism from a consideration of orbital interaction in the reaction of $^1\Delta_g$ molecular oxygen[16] and successively disclosed a common feature between singlet oxygen and benzyne as [2 + 2] cycloaddends by means of an HOMO–LUMO overlap analysis.[17] Both reagents have the LUMO's at low energy levels; they are powerful electron acceptors. These chemical species provide the LUMO rather than the HOMO for the significant orbital interaction with olefins. The interaction works most effectively at the nuclear arrangement in which two nucleophilic centers of the donor and one electrophilic atom of the acceptor form an isosceles triangle with the other reacting atom of the acceptor tailing out of the trigonal plane (**1** and