Structural Effects on the Reactivity of Carbon Radicals in Homolytic Aromatic Substitution. Part 4.[1] The Nucleophilicity of Bridgehead Radicals[2]

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The reactions of 1-adamantyl (1), 3,3-dimethylbicyclo[2.2.2]octan-1-yl (2), and 7,7-dimethylbicyclo[2.2.1]-heptan-1-yl (3) radicals with protonated pyridines and quinoline have been investigated and the relative rates of substitution have been determined. The results obtained showed that the three bridgehead radicals have nucleophilic properties which decrease in the order: (1) > (2) > (3). This behaviour is explained on the basis of a different degree of charge development in the transition state of the addition step of the radicals to the protonated substrates, as a consequence of different ring strain in the three polycyclic systems. A comparison of the present results with those already available for other alkyl radicals is also reported, in order to evaluate the effect of electronic configuration on the reactivity of carbon radicals in homolytic aromatic substitution.

ISOMER distribution and relative reactivity data for the reactions of 1-adamantyl[1] and 1-norbornyl[3] radicals with monosubstituted benzene derivatives have recently been reported and the reactions of these two radicals, as well as that of the bicyclo[2.2.2]octan-1-yl, with *p*-difluorobenzene have also been investigated.[4] The results show that bridgehead radicals have nucleophilic properties which are more or less pronounced depending upon the structure of the polycyclic system. Differing behaviour was more clearly evident for substrates with strongly electron-withdrawing substituents; thus methyl benzoate is 10.9 and 3.5 times more reactive than benzene with respect to 1-adamantyl and 1-norbornyl radicals, respectively, and benzonitrile reacted with 1-adamantyl radical 21.1 times faster than benzene. Other substituents in the benzene ring produced smaller reactivity differences.

The nucleophilic character of several alkyl radicals has been studied by Minisci and his co-workers[5] using the highly electron-deficient protonated pyridines as substrates; the differences in reactivity between alkyl radicals with different structures were greatly enhanced in this system and have been interpreted on the basis of a transition state for the addition step similar to a charge transfer complex with a consequently large contribution by polar forms. In the light of these results it seemed interesting to investigate the behaviour of bridgehead radicals with protonated pyridines in order to define more clearly the differences in polar character and to evaluate the influence of ring strain on the reactivity of carbon radicals which, because of the structural requirements of the molecule, have a pure or almost pure sp^3 configuration. Moreover, the results of this investigation allow comparison with other alkyl radicals (generated under the same experimental conditions) and give deeper insight into the effect of the electronic configuration of carbon radicals upon their reactivity in homolytic aromatic substitution.

RESULTS

Substrates and Products.—The bridgehead radicals investigated, 1-adamantyl (1), 3,3-dimethylbicyclo[2.2.2]octan-1-yl (2), and 7,7-dimethylbicyclo[2.2.1]heptan-1-yl (3) were produced by the silver-catalyzed decarboxylation of the corresponding carboxylic acid by ammonium persulphate,[6] according to the mechanism in the Scheme.

The carboxylic acids employed to produce the radicals (1) and (3) are known compounds, while 3,3-dimethylbicyclo[2.2.2]octane-1-carboxylic acid was prepared from the methyl ester of the 7,7-dimethylbicyclo[2.2.1]heptane-1-carboxylic acid according to reaction (1). Under the

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[1] Part 3, L. Testaferri, M. Tiecco, P. Spagnolo, P. Zanirato, and G. Martelli, *J.C.S. Perkin II*, 1976, 662.

[2] Taken from the Tesi di Laurea of Drs. M. Di Napoli and D. Contino, University of Bari.

[3] L. Testaferri, M. Tiecco, P. Spagnolo, and P. Zanirato, *Gazzetta*, 1975, **105**, 761.

[4] A. Mangini, P. Spagnolo, D. Tassi, M. Tiecco, and P. Zanirato, *Tetrahedron*, 1972, **28**, 3485.

[5] F. Minisci and O. Porta, *Adv. Heterocyclic Chem.*, 1974, **16**, 123.

[6] J. M. Anderson and J. K. Kochi, *J. Amer. Chem. Soc.*, 1970, **92**, 1651.

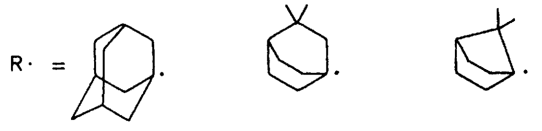
experimental conditions described earlier, radicals (1) and (2) were easily produced; radical (3) was generated in lower

$$S_2O_8^{2-} + Ag^+ \longrightarrow Ag^{2+} + SO_4^{2-} + SO_4^{-\cdot}$$

$$SO_4^{-\cdot} + Ag^+ \longrightarrow SO_4^{2-} + Ag^{2+}$$

$$RCO_2H + Ag^{2+} \longrightarrow RCO_2^{\cdot} + Ag^+ + H^+$$

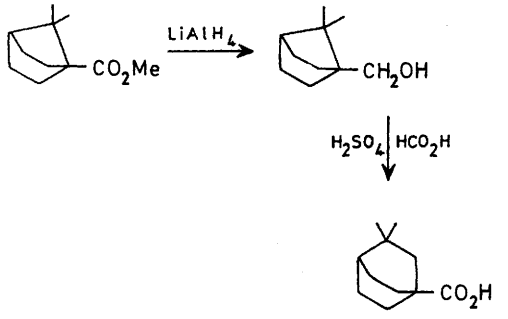
$$RCO_2^{\cdot} \longrightarrow R\cdot + CO_2$$



(1) (2) (3)

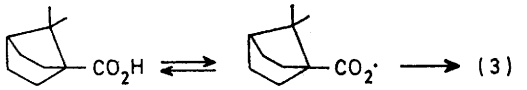
Scheme

yield and most of the starting acid was recovered unchanged. This can be attributed to the known[7] greater difficulty of decarboxylation of the acyloxyl radical of the 1-norbornyl system, which consequently can give rise



(1)

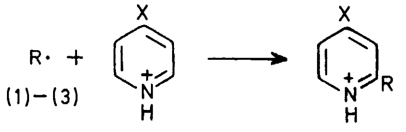
to other competitive reactions, among which hydrogen abstraction (2) to revert to the starting acid is preferred.



(2)

In order to obtain satisfactory yields of substitution products, it was therefore necessary to employ an excess of ammonium persulphate.

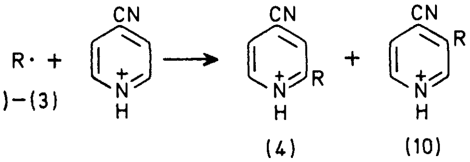
The reactions of the radicals (1)—(3) with protonated 4-substituted pyridines were carried out in aqueous acid solutions in the presence of acetonitrile to ensure complete solubility of the carboxylic acids; as already found for other alkyl radicals,[5] substitution takes place at the 2- and 4-positions. In the case of 4-cyanopyridine only a small



(4) X = CN (8) X = Me
(5) X = COMe (9) X = OMe
(6) X = Cl
(7) X = H

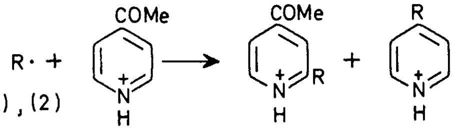
a; R = (1) b; R = (2) c; R = (3)

amount of the 3-substitution product was formed for all three bridgehead radicals. From the reactions of radicals (1) and (2) with 4-acetylpyridine, together with the 2-substitution products (5), by-products were observed, which were identified as 4-(1-adamantyl)pyridine (11a) and 4-(3,3-dimethylbicyclo[2.2.2]octan-1-yl)pyridine (11b) respectively. Substitution of the acyl group becomes much more important when the α-positions are not available and with other nitrogen-containing heteroaromatic compounds.[8] To our knowledge this displacement of the acyl group by alkyl radicals is unprecedented and we are presently investigating the mechanism of this S_R reaction. Reactions of the radicals (1)—(3) with pyridine afforded a mixture of the 2- (7) and 4-substituted pyridines (11); a third compound was obtained in small yield with the radicals (1) and (2), and was identified as adamantan-1-ol and 3,3-dimethylbicyclo[2.2.2]octan-1-ol, respectively. The amount of alcohol increased considerably with less reactive substrates like 4-methyl- and 4-methoxy-pyridine; in the latter case reaction with the 1-adamantyl radical did not give any substitution compound and the only product was adamantan-1-ol. The formation of the alcohols can be accounted for by assuming initial oxidation of the bridgehead radical to the corresponding cation followed by nucleophilic attack by water; in this respect the results obtained are in agreement with the expected ionization potential of the three bridgehead radicals (see Discussion section).



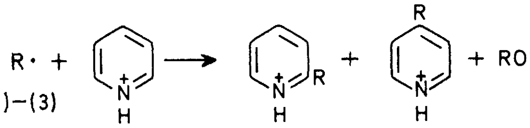
(4) (10)

(4a):(10a) = 92:8; (4b):(10b) = 90:10; (4c):(10c) = 86:14



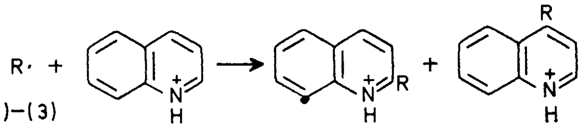
(5) (11)

(5a):(11a) = 92:8; (5b):(11b) = 95:5



(7) (11)

(7a):(11a) = 21:79; (7b):(11b) = 28:72; (7c):(11c) = 45:55



(12) (13)

(12a):(13a) = 97:3; (12b):(13b) = 97:3; (12c):(13c) = 65:35

The reactions with protonated quinoline were carried out in a similar way; in every case a mixture of the 2-(12) and 4-substituted quinolines (13) were obtained, with the 2-isomer predominating.

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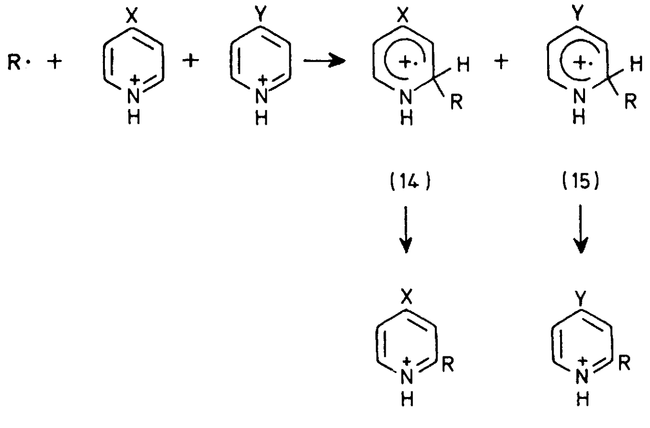
[7] C. Rüchardt, *Angew. Chem. Internat. Edn.*, 1970, **9**, 830.

[8] M. Fiorentino, L. Testaferi, M. Tiecco, and L. Troisi, *J.C.S. Chem. Comm.*, 1976, 329.

Relative Rate Determinations.—The reactivities of the 4-substituted pyridines relative to pyridine towards the bridgehead radicals (1)—(3) were determined by means of competitive experiments using an excess of a mixture of two bases in aqueous sulphuric acid; with the assumption that neither the starting compounds nor the reaction products are selectively removed by side reactions and that the σ-complex intermediates (14) and (15) are not selectively consumed to give products different from (4)—(9), the product ratios should give directly the values of the relative rates. Unfortunately g.l.c. analyses of mixtures containing small quantities of substitution products and a large amount of unchanged substrates could not be made with confidence, the ratios of products being dependent upon the quantity of the ammonium persulphate added. This was particularly evident when the two substrates in competition had large differences in reactivity. The reactions were therefore followed by adding the persulphate in portions and the ratios of substitution products were plotted against the amount of the added oxidizing agent; graphical extrapolation to zero should give the correct value of the relative rate. This procedure was in some cases confirmed by simultaneously measuring the disappearance of the two starting pyridines and applying the equation $K_a/K_b = \log(a/a-x)/\log(b/b-x)$, where $(a/a-x)$ and $(b/b-x)$ are the fractions of unchanged substrates; plots of $\log(a/a-x)$ against $\log(b/b-x)$ gave straight lines whose slopes represented the values of the relative rates. The results obtained with the two methods were in excellent agreement indicating that the extrapolation procedure gives satisfactory results. A further important conclusion can be drawn from these data; the coincidence of the relative rates determined from the measurement of the starting compounds and of the substitution products establishes the fact that neither the starting compounds or the products formed nor the intermediate σ-complexes are selectively removed to give other products; thus we are dealing with a clean substitution process. This is particularly interesting considering the objections which can be raised to the competitive method when applied to homolytic substitutions in the homoaromatic series, where the relative rates are usually determined by measuring the ratios of the products formed.[9]



Owing to the large differences in reactivity between some 4-substituted pyridines and pyridine, direct determination of the relative rates gives rise to serious analytical problems. These were overcome by carrying out competition experiments between pairs of substrates with similar rates (*i.e.* CN–COMe, COMe–Cl *etc.*); from combined values the reactivities relative to pyridine can be calculated. Moreover the initial concentrations of the two substrates were adjusted so that comparable amounts of substitution products could be obtained; statistical corrections were then applied (see Table 7). This procedure is similar to that employed with other alkyl radicals.[10]

The results are collected in Table 1. From the relative rates reported in Table 1 and the isomer ratios obtained for substitution of pyridine, the reactivities of the 2-positions of 4-substituted pyridines with respect to the 2-position of pyridine can be calculated for the three bridgehead radicals (1)—(3) (Table 2).

TABLE 1

Relative rates for the substitution of protonated 4-substituted pyridines by radicals (1)—(3)

		Radical	
Substituent	(1)	(2)	(3)
CN	56.0	12.30	10.08
COMe	19.0	6.92	3.66
Cl	1.83	1.71	1.61
H	1.00	1.00	1.00
Me	0.021	0.03	0.26
OMe		0.002 2	0.112

The reactivity of protonated quinoline relative to protonated pyridine was also determined indirectly from competitive experiments between quinoline and 4-acetyl- or 4-cyano-pyridine [19.02, 12.24, and 10.10 for radicals (1)—(3) respectively]. The reactivity of the 2-position of protonated quinoline relative to the 2-position of protonated pyridine can be obtained from these values and the isomer ratios reported above for the two bases; the corresponding values are 175.7, 84.8, 29.2 for (1)—(3) respectively.

TABLE 2

Relative rates for the substitution of the 2-positions of protonated 4-substituted pyridines by radicals (1)—(3)[a]

		Radical	
Substituent	(1)	(2)	(3)
CN	245.3	39.5	19.3
COMe	90.5	24.7	8.13
Cl	8.7	6.1	3.6
H	1.0	1.0	1.0
Me	0.1	0.11	0.58
OMe		0.01	0.25

[a] As already observed for simple alkyl radicals,[10] Hammett correlations of these partial relative rates with the σ_m values of substituents were not very satisfactory; however, good correlations were obtained with the chemical shifts of pyridinium 2-H, the slopes being 6.0, 4.8, and 2.9 for radicals (1)—(3) respectively.

DISCUSSION

In agreement with the results obtained for the benzene series,[1,3] the effect of substituents in the protonated pyridines confirms that the three bridgehead radicals have nucleophilic character which gradually decreases on passing from (1) to (3). The selectivity shown in the present case is however considerably enhanced. Thus in the case of the 1-adamantylation the presence of a cyano-group produces an increase of the reactivity of

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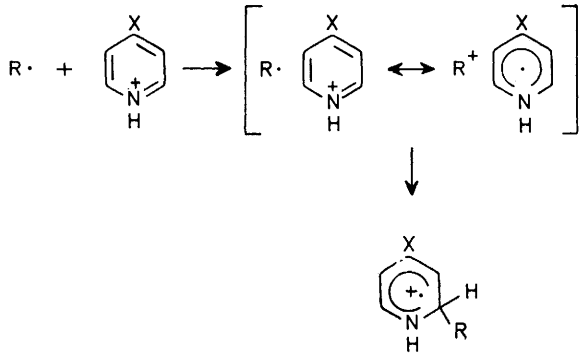
[9] M. J. Perkins, *Free Radicals*, 1973, **2**, 231; D. C. Nonhebel and J. C. Walton, 'Free Radical Chemistry,' The University Press, Cambridge, 1974, p. 417.

[10] F. Minisci, R. Mondelli, G. P. Gardini, and O. Porta, *Tetrahedron*, 1972, **28**, 2403.

the protonated pyridine (${}^{CN}K/{}^{H}K = 56$) which is considerably higher than that produced in benzene (${}^{CN}K/{}^{H}K = 21.1$);[1] on the other hand the methyl group deactivates pyridine (${}^{Me}K/{}^{H}K = 0.021$) more than benzene (${}^{Me}K/{}^{H}K = 0.48$).[1] This effect is much less pronounced with radical (3).[3] This increased sensitivity of nucleophilic carbon radicals to substituent effects can be attributed, as already suggested by Minisci,[10] to a difference in the nature of the transition state for the two systems. In the case of benzene derivatives the transition state would be similar to a σ-complex in which polar species give a substantial contribution only under favourable circumstances[1] (when strongly electron-withdrawing substituents are present), while in the case of protonated pyridines the transition state is similar to a charge transfer complex in which the radical acts as donor and the substrate as acceptor. Thus, electron-withdrawing substituents will increase and electron-releasing substituents decrease the acceptor ability of the protonated pyridine. On the other hand the charge separation in the transition state implies the development of positive charge at the carbon atom of the nucleophilic radical and the degree to which this process will occur, for a given substrate, will depend upon the ability of this carbon atom to accommodate positive charge. In the case of radical (3), the formation of an incipient carbocation at the bridgehead position is difficult because of the highly strained nature of the polycyclic system; the absence of severe ring strain, on the other hand, allows a developing positive charge to be more easily accommodated at the 1-position of adamantane.[11] Radical (2) shows intermediate behaviour. These characteristics will be reflected in the nucleophilic properties of the three bridgehead radicals. The charge separation for the radical (3) will occur to a very low extent and it is the least selective of the series; this is confirmed by the values of the relative rates as well as by the isomer ratios in the substitution of pyridine, 4-cyanopyridine, and quinoline. A further point of interest in this respect is offered by the results obtained with weakly electron-deficient substrates like 4-methyl- and 4-methoxy-pyridine; only the 1-adamantyl and 3,3-dimethylbicyclo[2.2.2]octan-1-yl radicals afforded the corresponding alcohols indicating their ability to be oxidized (probably by Ag^{2+}) to the corresponding carbocations, while radical (3) reacts with the substrates. In the absence of protonated pyridines radicals (1) and (2) easily oxidize to give alcohols, while radical (3) does not undergo the electron transfer process and only dimerization and hydrogen abstraction are observed. This behaviour is quite similar to that of cyclopropyl radical in the presence of Cu^{2+} ions.[12]



Our results can be used to elucidate fully the effect of the hybridization of the orbital carrying the unpaired electron upon the polar nature of carbon-centred radicals. An increase of the *s* character of a hybrid orbital will result in an increase of its electronegativity and a decrease of the donor ability of the corresponding radical with consequently less pronounced nucleophilic character. These conclusions were already drawn from studies in the homocyclic series[13] and are confirmed by the data here. According to the nature of the orbital occupied by the odd electron the following nucleophilicity sequence obtains carbon radicals: $p > sp^3 > sp^2 > sp$. The *sp* configuration confers slightly electrophilic character.[13] Table 3 collects the available data of relative rates of substitutions of 4-substituted pyridines by carbon radicals with different hybridization; for the sake of homogeneity 4-methylpyridine has been chosen as the reference.

The two radicals at the extremes of this sequence, $Me_3C\cdot$ and $Ph\cdot$, represent examples of radicals with the unpaired electron on a *p* and an sp^2 orbital respectively. The three bridgehead radicals should have a pyramidal configuration; however, progressively enhanced *s* character of the orbital carrying the unpaired electron is expected on passing from (1) to (3) as a result of the different ring strain in the three systems. Recent e.s.r. investigations[14,15] showed that the best agreement between the experimental and the INDO-calculated hyperfine splitting constants was obtained by considering that the spin-bearing carbon atoms do not suffer much

TABLE 3

Relative rates of substitution in the 2-position of protonated 4-substituted pyridines by carbon radicals

	Substituent X				
Radical	CN	COMe	Cl	CH_3	Ref
t-Butyl	12 600	960	74	1	10
(1)	2 453	905	87	1	This work
(2)	359	225	55	1	This work
(3)	33.3	14	6.2	1	This work
Cyclopropyl	13.9	6.2		1	*a*
Phenyl	3.3		2.9	1	*b*

[a] A. Clerici, F. Minisci, and O. Porta, *J.C.S. Perkin II*, 1974, 1699. [b] A. Clerici, F. Minisci, and O. Porta, *Gazzetta*, 1973, **101**, 171.

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[11] R. C. Fort and P. v. R. Schleyer, *Adv. Alicyclic Chem.*, 1966, **1**, 283.

[12] J. K. Kochi and A. Bemis, *J. Amer. Chem. Soc.*, 1968, **90**, 4038.

[13] P. Spagnolo and M. Tiecco, *Tetrahedron Letters*, 1968, 2313; G. Martelli, P. Spagnolo, and M. Tiecco, *J. Chem. Soc.* (*B*), 1970, 1413.

[14] P. J. Krusic, T. A. Rettig, and P. v. R. Schleyer, *J. Amer. Chem. Soc.*, 1972, **94**, 995.

[15] T. Kawamura, M. Matsunaga, and T. Yonezawa, *J. Amer. Chem. Soc.*, 1975, **97**, 3234.

geometrical change with respect to the corresponding hydrocarbons. The amount of *s* character of the orbitals employed to form the bridgehead C–H bonds can be estimated from the $J_{^{13}\mathrm{CH}}$ values; the percentage *s* character for bicyclo[2.2.1]heptane [16] and bicyclo[2.2.2]-octane [17] is 28 and 27%, respectively, indicating a larger *s* character than in adamantane where the orbital is presumably pure sp^3.[18] More reliable information on the relative geometries of the radical sites could be obtained [14] from bridgehead ^{13}C hyperfine coupling data which unfortunately are not yet available. In cyclopropane the $J_{^{13}\mathrm{CH}}$ coupling constant indicates that the C–H bonds have 32% *s* character, *i.e.* slightly less than in sp^2 bonds.[19] The low value of the hyperfine splitting constant of the α-proton ($a_{\alpha\text{-H}}$ 6.5 G) suggests non-planarity of the radical centre [20] in the cyclopropyl radical which is considered to be nearly sp^2 hybridized, like the corresponding hydrocarbon.[21] These results are in agreement with the experimental behaviour of this radical which has a selectivity intermediate between those of the radical (3) and the phenyl radical in reactions with protonated pyridines.

TABLE 4

Physical, spectral (n.m.r. in CS_2 at 100 MHz) and analytical data of the 1-adamantyl derivatives of 4-substituted pyridines and quinoline

Compound	M.p. (°C)	Chemical shifts (δ) 2	3	4	5	6	Coupling constants (Hz) $J_{3.5}$	$J_{3.6}$	$J_{5.6}$	Analytical data (%) Found C	H	N	Calc. C	H	N
(4a)	144—145 [b]	*e*	7.47		7.29	8.80	1.5	1.1	5.0	80.6	7.6	11.9	80.7	7.55	11.75
(5a) [a]	75—76 [b]	*e*	7.67	2.52 [f]	7.49	8.75	1.5	1.1	5.0	80.0	8.15	5.6	79.95	8.25	5.5
(6a) [a]	106—107 [b]	*e*	7.25		7.10	8.50	1.5	*k*	5.0	73.0	7.4	5.65	72.7	7.3	5.65
(7a)	37—38 [c]	*e*	7.14	7.52	6.97	8.41	1.5	1.1	5.0	84.5	9.0	6.45	84.5	8.95	6.5
(11a)	76—77 [c]	8.50	7.20	*g*	7.20	8.50	*m*			84.7	9.0	6.4			
(8a)	103—104 [c]	*e*	6.90	2.27	6.74	8.24	1.5 [n]	0.8	5.0	84.3	9.3	6.0	84.6	9.25	6.15
(10a)	146—147 [b]	8.84	*h*		7.55	8.70			5.0	79.95	7.55	11.7	80.7	7.55	11.75
(12a)	95—96 [d]	*h*	7.3	7.86	7.1—7.6 [j]			$J_{3.4}$ 9.0		86.6	7.9	5.4	86.7	8.0	5.3

[a] At 60 MHz. [b] From light petroleum (b.p. 100—120°). [c] From MeOH–H_2O. [d] From hexane. [e] 1-Adamantyl group, δ 1.75br (6 H, s, δ-H), 1.95br (6 H, s, β-H), and 2.0br (3 H, s, γ-H). [f] COMe, $\nu_{max.}$ 1 700 cm^{-1} (CS_2). [g] 1-Adamantyl group, δ 1.85 (12 H, m, β- and δ-H) and 2.1br (3 H, s, γ-H). [h] 1-Adamantyl group, δ 1.75br.(6 H, s, δ-H) and 2.1br (9 H, s, β- and γ-H). [i] Methyl group. [j] 5-, 6-, 7-, and 8-H. [k] Not resolved. [l] $J_{3.4}$ 8.0, $J_{4.5}$ 7.6, $J_{4.6}$ 1.9 Hz. [m] Not analysed. [n] $J_{3.Me} = J_{5.Me}$ 0.7, $J_{6.Me}$ 0.2 Hz.

TABLE 5

Physical, spectral (n.m.r. in CS_2 at 100 MHz) and analytical data of the 3,3-dimethylbicyclo[2.2.2]octan-1-yl derivatives of 4-substituted pyridines and quinoline

Compound	M.p. or b.p. (°C) [*p*/mmHg]	Chemical shifts (δ) 2	3	4	5	6	Coupling constants (Hz) $J_{3.5}$	$J_{3.6}$	$J_{5.6}$	Analytical data (%) Found C	H	N	Calc. C	H	N
(4b)	51—52 [a]	*b*	7.03		7.15	8.6	1.5	0.9	5.0	80.1	8.8	11.7	79.95	8.4	11.65
(5b)	154—156 [0.1]	*b*	7.35	2.45 [c]	7.5	8.55	1.5	0.9	5.0	79.35	8.9	5.25	79.35	9.0	5.54
(6b)	109—111 [0.05]	*b*	7.08		6.95	8.29	2.0	0.7	5.0	72.5	8.1	5.5	72.1	8.05	5.6
(7b)	89—91 [0.05]	*b*	7.03	7.43	6.88	8.36	1.3 [d]	1.0	5.0	83.65	9.95	6.45	83.65	9.8	6.5
(11b)	98—100 [0.05]	8.30	7.03	*b*	7.03	8.30	*e*			83.5	9.75	6.6			
(8b)	128—130 [0.5]	*b*	6.86	2.25 [f]	6.78	8.20	1.5 [g]	0.8	5.0	83.6	9.95	6.2	83.8	10.1	6.1
(9b)	105—107 [0.1]	*b*	6.53	3.68 [h]	6.42	8.15	2.4	0.7	5.5	78.4	9.35	5.8	78.3	9.45	5.7
(10b)	52—54 [a]	8.54	*i*		7.28	8.44			5.0	80.2	8.6	11.7	79.95	8.4	11.65
(12b)	150—151 [0.05]	*j*	7.26	7.86	7.25—7.6 [k]			$J_{3.4}$ 9.0		86.1	8.7	5.2	86.05	8.7	5.25

[a] From MeOH–H_2O. [b] Bicyclo-octyl group, δ 1.05 (6 H, s, $2CH_3$), 1.2 (1 H, m), 1.5 (2 H, s), and 1.7 (8 H, m). [c] COMe, $\nu_{max.}$ 1 690 cm^{-1} (CS_2). [d] $J_{3.4}$ 8.0, $J_{4.5}$ 7.4, $J_{4.6}$ 1.9 Hz. [e] Not analysed. [f] Methyl group. [g] $J_{3.Me} = J_{5.Me}$ 0.75, $J_{6.Me}$ 0.3 Hz. [h] OMe. [i] Bicyclo-octyl group, δ 1.1 (6 H, s, $2CH_3$), 1.3 (1 H, m), 1.7 (2 H, s), and 1.9 (8 H, m). [j] Bicyclo-octyl group, δ 1.05 (6 H, s, $2CH_3$), 1.2 (1 H, m), 1.6 (2 H, s), and 1.8 (8 H, m). [k] 5-, 6-, 7-, and 8-H.

EXPERIMENTAL

G.l.c. analyses were performed on a Hewlett–Packard 5700 instrument equipped with a flame ionization detector, using a 10% Silicone GE XE-60 on Aeropak 30(100—120 mesh) column. Quantitative analyses were effected with internal standards and calibrations for area response differences were carried out for each reaction using pure samples of the various substituted cycloalkylpyridines and quinolines.

Materials.—The 4-substituted pyridines and the adamantane-1-carboxylic acid were commercial products. 7,7-Dimethylbicyclo[2.2.1]heptane-1-carboxylic acid was prepared as described in the literature.[22]

3,3-*Dimethylbicyclo*[2.2.2]*octane*-1-*carboxylic Acid.*—A solution of 7,7-dimethylbicyclo[2.2.1]heptane-1-carboxylic acid (7 g) in methanol (80 ml) and concentrated H_2SO_4 (4 ml) was refluxed for 7 h. Solvent was removed and the residue poured onto ice. The mixture was extracted with

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ether and the organic layer was washed with 10% $NaHCO_3$ and water, dried, and evaporated. The crude ester dissolved in ether (15 ml) was added dropwise to a suspension of $LiAlH_4$ (1.6 g) in ether (80 ml); the mixture was refluxed for 1 h and dilute HCl was added. The organic layer was washed, dried, and the solvent removed. A solution of the crude alcohol (5.3 g) in formic acid (25 ml) was added dropwise, at 10°, to a stirred mixture of concentrated H_2SO_4 (95 ml), 20% oleum (25 ml), and formic acid (3 ml). After 2 h the mixture was poured onto ice and the precipitate was taken up in ether; the solution was washed with water and then extracted with 10% NaOH. Acidification of the alkaline solution afforded 3,3-*dimethylbicyclo*[2.2.2]*octane*-1-*carboxylic acid* (4.2 g), m.p. 105—106° (from MeOH–H_2O) (Found: C, 72.5; H, 9.9. $C_{11}H_{18}O_2$ requires C, 72.5; H, 9.95%). δ (CS_2) 1.0 (6 H, s, 2Me), 1.15 (1 H, m), 1.4 (2 H, s), 1.7 (8 H, m), and 11.1br (1 H, s, CO_2H), $\nu_{max.}$ (CS_2) 1 700 cm^{-1}.

TABLE 6

Physical, spectral (n.m.r. in CS_2 at 100 MHz), and analytical data of the 7,7-dimethylbicyclo[2.2.1]heptan-1-yl derivatives of 4-substituted pyridines and quinoline

		Chemical shifts (δ)					Coupling constants (Hz)			Analytical data (%) Found			Calc.		
Compound	M.p. or b.p. (°C) [*p*/mmHg]	2	3	4	5	6	$J_{3,5}$	$J_{3,6}$	$J_{5,6}$	C	H	N	C	H	N
(4c)	57—59 ^{a}	*b*	7.37		7.17	8.61	1.5	0.85	5.0	79.7	8.05	12.5	79.6	8.0	12.4
(6c)	31—32 ^{a}	*b*	7.58	2.45 ^{c}	7.37	8.62	1.6	0.9	5.0	78.85	8.55	5.7	79.0	8.65	5.75
(6c)	159—161 [1]	*b*	7.18		6.98	8.33	2.0	0.7	5.0	71.3	7.7	5.95	71.35	7.65	5.95
(7c)	140—143 [1]	*b*	7.14	7.44	6.95	8.42	1.4 ^{d}	1.1	5.0	83.45	9.4	6.8	83.6	9.45	6.95
(11c)	92—94 ^{a}	8.33	7.13	*b*	7.13	8.33	*e*			83.55	9.5	6.95			
(8c)	43—44 ^{a}	*b*	6.95	2.27 ^{f}	6.75	8.25	1.5 ^{g}	0.75	5.0	83.7	9.85	6.55	83.7	9.8	6.5
(9c)	160—162 [1]	*b*	6.6	3.68 ^{h}	6.48	8.2	2.4	0.7	5.5	77.7	9.2	5.95	77.9	9.1	6.05
(10c)	90—91 ^{a}	8.78	*i*		7.34	8.4			5.0 ^{j}	79.55	8.5	12.25			
(12c)	43—45 ^{a}	*k*	7.34	7.89	7.23—7.69 ^{l}			$J_{3,4}$ 9.0		86.15	8.5	5.65	86.05	8.35	5.6
(13c)	166—168 ^{a}	8.6	7.3	*m*	*n*			$J_{2,3}$ 5.0		85.95	8.5	5.5			

[a] From MeOH–H_2O. [b] Bicycloheptyl group, δ 2.4br (2 H, t), 1.1—2.0 (7 H), and 0.9 (6 H, s, $2CH_3$). [c] COMe, $\nu_{max.}$ 1 690 cm^{-1} (CS_2). [d] $J_{3,4}$ 8.0, $J_{4,5}$ 7.4, $J_{4,6}$ 1.9 Hz. [e] Not analysed. [f] Methyl group. [g] $J_{3,Me} = J_{5,M}$ 0.7 Hz. [h] OMe. [i] Bicycloheptyl group, δ 1.6—2.4 (8 H), 1.4 (1 H), and 1.2 (6 H, s, $2CH_3$). [j] $J_{2,5}$ 0.9 Hz. [k] Bicycloheptyl group, δ 2.5br (2 H, t), 1.2—2.1 (7 H), and 1.0 (6 H, s, $2CH_3$). [l] 5-, 6-, 7-, and 8-H. [m] Bicycloheptyl group, δ 2.5br (2 H, t), 1.9 (4 H, m), 1.7 (2 H, m), 1.4 (1 H, m), and 1.3 (6 H, s, $2CH_3$). [n] δ 8.20 (1 H), 7.93 (1 H), 7.45 (1 H), and 7.35 (1 H).

TABLE 7

Relative reactivities ^{a} of pairs of protonated 4-(X-/Y-) pyridines towards radicals (1)—(3)

	Radical (1)			Radical (2)			Radical (3)		
X/Y	Molar ratio	Relative rate	Average ^{b}	Molar ratio	Relative rate	Average ^{b}	Molar ratio	Relative rate	Average ^{b}
CN/H							1 : 5	10.02	10.08
							1 : 10	10.14	
CN/COMe	1 : 1	2.94	2.95	1 : 2	1.80	1.78	1 : 1	2.77	2.75
	1 : 2	2.97		1 : 1	1.76		1 : 2	2.74	
	1 : 3	2.95		1 : 1	1.80 ^{c}		1 : 1	2.75 ^{c}	
	1 : 1	2.96 ^{c}							
COMe/H	1 : 5	19.2	19.0	1 : 3	7.02	6.92			
	1 : 10	19.0		1 : 5	6.82				
	1 : 20	18.8							
COMe/Cl	1 : 3	10.30	10.38	1 : 2	3.98	4.06	1 : 1	2.29	2.27
	1 : 10	10.46		1 : 4	4.10		1 : 2	2.25	
Cl/H	1 : 1	1.78	1.83	1 : 1	1.74	1.71	1 : 1	1.61	1.61
	1 : 2	1.88		1 : 2	1.68		1 : 2	1.60	
							1 : 1	1.61 ^{c}	
Cl/Me	1 : 10	85.95	85.14 ^{d}	1 : 5	59.4	59.0 ^{d}	1 : 2	6.20	6.19
	1 : 20	84.33		1 : 10	58.6		1 : 5	6.18	
Me/H	5 : 1	0.021	0.021	5 : 1	0.027	0.03			
	10 : 1	0.020 8		10 : 1	0.032				
	5 : 1	0.021 ^{c}		5 : 1	0.029 ^{c}				
Me/OMe				1 : 2	13.75	13.65	1 : 1	2.29	2.32
				1 : 5	13.52•		1 : 2	2.35	
OMe/H							2 : 1	0.110	0.112
							5 : 1	0.115	
Quinoline/CN	3 : 1	0.32	0.34	1 : 1	0.98	1.0	1 : 1	1.01	1.01
	2 : 1	0.36		2 : 1	1.02		1 : 2	1.02	
Quinoline/COMe	1 : 1	0.98	1.00	1 : 1	1.78	1.76	1 : 3	2.80	2.72
	1 : 1	1.02		1 : 3	1.74		1 : 3	2.65	

[a] Values obtained from the ratios of products formed (see Results section). [b] From these data the relative rates collected in Table 1 were calculated. [c] Values obtained from the ratios of unchanged starting substrates (see Results section). [d] These values are slightly different from those expected and are probably due to analytical difficulties because of the large difference in reactivity between the two substrates; they are therefore not employed to calculate the data in Table 1.

The 4-cycloalkylpyridines and cycloalkylquinolines necessary for the present investigation were obtained by the following general procedure. To a stirred solution of a heteroaromatic substrate (0.01 mol), a bridgehead carboxylic acid (0.02 mol), and $AgNO_3$ (0.001 mol) in 10% H_2SO_4 (35 ml) and MeCN (35 ml), heated at 90°, a solution of ammonium persulphate (0.02 mol; 0.04 mol in the case of the bicycloheptanecarboxylic acid) in water (10 ml) was added dropwise over *ca.* 20 min. Stirring and heating was continued for 30 min, and the cooled solution was then poured onto ice and NH_3; the mixture was extracted with chloroform and the organic layer was washed with 5% NaOH. From the combined aqueous solutions unchanged acid was recovered by acidification. The washed organic solution was dried and solvent was removed. The residue was chromatographed through a silica gel column using light petroleum (b.p. 40—60 °C)–ethyl acetate (9 : 1) as eluant. The separation of the various components was monitored by g.l.c. and t.l.c. The compounds obtained from the various reactions are described in the Results section. Their characterization was accomplished by elemental analyses, 60 or 100 MHz n.m.r. spectroscopy (Varian HA 100 or JEOL Minimar), and by i.r. spectroscopy (Perkin-Elmer 257); pertinent data are collected in Tables 4—6. No accurate determination of the yields was made, the purpose being to obtain pure samples for g.l.c. analyses of competitive experiments; for radicals (1) and (2) however yields based on the bases employed were in the range 60—70%, for (3), 40—50%.

Adamantan-1-ol and 3,3-dimethylbicyclo[2.2.2]octan-1-ol were also obtained from reactions carried out in the absence of pyridines; they were identified by comparison with authentic samples.[23]

Competitive Experiments.—To a stirred solution of two heteroaromatic substrates (0.01 mol) (the pairs of bases and their molar ratios are reported in Table 7) a bridgehead carboxylic acid (0.01 mol) and $AgNO_3$ (0.001 mol) in 10% H_2SO_4 (35 ml) and MeCN (35 ml), heated at 90°, a solution of ammonium persulphate (0.005 mol) in water (10 ml) was added in 1 ml portions. After each addition, samples were analysed by g.l.c. and the ratio of products formed determined; in some cases (see Table 7) the ratios of unchanged starting substrates were simultaneously determined. The results obtained were employed, as described in the Results section, to determine the values of the relative rates which are collected in Table 7.

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