Evaluation of the Polar–Inductive and Mesomeric Effects exerted on Contiguous Functionalities by *N*-Oxidopyridinium Groups

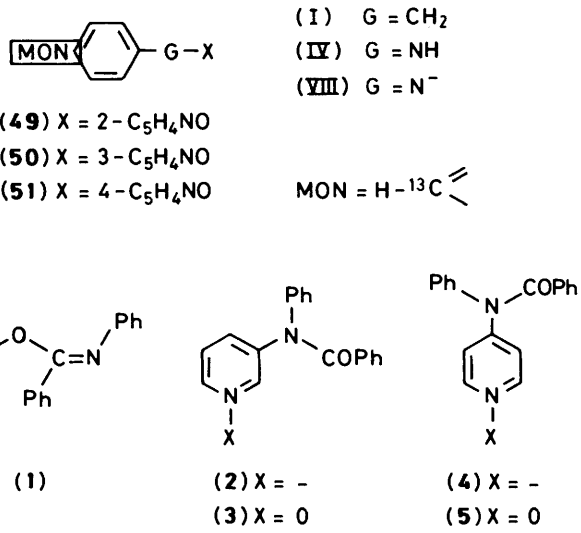
Emma Barchiesi, Silvia Bradamante, Carla Carfagna, Raffaella Ferraccioli, and Giorgio A. Pagani*

Dipartimento di Chimica Organica e Industriale dell'Università and Centro CNR Speciali Sistemi Organici, Via C. Golgi 19, 20133 Milano, Italy

The polar–inductive and mesomeric effects (and mixtures thereof) of *N*-oxidopyridinium-2-, -3-, and 4-yl functionalities have been evaluated in terms of the σ_{I_B}, σ_{R^-}, and $\sigma_{\bar{C}}$ scales previously defined. Values were generated from the phenyl *para*-^{13}C shifts of $PhCH_2C_5H_4NO$ and $PhNHC_5H_4NO$, respectively. The parameters obtained successfully account for the phenyl *para*-^{13}C shifts of the sodium salts of anilinopyridine 1-oxides (**VII**), prepared in turn by deprotonation of the corresponding precursor nitrogen acids by sodium methylsulphinylmethanide. Results show that the *N*-oxidopyridinium ring exerts considerably more electron-withdrawing power, by both polar–inductive and mesomeric mechanisms, than in the absence of the *N*-oxide function.

Polar–inductive and mesomeric effects exerted by *para*-substituted aryl groups on continguous electron-rich functionalities (G) have been described in terms of the benzylic σ_{I_B}, the mixed $\sigma_{\bar{C}}$, and the resonance σ_{R^-} constants.[1] Analogous effects exerted by the 2-, 3-, and 4-pyridyl groups have been described previously within the frame of a scale of effects exerted by primary functionalities.[2] Our approach for obtaining the σ constants is based on the response of a *para* magnetic monitor [$^1H(p)$, $^{19}F(p)$, or $^{13}C(p)$] and offers the great advantage of providing an experimental discriminative access to both the polar–inductive and the resonance contributions exerted by the (hetero)aromatic systems. So far the method has proved to be of general validity and applicability.[1–5]

Although the electron-withdrawing capabilities of the pyridyl rings have been extensively documented,[6] much less is known in quantitative terms about the corresponding *N*-oxides. Available acidity,[7] n.m.r.,[8] and kinetic[9] data indicate an enhanced electron deficiency for the *N*-oxides relative to the *N*-unsubstituted pyridine rings. We report here the polar–inductive and mesomeric effects exerted by the *N*-oxides of pyridyl rings as substituents. Accordingly, we have analysed the ^{13}C n.m.r. spectra of the 2-, 3-, and 4-benzylpyridine 1-oxides (**I-49**)—(**I-51**)† and of the corresponding 2-, 3-, and 4-anilinopyridine 1-oxides (**IV-49**)—(**IV-51**). To check the consistency of the interpolated σ values, we then prepared the sodium salts (**VII-49**)—(**VII-51**) of the anilinopyridine 1-oxides and we verified that the constants obtained accounted satisfactorily for their $^{13}C(p)$ shifts in terms of the general relationships already described for the PhN^-X family (**VII**).



Results and Discussion

Synthesis of the N-*Oxides.*—The benzylpyridine 1-oxides were prepared by oxidation of the corresponding benzylpyridines with *m*-chloroperbenzoic acid. The 2-anilinopyridine 1-oxide (**IV-49**) was prepared by nucleophilic substitution of 2-chloropyridine 1-oxide with aniline. Since preliminary experiments showed that oxidation of anilinopyridines with *m*-chloroperbenzoic acid would probably take place other than at the pyridyl nitrogen, protection of the secondary amine nitrogen had to be considered. Indeed oxidation at the pyridyl nitrogen could be carried out successfully with the *N*-benzoylanilinopyridines (**2**) and (**4**): the 4-isomer (**4**) was obtained by direct benzoylation of 4-anilinopyridine, and the 3-isomer (**3**) was obtained by Chapman rearrangement of the α-phenyliminobenzyl 3-pyridyl ether (**1**), in turn obtained from α-phenyliminobenzyl chloride and 3-hydroxypyridine. Alkaline hydrolysis of the amides (**3**) and (**5**) afforded the desired compounds (**IV-50**) and (**IV-51**). As previously,[5] the sodium amides (**VII-49**)—(**VII-51**) were obtained directly in the n.m.r. tubes by deprotonation of the corresponding nitrogen acids of family (**IV**) using as a base sodium methylsulphinylmethanide in Me_2SO solution.

^{13}C *N.m.r. Spectra.*—Table 1 collects the ^{13}C shift data for the *N*-oxidopyridinium-2-, -3-, and -4-yl compounds belonging to families (**I**), (**IV**), and (**VII**). The major C–H coupling constants of the heterocyclic rings in compounds (**49**)—(**51**) of families (**I**), (**IV**), and (**VII**) are reported in Table 2. Detailed description of *all* the coupling constants of the heterocyclic moiety was outside the aim of the present investigation: indeed attention was particularly focused on those parameters that could allow us to discriminate between the resonances of carbon atoms present in

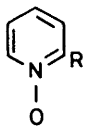
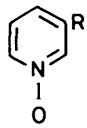
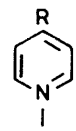
† As before,[1–5] substituents are identified by an arbitrary progressive arabic numbering; families are identified by roman numbers.

Table 1. ^{13}C Chemical shifts of substituted pyridine 1-oxides[a]

Compound	C(2)	C(3)	C(4)	C(5)	C(6)	C(*ipso*)	C(*ortho*)	C(*meta*)	C(*para*)	CH_2
(I-49)	150.30	126.28	124.74	124.38	138.93	137.18	128.38	129.07	126.47	35.44
(IV-49)	147.54	107.38	127.09	113.94	137.32	138.46	121.73	129.30	123.86	
(VII-49)[b]	155.64	107.48	127.01	101.91	138.26	154.30	122.50	128.52	118.03	
(I-50)	136.46	140.59	125.57	126.14	138.39	139.34	128.58	128.69	126.45	37.36
(IV-50)	126.70	143.35	112.19	126.20	129.76	141.00	119.17	129.44	122.17	
(VII-50)[b]	126.63	154.93	112.47	124.46	118.28	155.94	119.69	128.31	114.49	
(I-51)	138.36	126.49	139.45[c]	126.49	138.36	139.24[c]	128.71	128.58	126.38	39.07
(IV-51)	138.70	111.30	140.49[c]	111.30	138.70	141.80[c]	119.27	129.28	122.24	
(VII-51)[d]	137.27	109.27	155.65[c]	109.27	137.27	153.70[c]	120.80	128.43	116.32	

[a] Shifts are relative to Me_4Si for 0.33M-solutions in $(CD_3)_2SO$; numbering of carbon atoms refers to the heterocyclic ring. [b] Shifts are relative to Me_4Si as external standard; solutions in Me_2SO, 0.33M in substrate and 0.66M in base. [c] Assignments may be interchanged. [d] Solution in Me_2SO, 0.11M in substrate and 0.22M in base.

Table 2. C–H Coupling constants (Hz) of the 1-oxidopyridinium groups

		R = CH_2Ph			R = NHPh			R = N^-Ph		
Systems	C	$^1J_{CH}$	$^2J_{CCH}$	$^3J_{CCCH}$	$^1J_{CH}$	$^2J_{CCH}$	$^3J_{CCCH}$	$^1J_{CH}$	$^2J_{CCH}$	$^3J_{CCCH}$
	2		J_{C,CH_2} = 6	$J_{C,H(6)}$ = 4.3; $J_{C,H(4)}$ = 8.5			$J_{C,H(4)}$ = 8.6; $J_{C,H(6)}$ = 5.2			$J_{C,H(4)}$ = 8; $J_{C,H(6)}$ = 4.1
	3	164.7		$J_{C,H(5)}$ = 8.4; J_{C,CH_2} = 4	167.1		$J_{C,H(5)}$ = 8.2	161.5		$J_{C,H(5)}$ = 8
	4	169.2		$J_{C,H(6)}$ = 7	167.4		$J_{C,H(6)}$ = 8.1	160.1		$J_{C,H(6)}$ = 8.3
	5	167.7	$J_{C,H(4)}$ = $J_{C,H(6)}$ = 4	$J_{C,H(3)}$ = 7.2	168.7	$J_{C,H(6)}$ = 2.8	$J_{C,H(3)}$ = 8.3	169	$J_{C,H(6)}$ = 2.4	$J_{C,H(3)}$ = 8.8
	6	187	$J_{C,H(5)}$ = 4.3	$J_{C,H(4)}$ = 5.7	185.8	$J_{C,H(5)}$ = 4	$J_{C,H(4)}$ = 7.4	178.2	$J_{C,H(5)}$ = 4	$J_{C,H(4)}$ = 8
	2	188.1		$J_{C,H(6)}$ = 3.7; $J_{C,H(4)}$ = 8.5; J_{C,CH_2} = 6	184.8		$J_{C,H(4)}$ = 9; $J_{C,H(6)}$ = 4.7	180.1		$J_{C,H(4)}$ = 8.9; $J_{C,H(6)}$ = 4.5
	3			[a]			$J_{C,H(5)}$ = 10.4		$J_{C,H(2)}$ = 2.8	$J_{C,H(5)}$ = 9
	4	167.6		$J_{C,H(2)}$ = $J_{C,H(6)}$ = 5.6; J_{C,CH_2} = 5.7	169.1		$J_{C,H(6)}$ = 10.8; $J_{C,H(2)}$ = 5.7[b]	156.3		$J_{C,H(6)}$ = 10.6; $J_{C,H(2)}$ = 5.7[b]
	5	168.2	$J_{C,H(6)}$ = 4.7		168.4	$J_{C,H(6)}$ = 4.8		159.9	$J_{C,H(6)}$ = 5.2	
	6	186.1		$J_{C,H(4)}$ = 8; $J_{C,H(2)}$ = 6	188	$J_{C,H(5)}$ = 4	$J_{C,H(4)}$ = 8.3; $J_{C,H(2)}$ = 4.2	187	$J_{C,H(5)}$ = 4.5	
	2	188.2	$J_{C,H(3)}$ = 4	$J_{C,H(6)}$ = 6.7	185.5	$J_{C,H(3)}$ = 2	$J_{C,H(6)}$ = 4.4	179	$J_{C,H(3)}$ = 3.6	$J_{C,H(6)}$ = 6.5
	3	170.1	$J_{C,H(2)}$ = 4.8	$J_{C,H(5)}$ = 4.8	164.8	$J_{C,H(2)}$ = 4.6	$J_{C,H(5)}$ = 5.7	163	$J_{C,H(2)}$ = 3.9	$J_{C,H(5)}$ = 5.7
	4		J_{C,CH_2} = 6.8[c]	$J_{C,H(2)}$ = $J_{C,H(6)}$ = 6.8;			$J_{C,H(2)}$ = $J_{C,H(6)}$ = 8.3			$J_{C,H(2)}$ = $J_{C,H(6)}$ = 8
	5	170.1	$J_{C,H(6)}$ = 4.8	$J_{C,H(3)}$ = 4.8	164.8	$J_{C,H(6)}$ = 4.6	$J_{C,H(3)}$ = 5.7	163	$J_{C,H(6)}$ = 3.9	$J_{C,H(3)}$ = 5.7
	6	188.2	$J_{C,H(5)}$ = 4	$J_{C,H(2)}$ = 6.7	185.5	$J_{C,H(5)}$ = 2	$J_{C,H(2)}$ = 4.4	179	$J_{C,H(5)}$ = 3.6	$J_{C,H(2)}$ = 6.5

[a] Broad multiplet. [b] Assignment uncertain. [c] Tentative interpretation.

the various heterocyclic and benzenoid positions. The assignment of the ^{13}C resonances was based on data from proton-coupled spectra, with the aid of literature reports concerning the parameters both of pyridine *N*-oxides[10] and of the non-oxidised rings: in a number of cases selective decouplings were also performed. Once the carbon resonances of the heterocyclic portion had been attributed, the assignment of the C(*p*) peak was usually straightforward. In particular, the assignment of the ^{13}C peaks in the benzylpyridine 1-oxides was somewhat aided by the application of substituent shift effects known[11] to affect the values of the unsubstituted ring, and by the availability of the non-oxidised benzyl precursors. Two features were generally exploited for the assignments: (*a*) the fact that signals of carbon atoms at positions 2, 4, and 6 in the *N*-oxides are displaced *ca.* 10 p.p.m. to high field relative to the non-oxidised counterparts; and (*b*) the increase in $^1J_{CH}$ in the *N*-oxides.

In the case of the 2-benzylpyridine 1-oxide there was a particular uncertainty in the assignment of peaks to C(3) and C(5) because neither chemical shift is under the direct influence of the *N*-oxide group. Both C(3) and C(5) signals are present as two quintets, whereas that of C(4) appears as a double doublet. However, a 'tickling' experiment showed that C(3) is coupled with the protons of the benzylic methylene group, whereas C(5) shows couplings with H(3), H(4), and H(6), the sizes of the long-distance couplings being in the usual range.[11] On the basis of the identification of C(3), the distinction of C(*p*) from C(3) is straightforward.

In the case of the 3-benzylpyridine 1-oxide, distinction had to be made between C(2) and C(6), and among C(4), C(5), and C(*p*). The long-distance couplings and the couplings with protons of the benzylic methylene group allowed distinction of C(2) from C(6) and of C(4) from C(5). Furthermore the value of $^1J_{CH}$ allowed the distinction of C(*p*) ($^1J_{CH}$ 160 Hz) from C(4) and C(5). Upon selective irradiation at the frequency of the benzylic protons, the C(3) signal became a double doublet because of couplings with H(5) and H(2). Furthermore, the coupling between C(4) and CH_2 also vanished, thus allowing

Table 3. Master equations relating C(*p*) of families (**I**), (**IV**), and (**VII**) to polar–inductive (σ_{IB}), resonance (σ_{R-}), and mixed (σ_C^-) substituent parameters

No.	Family	G	Relationship	*r*	*n*	Substituents
(1)	(**I**)	CH_2	$C(p) = (5.127 \pm 0.064)\sigma_{IB} + (125.29 \pm 0.01)$	0.998	24	H, Ph, $CONMe_2$, CO_2Me, COMe, COPh, $COCF_3$, NO_2, CN, SOMe, SO_2Me, SOPh, SO_2Ph, $PO(OEt)_2$, 2-C_5H_4N, 3-C_5H_4N, 4-C_5H_4N, CH_2CN, CH_2COMe, NH_2, NHCOMe, NMe_3^+, Br, SPh
(2)	(**IV**)	NH	$C(p) = (8.46 \pm 0.29)\sigma_C^- + (115.56 \pm 0.08)$	0.991	17	H, Ph, $CONMe_2$, CO_2Me, COMe, COPh, CHO, $COCF_3$, NO_2, CN, SO_2Me, SOPh, SO_2Ph, $PO(OEt)_2$, 2-C_5H_4N, 3-C_5H_4N, 4-C_5H_4N
(3)	(**IV**)	NH	$C(p) = (6.71 \pm 0.18)\sigma_{IB} + (12.93 \pm 0.29)\sigma_{R-} + (115.42 \pm 0.09)$	0.999	18	as entry (2) + Me
(4)	(**VII**)	N^-	$C(p) = (16.17 \pm 0.60)\sigma_C^- + (102.58 \pm 0.21)$	0.991	15	H, Ph, $CONMe_2$, CO_2Me, COMe, COPh, CHO, $COCF_3$, NO_2, $PO(OEt)_2$, $POPh_2$, 2-C_5H_4N, 3-C_5H_4N, 4-C_5H_4N, Me
(5)	(**VII**)	N^-	$C(p) = (10.04 \pm 1.03)\sigma_{IB} + (26.10 \pm 1.40)\sigma_{R-} + (101.84 \pm 0.47)$	0.992	15	as entry (4)

the identification of C(4): the assignment of C(5) followed as a consequence.

In the case of the 4-benzylpyridine 1-oxide, no problems arose in distinguishing signals for C(2) and C(6) from those for C(3) and C(5) and the phenyl resonances. However no clear distinction could be made between C(4) and C(*ipso*) of the phenyl ring.

Distinctive upfield shifts were found for the carbon atoms *ortho* and *para* to the amino group in the *N*-oxides of anilinopyridines. In the case of 2-anilinopyridine 1-oxide (**IV-49**) the distinction of C(3) from C(5) is based on the fact that the C(3) signals was a double doublet whereas that of C(5) was a double set of double doublets. The C(4) resonance was present as a double doublet and the C(*p*) resonance as a classical double triplet.

In the case of 3-anilinopyridine 1-oxide the C(5) signal was present as a double doublet and that of C(4) as an unresolved double multiplet. To distinguish between C(2) and C(6) we assumed a larger multiplicity for C(6) (two ^3J and one ^2J couplings) than for C(2) (two ^3J couplings).

In the case of 4-anilinopyridine 1-oxide the distinction of signals for C(3) and C(5) from those for C(2) and C(6) was based on the size of the corresponding $^1J_{CH}$ couplings (165 and 185 Hz, respectively). Distinction of C(*o*) and C(*m*) of the phenyl ring from C(2)/C(6), and C(3)/C(5) [C(*o*) and C(*m*) are present with approximately the same intensity as C(3)/C(5), and C(2)/C(6)] was based on the slightly smaller $^1J_{CH}$ value (159 Hz)[2b] in the benzene ring than in the heterocycle. Both the quaternary carbon atoms C(4) and C(*ipso*) of the phenyl ring had long-range couplings, of 8.3 and 7.2 Hz. Since in general the carbon atoms of the heterocycle showed larger ^3J couplings than the carbon atoms of the phenyl ring, it seemed logical to assign the 140.49 p.p.m. resonance with a larger coupling to C(4) of the pyridine ring.

The effect of the negative charge in the sodium *N*-phenyl-*N*-(1-oxidopyridiniumyl)amides was to move upfield the shifts of the carbon atoms carrying some charge and to decrease slightly some ^1J values. The spreading of the shifts and the analogy of the pattern of the anions with those of the neutral precursors made the assignments straightforward. As an example, in the anion of 2-anilinopyridine 1-oxide, analogously to the neutral species, the C(3) resonance is present as a double doublet, the C(5) signal as two sets of double doublets, and the C(6) resonance, as expected, as a double triplet.

Correlative Analysis and Electron Demands of the Oxidopyridiniumyl Substituents.—Table 3 reports the 'master' relationships that control the variation of the C(*p*) monitor of PhGX as a function of the electron demand of the substituent.[2–5] Thus equation (1) is valid for the $PhCH_2X$ systems and C(*p*) is a function only of the polar–inductive effect of the substituent as expressed in terms of σ_{IB}. The polar–inductive effects exerted by the oxidopyridinium groups can be interpolated once the C(*p*) values for the benzylpyridine 1-oxides (**I-49**)—(**I-51**) are introduced into equation (1): the σ_{IB} values obtained are reported in Table 4. Equation (2) is valid for the PhNHX systems and C(*p*) is a function both of the polar–inductive and of the mesomeric effects exerted by the substituent as expressed by the mixed parameter σ_C^-. Values of σ_C^- for the pyridine 1-oxide substituents can be interpolated once the C(*p*) values of the anilinopyridine 1-oxides are introduced into equation (2): such values are also reported in Table 4. Equation (3) is a dual-parameter relationship linking the variation of C(*p*) in PhNHX to the polar–inductive effect exerted by X and expressed by σ_{IB}, and to the mesomeric effect as expressed by σ_{R-}. The mesomeric component of the total substituent effect exerted by the 1-oxidopyridinium substituents can be obtained in terms of σ_{R-} once the C(*p*) of anilinopyridine 1-oxides and the corresponding σ_{IB} values are introduced into equation (3). The values of σ_{R-} can also be calculated from the relationship that is obtained by making equal the two right-hand-side expressions of equations (2) and (3): $\sigma_{R-} = 0.654\,\sigma_C^- - 0.519\,\sigma_{IB} + 0.01$. The relationship links directly σ_C^-, σ_{IB}, and σ_{R-}. The values of σ_{R-} for the 1-oxidopyridinium substituents are also reported in Table 4.

Table 4. Polar–inductive σ_{IB}, resonance σ_{R-}, and mixed σ_C^- constants for the 2-, 3-, and 4-pyridyl groups and their *N*-oxides

Substituent	σ_{IB}	σ_{R-}	σ_C^-
2-C_5H_4N	0.12	0.31	0.55
2-C_5H_4NO	0.23	0.53	0.98
3-C_5H_4N	0.15	0.31	0.58
3-C_5H_4NO	0.23	0.40	0.78
4-C_5H_4N	0.18	0.45	0.81
4-C_5H_4NO	0.21	0.425	0.80

It is interesting to compare the electron demands of the oxidopyridinium substituents with those of the pyridyl ring: for this reason we have included in Table 4 also the σ values for the 2-, 3-, and 4-pyridyl groups. All the σ values of the oxidopyridinium substituents are numerically greater than the corresponding parameters for the pyridyl rings. The largest increase is manifested by position 2 of the ring: thus the 1-oxidopyridinium-2-yl substituent is the most electron-

withdrawing group of the series, considerably more potent than the 4-isomer.

To test the general applicability of the σ parameters obtained for the 1-oxidopyridinium functionalities, we have incorporated these values into equation (4) of Table 3 to treat the C(*p*) shifts of the sodium amides (**VII-49**)—(**VII-51**). The result is highly satisfactory since the new fitting parameters after the incorporation are: $\delta C(p) = (16.12 \pm 0.57)\sigma_C^- + (102.59 \pm 0.18)$ ($n = 18$, $r = 0.990$).

The same C(*p*) data for (**VII-49**)—(**VII-51**) were further incorporated into the biparametric equation (5) of Table 3. The result was satisfactory in this case also since the new parameters after the incorporation were: $\delta C(p) = (10.84 \pm 0.99)\sigma_{IB} + (26.16 \pm 1.29)\sigma_R^- + (101.85 \pm 0.46)$ ($n = 18$).

The present results confirm the high rank occupied by the 1-oxidopyridinium ring in the scales of electron-poor functionalities, and are in qualitative good accord with results of nucleophilic aromatic subtitutions carried out on halogenopyridine 1-oxides.[9] The use of the 1-oxidopyridinium ring as a substitutent may be useful in the design of synthons in which there is need for a potent electron-withdrawing group.

Experimental

Materials.—2-Benzylpyridine, 4-benzylpyridine, 3-hydroxymethylpyridine, and 2-chloropyridine 1-oxide were commercial products (Fluka or Aldrich). 3-Benzylpyridine was prepared according to reported procedures.[12]

2-Benzylpyridine 1-Oxide (**I-49**).—A solution of 2-benzylpyridine (1 g, 5.9 mmol) in CH_2Cl_2 (7 ml) was added dropwise to a stirred solution of *m*-chloroperbenzoic acid (1.78 g; 70% oxidimetric titre; 7.2 mmol; 22% molar excess) in CH_2Cl_2 (30 ml). The mixture was stirred at room temperature for 72 h, washed with aq. 10% Na_2CO_3 (50 ml), then with water, dried ($MgSO_4$), and evaporated to dryness. The oily residue was taken up in a mixture of ethyl acetate, benzene, and n-hexane (1:1:1) to give a solid which upon crystallisation afforded the *N*-oxide (**I-49**) (500 mg, 45.5%), m.p. 104—105 °C (from PhH) (lit.,[13] 103 °C; 106 °C) (Found: C, 77.7; H, 6.2; N, 7.4. Calc. for $C_{12}H_{11}NO$: C, 77.8; H, 6.0; N, 7.6%); δ_H (90 MHz; $CDCl_3$) 4.3 (2 H, s, CH_2), 7.1 (3 H, m, aromatic), 7.3 (5 H, m, aromatic), and 8.33 (1 H, br t, H-6 of pyridyl).

3-Benzylpyridine 1-Oxide (**I-50**).—A solution of 3-benzylpyridine (4 g, 23.6 mmol) in CH_2Cl_2 (28 ml) was added dropwise to a stirred solution of *m*-chloroperbenzoic acid (6.26 g; 85% oxidimetric titre; 30.8 mmol; 30% molar excess) in CH_2Cl_2 (75 ml). The mixture was treated as described for (**I-49**). The oily residue obtained after evaporation of the solvent solidified upon treatment with ethyl acetate–n-hexane (9:1); the isolated solid was distilled (130 °C at 0.1 mmHg) to give the N-*oxide* (**I-50**) (1.79 g, 41%), m.p. 50 °C (Found: C, 77.3; H, 5.9; N, 7.3. $C_{12}H_{11}NO$ requires C, 77.8; H, 6.0; N, 7.6%); δ_H (90 MHz; $CDCl_3$) 3.9 (2 H, s, CH_2), 7.25 (7 H, m, aromatic), and 8.1 (2 H, m, H-2 and H-6 of pyridyl).

4-Benzylpyridine 1-Oxide (**I-51**).—A solution of 4-benzylpyridine (5 g, 29.5 mmol) in CH_2Cl_2 (35 ml) was added dropwise to a stirred solution of *m*-chloroperbenzoic acid (7.83 g; oxidimetric titre 70%; 38.5 mmol; 31% molar excess) in CH_2Cl_2 (94 ml). The mixture was treated as described for (**I-49**) to give the *N*-oxide (**I-51**) (2 g, 36%), m.p. 105 °C (from PhH) (lit.,[14] 105—107 °C; lit.,[13b] 151 °C) (Found: C, 77.7; H, 5.9; N, 7.4. Calc. for $C_{12}H_{11}NO$: C, 77.8; H, 6.0; N, 7.6%); δ_H (90 MHz; $CDCl_3$) 4.0 (2 H, s, CH_2), 7.25 (7 H, m, aromatic), and 8.15 (2 H, d, H-2 and H-6 of pyridyl).

2-Anilinopyridine 1-Oxide (**IV-49**).—Aniline (6.69 g, 72 mmol) was added to a solution of 2-chloropyridine 1-oxide hydrochloride (3 g, 18 mmol) in acetonitrile (7 ml); the mixture was refluxed for 4 h and evaporated to dryness, and the residue was taken up in methylene dichloride and water. The organic phase was dried (Na_2SO_4) and evaporated to dryness. The residue was chromatographed on silica with ethyl acetate–methanol (9:1) to give the N-*oxide* (**IV-49**) (540 mg, 16%), m.p. 120—121 °C (Found: C, 71.1; H, 5.5; N, 15.2. $C_{11}H_{10}N_2O$ requires C, 70.95; H, 5.4; N, 15.0%); δ_H (90 MHz; $CDCl_3$) 6.7 (1 H, triple doublet, H-5 of pyridyl, $J_{5,6} \simeq J_{4,5}$ 6.5 Hz, $J_{3,5}$ 3.5 Hz), 7.3 (7 H, m, aromatic), 8.2 (1 H, dd, H-6 of pyridyl, $J_{5,6}$ 6.5 Hz, $J_{4,5}$ *ca.* 1 Hz), and 8.8 (1 H, br s, NH).

α-Phenyliminobenzyl 3-Pyridyl Ether (**1**).—3-Hydroxypyridine (5.94 g, 62.5 mmol) was added to ethanol (30 ml) in which metallic sodium (1.43 g, 62.5 mmol) had been previously dissolved; to the solution α-phenyliminobenzyl chloride[15] (12.59 g, 58.4 mmol) in ether (28 ml) was slowly added. The mixture was stirred at room temperature for 12 h, then evaporated at reduced pressure, and the residue was treated with water to give a solid, which was filtered off and dried. Chromatography on silica with methylene dichloride–ethyl acetate (8:2) gave the *imino ether* (**1**) (8 g, 50%), m.p. 46—48 °C (Found: C. 78.3; H, 5.1; N, 10.2. $C_{18}H_{14}N_2O$ requires C, 78.8; H, 5.1; N, 10.2%); δ_H (90 MHz; $CDCl_3$) 7.33 (12 H, m, aromatic) and 8.45 (2 H, m, H-2 and H-6 of pyridyl).

N-Benzoyl-3-anilinopyridine 1-Oxide.—To perform the Chapman rearrangement,[16] the imino ether (**1**) (6 g, 21.8 mmol) was heated, in a small apparatus immersed in an oil-bath, to the m.p. and then cautiously at 280—290 °C for 30 min; the temperature was monitored by a thermometer immersed in the melt. The mixture was cooled and a solid was obtained upon treatment with n-hexane. Chromatography on silica with methylene dichloride–ethyl acetate (9:1) gave *N*-benzoyl-3-anilinopyridine, m.p. 159 °C; δ_H (90 MHz; $CDCl_3$) 7.45 (12 H, m, aromatic) and 8.5 (2 H, m, H-2 and H-6 of pyridine). A solution of this amide (2 g, 7.29 mmol) in methylene dichloride (14 ml) was added dropwise to a stirred solution of *m*-chloroperbenzoic acid (1.91 g; oxidimetric titre 85%; 9.40 mmol; 30% molar excess) in methylene dichloride (34 ml). The mixture was stirred at room temperature for 72 h, washed with aq. 10% Na_2CO_3 (3 × 25 ml), then with water, dried (Na_2SO_4), and evaporated to dryness to leave a yellowish solid, crystallisation of which gave the N-*oxide* (2 g, 94.5%), m.p. 153—155 °C (from ethyl acetate) (Found: C, 74.7; H, 5.0; N, 9.8. $C_{18}H_{14}N_2O_2$ requires C, 74.5; H, 4.9; N, 9.6%); δ_H (90 MHz; $CDCl_3$) 7.33 (12 H, m, aromatic) and 8.15 (2 H, m, H-2 and H-6 of pyridine).

3-Anilinopyridine 1-Oxide (**IV-50**).—To a solution of *N*-benzoyl-3-anilinopyridine 1-oxide (2 g, 6.88 mmol) in ethanol (21 ml) was added aq. 50% potassium hydroxide (4.3 ml); the mixture was refluxed under nitrogen for 1 h, then evaporated to dryness. The residue was taken up in brine (40 ml), and extracted with ether (4 × 40 ml); the organic extracts were dried (Na_2SO_4) and evaporated to dryness and the residue upon crystallisation afforded the mono-hydrated N-*oxide* (900 mg, 70%), m.p. 75 °C (from PhH) (Found: C, 64.5; H, 5.3; N, 13.4. $C_{11}H_{10}N_2O{\cdot}H_2O$ requires C, 64.7; H, 5.8; N, 13.7%). The *anhydrous compound* was obtained by heating the monohydrated form for a few hours at 60 °C and 0.1 mmHg, to constant m.p. 135—136 °C (Found: C, 70.9; H, 5.5; N, 15.0. $C_{11}H_{10}N_2O$ requires C, 70.95; H, 5.4; N, 15.0%); δ_H (90 MHz; $CDCl_3$) 2.5 (1 H, br s, NH), 7.2 (7 H, m, aromatic), 7.8 (1 H, m, H-6 of pyridine), and 8.1 (1 H, s, H-2 of pyridine).

4-(N-*Benzoylanilino*)*pyridine* (**4**).—A stirred suspension of 4-anilinopyridine[17] (3 g, 17.6 mmol) in pyridine (30 ml) was treated with benzoyl chloride (3.22 g, 22.9 mmol): after 30 min the mixture was diluted with water (30 ml), aq. 10% K_2CO_3 was added (80 ml), and the solution was filtered to give the amide (3.72 g, 77%), m.p. 164—165 °C (lit.,[18] 166—167 °C) (Found: C, 79.1; H, 5.2; N, 10.2. Calc. for $C_{18}H_{14}N_2O$: C, 78.8; H, 5.1; N, 10.2%); δ_H (90 MHz; $CDCl_3$) 8.5 (2 H, d, H-2 and H-6 of pyridine) and 7.6—7.0 (12 H, m, aromatic).

4-(N-*Benzoylanilino*)*pyridine* 1-*Oxide* (**5**).—A solution of 4-(*N*-benzoylanilino)pyridine (6 g, 21.87 mmol) in methylene dichloride (42 ml) was added dropwise to a stirred solution of chloroperbenzoic acid (5.80 g; oxidimetric titre 85%; 28.56 mmol; 30% molar excess) in methylene dichloride (110 ml). The mixture was stirred at room temperature for 8 h, washed with aq. 10% Na_2CO_3 (3 × 180 ml), then with water (2 × 180 ml), dried (Na_2SO_4), and evaporated to dryness. The yellowish solid afforded upon crystallisation the N-*oxide* (**5**) (5 g, 79%), m.p. 182—183 °C (from ethyl acetate) (Found: C, 74.55; H, 4.8; N, 9.6. $C_{18}H_{14}N_2O_2$ requires C, 74.5; H, 4.9; N, 9.65%); δ_H (90 MHz; $CDCl_3$) 7.1—7.6 (12 H, m, aromatic) and 8.15 (2 H, d, H-2 and H-6 of pyridine, $J_{5,6}$ 7.5 Hz).

4-*Anilinopyridine* 1-*Oxide* (**IV-51**).—To a solution of 4-(*N*-benzoylanilino)pyridine 1-oxide (4 g, 13.77 mmol) in ethanol (64 ml) was added aq. 50% potassium hydroxide (8 ml); the mixture was stirred at room temp. for 8 h and was then evaporated to dryness. Treatment with water (150 ml) induced the formation of small white needles of the *amine* (2.20 g, 86%), m.p. 222 °C (Found: C, 70.55; H, 5.3; N, 14.8. $C_{11}H_{10}N_2O$ requires C, 70.95; H, 5.4; N, 15.05%); δ_H [80 MHz; $(CD_3)_2SO$] 6.90—7.34 (8 H, m, aromatic), and 7.93 (2 H, d, *J* 7.5 Hz, H-2 and H-6 of pyridine).

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