215. Nucleophilic and Electrophilic Properties of Carbenes, II. 4-Biphenylyl-4-pyridylcarbene

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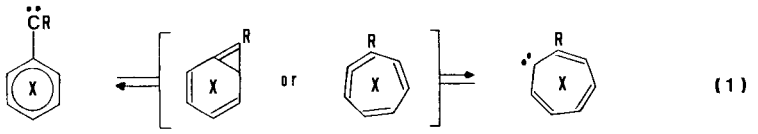
Summary. Flash pyrolysis of 4-biphenylyl-4-pyridyldiazomethane (**4**) gave 7-phenyl-2-azafluorene (**5**), which was also synthesized from 3-mesitoylpyridine in four steps. 4-Biphenylyl-4-pyridyl-[^{13}C]-diazomethane (**9**) was prepared from isonicotinic [^{13}C]-acid chloride in three steps. Flash pyrolysis of **9** established that 4a- and 4b-[^{13}C]-7-phenyl-2-azafluorenes are formed in a carbene-carbene rearrangement in which ring expansion of the biphenyl part dominates over that of the pyridine ring. These results support the postulate that carbene-carbene rearrangements are favoured by a nucleophilic interaction between the filled singlet carbene sp^2 (σ) orbital and the lowest unoccupied molecular orbital (LUMO) of the aromatic ring.

Recently we have postulated that the ring expansion in arylcarbenes (equation 1) is governed by simultaneous nucleophilic and electrophilic interactions between the



(1)

R = aryl, X = CH or N

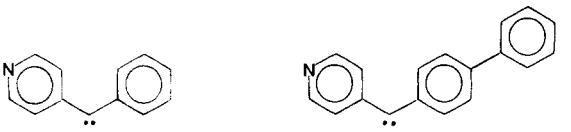
carbene centre and the aromatic ring [1]. According to this theory the carbene reacts preferentially with the ring which possesses a low LUMO energy in conjunction with a large LUMO coefficient in the position to which the carbene centre is attached (σ-LUMO interaction). At the same time, the vacant carbene p orbital undergoes an electrophilic substitution unto the *ortho* position, a reaction which is favoured by a high-lying ring-HOMO and large HOMO-coefficient in the *ortho* position (p-HOMO interaction). These interactions can be visualized by means of the perturbational MO diagram shown in Fig. 1, or the 'electron pushing' formula **1**.

1

Fig. 1. *Schematic representations of the interactions between arene MO's and a carbene substituent*

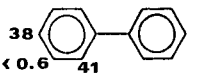
Thus, phenyl-(2-pyridyl)-carbene expands exclusively into the pyridine ring; phenyl-(4-pyridyl)-carbene (**2**) expands 92% into the pyridine ring and 8% into the benzene ring. (2-Pyridyl)-(2-naphthyl)-carbene undergoes expansion of both rings [1].

(4-Biphenylyl)-(4-pyridyl)-carbene (**3**) can be used as an important test of this theory. While the electronic properties of the pyridine rings in **2** and **3** are similar,



2 **3**

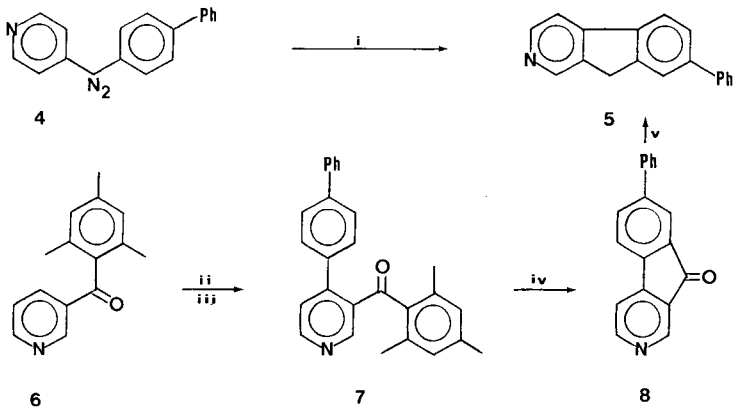
the benzenoid part in **3** has a low-lying LUMO with a large coefficient in the *para* position, where the carbene moiety is attached [2] (for a review of theoretical reactivity indices see *Streitwieser* [3]). The *meta* positions in biphenyl have reactivity indices identical with or lower than those in benzene [3]. The following partial rate factors for nitration of biphenyl [4] (relative to benzene) indicate that the *meta* positions are indeed less reactive than benzene in electrophilic substitution.



If the carbene rearrangements were governed essentially by electrophilic interactions between the carbene p-orbital and the neighbouring ring positions, we should, therefore, expect that **3** reacts in much the same way as **2**, *i.e.* by $\geqslant 92\%$ pyridine expansion and $\leqslant 8\%$ benzene expansion. If the nucleophilic σ-LUMO interaction is dominating, **3** should undergo a higher degree of benzenoid ring expansion than observed in **2**. The latter has now been found to be true.

Results and Discussion. – (4-Biphenylyl)-(4-pyridyl)-diazomethane (**4**) was obtained by treatment of the corresponding ketone with hydrazine hydrate followed by oxidation with active manganese dioxide. Flash pyrolysis of **4** at 400° ($5 \cdot 10^{-5}$ Torr) yielded 7-phenyl-2-azafluorene (7-phenylindeno[2,1-*c*]pyridine) (**5**) which was purified by chromatography and identified by direct comparison with a sample prepared from 3-mesitoylpyridine (**6**) by an application of *Fuson*'s method [5] (*Scheme 1*).

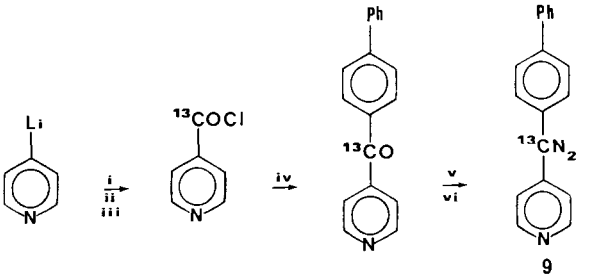
Scheme 1



i) 400° (5×10^{-5} Torr); ii) 4-biphenylylmagnesium bromide; iii) chloranil; iv) polyphosphoric acid, 200°; v) Zn—$HgCl_2$/HCl.

The ^{13}C-labelled diazomethane (**9**) was prepared from 4-pyridyllithium and $^{13}CO_2$ followed by conversion of the isonicotinic[^{13}C]-acid to the acid chloride, and *Friedel-Crafts* reaction with biphenyl. Treatment of the purified 4-biphenylyl 4-pyridyl [^{13}C]-ketone with hydrazine hydrate and MnO_2 as above yielded the red crystalline diazo-compound **9** (*Scheme 2*).

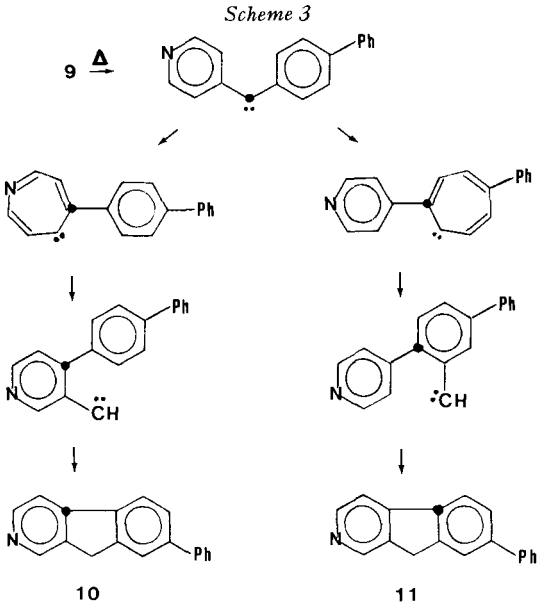
Scheme 2



i) $^{13}CO_2$;
ii) HCl;
iii) $SOCl_2$;
iv) biphenyl/$AlCl_3$/CS_2;
v) N_2H_4;
vi) MnO_2.

The pyrolysis of **9** can proceed in two different ways, as described in *Scheme 3*. Pyridine ring expansion and benzenoid ring expansion result in 4a- and 4b-[^{13}C]-labelled 7-phenyl-2-azafluorene (**10** and **11**), respectively.

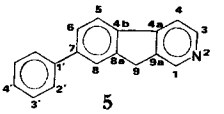
Scheme 3



Since we have previously analyzed the ^{13}C-NMR. spectra of azafluorenes in detail [1], the positions of label in **10** and **11** can readily be determined. The ^{13}C-NMR. spectrum of unlabelled **5** is reported in Table 1. The 7-phenyl-2-azafluorene isolated from the pyrolysis of **9** exhibited two ^{13}C-NMR. resonances at δ 148.8 and 138.3 ppm in the integrated ratio ~40:60 (relative to a 50:50 ratio in the unlabelled compound). The δ 148.8 ppm peak is unambiguously assigned to the 4a-position [1], *i.e.* compound

10; the δ 138.3 ppm peak corresponds to the 4b-position (compound **11**). The off-resonance decoupled spectrum confirmed that these two peaks are due to quaternary carbon atoms.

Table 1. *^{13}C-NMR. spectra of 7-phenyl-2-azafluorenes* (natural abundance (**5**), and ^{13}C-labelled (**10** + **11**))



5			**10 + 11**	**5**			**10 + 11**
δ_{TMS} (ppm) [a]	Type of C [b]	Attribution C No.	δ_{TMS} (ppm)	δ_{TMS} (ppm) [a]	Type of C [b]	Attribution C No.	δ_{TMS} (ppm)
148.8	qua	4a	148.8	128.7	tert	3′	
147.6	tert	1 (3)		127.4	tert	4′ (6)	
146.0	tert	3 (1)		127.0	tert	2′	
144.6	qua	(8a)		126.2	tert	6 (4′)	
142.3	qua	7 (1′)		123.9	tert	8	
140.7	qua	1′ (7)		121.5	tert	5	
138.3	qua	4b	138.3	114.6	tert	4	
138.0	qua	9a		34.6	sec	9	

[a] Chemical shift relative to tetramethylsilane.

[b] From off-resonance decoupling; qua = quaternary, tert = tertiary, sec = secondary carbon atom.

The NMR. assignment was corroborated by mass spectrometry. The mass spectra of fluorenones and azafluorenones show loss of CO and fragmentation to benzynes [1]. The mass spectrum of unlabelled 7-phenyl-2-azafluorenone (**8**) shows three fragment peaks at *m/e* 150, 151, and 152, the latter corresponding to the molecular ion of phenylbenzyne. The labelled azafluorenes **10**/**11** were oxidized in the air to the corresponding azafluorenones, the mass spectrum of which had the three fragment peaks at *m/e* 151, 152, and 153, thus indicating labelling of the biphenyl moiety.

We conclude therefore that (4-biphenylyl)-(4-pyridyl)-carbene (**3**) undergoes expansion of both rings, with benzenoid ring expansion dominating. This fact strongly supports the postulated importance of carbene-σ ring-LUMO interactions in aromatic carbene-carbene rearrangements.

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Experimental Part

The pyrolysis apparatus consisted of a 32 × 2 cm quartz tube, heated by a *Heraeus* RoK 3/30 oven, and leading directly into a cold-trap (liq. N_2), the whole being evacuated by an *Edwards* pumping system with ultimate vacuum 2×10^{-8} Torr, and pumping speed 135 l/s. The working pressure was measured on a *Penning* gauge after the cold-trap. ^{13}C-NMR. spectra were recorded for $CDCl_3$ solutions in microtubes on a *Fourier* transform *Bruker* WP-60 instrument. Chemical shifts (δ) were obtained relative to $CDCl_3$, and are reported in ppm relative to tetramethylsilane, using $\delta_{CDCl_3} = 76{,}9$ ppm. Integrated spectra were recorded with a delay of 10 s between the pulses in order to increase the intensities of the quaternary carbon signals. Mass spectra were recorded on a *CEC* 21-490 instrument at 70 eV, using direct inlet at a source temperature of 200°. TLC. was performed on *Merck* precoated silica gel 60F 254 (0.20 mm) aluminium plates ('Alurolle').

For column chromatography *Merck* silica gel 60 (70–230 mesh) or aluminium oxide 90 (standard, activity II–III) were used. Microanalyses were performed by Dr. *K. Eder*, Genève. $Ba^{13}CO_3$ was obtained from *Bio-Rad* laboratories, California. Melting points are corrected.

Hydrazone of 4-Biphenylyl 4-pyridyl ketone. A mixture of 4.30 g (16.6 mmol) of 4-biphenylyl 4-pyridyl ketone [6], 6 g of hydrazine hydrate, and 2 g of CaO was refluxed for 16 h. After filtering and removal of the solvent, the yellow solid was taken up in $CHCl_3$ and extracted several times with water in order to remove the remaining hydrazine. After drying and evaporating the organic phase, the residue was recrystallized from ethanol/light petroleum 90:10, yielding 2.60 g (57%) of yellow needles, m.p. 166–169°. – MS.: *m/e* 274 ($M^+ + 1$, 18%), 273 (M^+, 100), 257 (16), 243 (9), 154 (12), 152 (14), 78 (8). – IR. (KBr): 3100 *w*, 1600 *m*, 1560 *s*, 1400 *m*, 830 *s*, 760 *m*, 730 *m*, 690 cm^{-1}.

$C_{18}H_{15}N_3$ (273.34) Calc. C 79.10 H 5.54 N 15.37% Found C 79.00 H 5.63 N 15.36%

(4-Biphenylyl)-(4-pyridyl)diazomethane (**4**). The aforesaid hydrazone (2.50 g; 9.2 mmol) was dissolved in 30 ml of $CHCl_3$, and 3.5 g of active MnO_2 [7] was added. The mixture was stirred magnetically at 22° for 2 h, filtered, and the filtrate evaporated to dryness. Recrystallization from CH_2Cl_2/light petroleum 80:20 yielded 1.45 g (58%) of red needles, m.p. (dec.) 111–112°. – MS.: *m/e* 271 (M^+, 2%), 245 (40), 244 (38), 243 (100), 242 (23), 215 (16), 181 (7), 167 (10). – IR. (KBr): 2060 *vs*, 1600 *s*, 1500 *m*, 770 *m*, 690 *m* cm^{-1}.

$C_{18}H_{13}N_3$ (271.32) Calc. C 79.68 H 4.83 N 15.49% Found C 79.67 H 4.98 N 15.57%

Isonicotinic [^{13}C]-acid. This compound was prepared from 4-pyridyllithium and $Ba^{13}CO_3$ (91.8 atom-% ^{13}C) in the same way as described for the ^{14}C-labelled compound [1]. Yield: 61%.

4-Biphenylyl 4-pyridyl [^{13}C]-ketone. Isonicotinic [^{13}C]-acid (1.72 g; 14 mmol) and 17 g of freshly distilled $SOCl_2$ were refluxed with mechanical stirring for $1^1/_2$ h. The excess of $SOCl_2$ was removed in *vacuo*, and 15 ml of anhydrous CS_2 and 1.85 g (12 mmol) of biphenyl were added. The resulting mixture was treated at room temp. and under vigorous stirring with 5.5 g of finely powdered anhydrous $AlCl_3$. As soon as the addition was completed, the reaction mixture was brought to reflux and kept at this temperature for 3 h. Distillation of the CS_2 left a solid mass which was treated with 77 ml of ice water and 13 ml of 1.2N HCl. The yellow solid was filtered off, added to 77 ml of warm water, and basified with conc. NaOH until the precipitated aluminium hydroxide had dissolved. The resulting solution was extracted with CH_2Cl_2, the extract washed with water, and dried over $CaCl_2$. Distillation of the solvent and recrystallization from absolute ethanol yielded 1.6 g (51.3%), m.p. 153–155° (lit. [6] 155° for unlabelled material).

4-Biphenylyl-4-pyridyl-[^{13}C]-diazomethane (**9**). The ^{13}C-labelled ketone was converted to the hydrazone (55% yield) and then to the diazomethane (59% yield) in the same way as described for the unlabelled compound (**4**) above. – MS.: *m/e* 272 (M^+, 3%), 246 (56), 245 (45), 244 (100), 243 (38), 216 (17), 182 (25), 168 (14).

Pyrolysis of (4-biphenylyl)-(4-pyridyl)-diazomethane (**4**). The diazo-compound (300 mg) was sublimed into the pyrolysis tube from a flask kept at 60° during 24 h. The pyrolysis apparatus was maintained at 400° (5×10^{-5} mm). 255 mg of the starting material decomposed in the sublimation flask, presumably to the corresponding azine, which was not examined further. The pyrolysis product, isolated from the cold-trap (32 mg) was essentially 7-phenyl-2-azafluorene (**5**). After purification by chromatography on silica gel, eluting with CH_2Cl_2 followed by $CHCl_3$, it had thin layer chromatographic properties and mixed m.p. identical with those of the synthetic material (*vide infra*). – MS.: *m/e* 244 ($M^+ + 1$, 19%), 243 (M^+, 100), 242 (13), 215 (6), 213 (5), 166 (3).

Pyrolysis of (4-biphenylyl)-(4-pyridyl)-[^{13}C]-diazomethane (**9**). Under the same conditions as described in the preceding entry 174 mg of **9** yielded 20 mg of pyrolysate which, after chromatography furnished 12 mg of pure [^{13}C]-7-phenyl-2-azafluorene. The ^{13}C-NMR. spectrum exhibited two and only two signals at δ 148.8 and 138.3 ppm, with integral and intensity ratio $\approx 40:60$. The identity of these two peaks with the corresponding ones in the unlabelled compound (Table 1) was established by recording the ^{13}C-NMR. spectrum of a 1:50 mixture of the labelled and unlabelled 7-phenyl-2-azafluorene.

Slow air oxidation of a chloroform solution of the labelled 7-phenyl-2-azafluorene afforded 7-phenyl-2-azafluorenone, which was separated by thin layer chromatography, extracted with chloroform, and subjected to mass spectrometry. – MS.: *m/e* 258 (100%), 230 (3.4), 229 (6.5), 228 (6.0), 203 (7.5), 202 (6.0), 201 (8.0), 153 (6.0), 152 (8.0), 151 (3.5), 150 (1.5).

4-(4-Biphenylyl)-3-mesitoylpyridine (**7**). To 4.0 g of Mg turnings in a one-liter three-necked flask equipped with mechanical stirrer, condenser, and drying tube, was added dropwise a solution of 6.3 g of 4-bromobiphenyl in 30 ml of anhydrous ether. The reaction was initiated by gentle heating and stirring for 15 min. A further 32.2 g of 4-bromobiphenyl in 110 ml of ether was added in the course of 1 h with stirring. To the *Grignard* reagent so formed (theoretically 165 mmol) was added dropwise 18.4 g (82 mmol) of 3-mesitoylpyridine [5] in 40 ml of ether. A gummy yellow solid formed, which was stirred for a further 15 min, and then hydrolysed with 400 ml of a saturated NH_4Cl solution. The organic phase was separated, washed successively with aq. Na_2CO_3, aq. $NaHCO_3$, and water, and dried over $CaCl_2$. Distillation of the solvent and recrystallization of the yellow product from ethanol gave 16.0 g (52%) of 4-(4-biphenyl)-3-mesitoyl-1,4-dihydropyridine, m.p. 232–237°. 14.0 g of this material (37 mmol) was refluxed with 9.1 g of chloranil in 800 ml of benzene for 15 h. The solution was then extracted five times with 350 ml of 10% NaOH in order to eliminate the tetrachlorohydroquinone. Evaporation to dryness of the benzene solution left a brown solid, which was taken up in ethanol, and refluxed with active carbon. After filtering and concentrating, the product was recrystallized from ethanol, yielding 8.7 g (63%) of yellow plates, m.p. 193–194°. – MS.: *m/e* 378 (M^+ + 1, 25%), 377 (M^+, 85), 376 (35), 348 (100), 306 (19), 235 (18), 233 (18), 147 (44), 119 (22). – IR. ($CHCl_3$): 2980*m*, 1670*s*, 1610*m*, 1590*m*, 1270*m* cm^{-1}.

$C_{27}H_{23}NO$ (377.49) Calc. C 85.91 H 6.14 N 3.71% Found C 85.84 H 6.21 N 3.81%

7-Phenyl-2-azafluoren-9-one (7-phenylindeno[2,1-*c*]pyridin-9-one) (**8**). A mixture of 5 g (13.3 mmol) of 4-biphenyl-3-mesitoylpyridine and 100 g of polyphosphoric acid was heated at 200° with stirring for 1 h. The dark coloured reaction mixture was poured into 300 ml of ice water, and the resulting mixture was brought to pH 10 with 20% NaOH-solution. The product was extracted with $CHCl_3$, the extract was refluxed with active carbon, filtered, concentrated, and chromatographed on alumina, eluting with $CHCl_3$. Collection of the yellow band and recrystallization from ethanol gave 1.05 g (31%) of beautiful yellow needles, m.p. 185–186° (subl. *ca.* 167–186°). – MS.: *m/e* 257 (M^+, 100%), 256 (5.7), 229 (2.5), 228 (4.6), 227 (3.7), 202 (4.1), 201 (3.0), 200 (4.1), 152 (0.6), 151 (0.6), 150 (0.6), 128.5 (5). – IR. (KBr): 1715*s*, 1600*s*, 1450*m*, 1430*m*, 1310*m*, 1150*m*, 940*m*, 840*m*, 770*s*, 710*m*, 670*w* cm^{-1}.

$C_{18}H_{11}NO$ (257.29) Calc. C 84.03 H 4.31 N 5.44% Found C 83.87 H 4.46 N 5.40%

7-Phenyl-2-azafluorene (7-phenylindeno[2,1-*c*]pyridine) (**5**). The foregoing ketone (533 mg; 2.07 mmol), 1.3 g of Zn—$HgCl_2$ [8], 2.5 ml of conc. hydrochloric acid, and 0.9 ml of water were refluxed with magnetic stirring for 48 h. Every 8 h a further 0.9 ml of conc. hydrochloric acid was added. The reaction mixture was poured into a beaker and brought to pH 8 with 1N NaOH. The precipitate of zinc hydroxide was filtered off; the filtrate was extracted with $CHCl_3$, and the precipitate was boiled up several times with $CHCl_3$, and the solvent decanted. The combined extracts were dried over Na_2SO_4, filtered, and evaporated to dryness. The yellow solid so obtained was recrystallized from ethanol/light petroleum 80:20, yielding 220 mg (45%) of colourless plates, m.p. 170–171°. – MS.: *m/e* 244 (M^+ + 1, 19%), 243 (M^+, 100), 242 (12), 215 (7), 213 (6), 166 (3). – IR. (KBr): 1620*m*, 1610*s*, 1475*s*, 1430*s*, 830*s*, 785*s*, 765*s* cm^{-1}. – ^{1}H-NMR. ($CDCl_3$): δ 8.7–8.4 (*m*, 2H (H(C-1), H(C-3)); 7.8–7.2 (*m*, 9H, aromatic); 3.8 (*s*, 2H, H(C-9)) ppm. – ^{13}C-NMR.: see Table 1.

$C_{18}H_{13}N$ (243.31) Calc. C 88.86 H 5.39% Found C 88.56 H 5.47%

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