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# Nucleophilic Character of the Alkyl Radicals. 16. Absolute Rate Constants and the Reactivity–Selectivity Relationship in the Homolytic Aromatic Alkylation

**Attilio Citterio,* Francesco Minisci,* Ombretta Porta, and Giulio Sesana**

*Contribution from the Istituto di Chimica del Politecnico, Piazza L. da Vinci 32, Milano, Italy.* *Received March 11, 1977*

**Abstract:** The rate constants for the homolytic alkylation of protonated heteroaromatic bases (4-methyl- and 4-cyanopyridine, 4-methylquinoline, benzothiazole, and quinoxaline) were measured from 15 to 80 °C. A good agreement was obtained with two different kinetic models involving 5-hexenyl and *n*-heptyl radicals. The high values of the rate constants (a range of $10^5$–$10^8$ $M^{-1}$ $s^{-1}$ was obtained) explain the great synthetic interest of these reactions. On the contrary the homolytic alkylation of benzene derivatives has lower rate constants ($10^2$ L $mol^{-1}$ $s^{-1}$), and shows a very poor synthetic interest. The observed failure of the reactivity–selectivity principle (RSP) was discussed in terms of polar effects and frontier orbitals theory.

Free-radical reactions are often considered somewhat suspiciously by the synthetic organic chemists owing to their poor selectivity. This suspiciousness is largely justified by the fact that transient radicals[2] (the most important from the synthetic point of view) are very reactive species, and that the reactivity–selectivity principle (RSP) is generally held to be valid in either free-radical or ionic reactions.

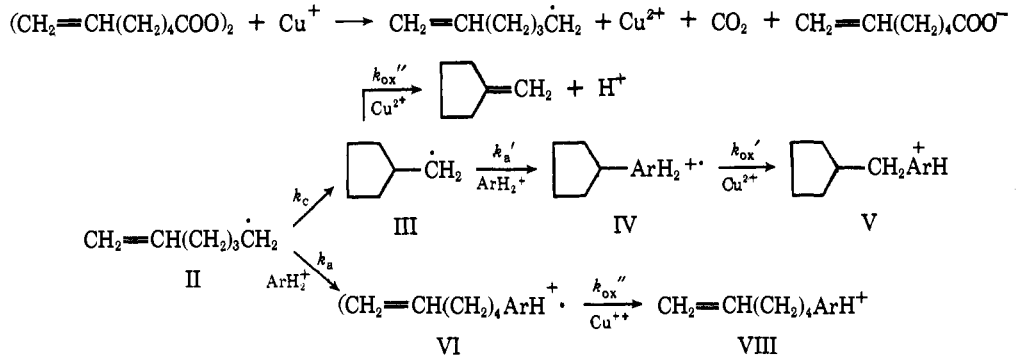
We[3] have recently described several reactions of transient radicals characterized by very high positional and substrate selectivity, which, in agreement with the RSP, should be characterized by low reactivity. On the contrary, the qualitative behavior suggested not only that these reactions were fast, but also that the selectivity increased with the reactivity.[3]

In particular, the homolytic alkylation of protonated heteroaromatic bases must be considered among the most important substitution reactions of this class of aromatic compounds owing to its high yields and selectivity, its cheap availability of a large variety of free-radical sources, and its very simple experimental conditions.[3,4] As no hydrogen abstraction takes place from alkyl groups in protonated heteroaromatic bases (also with high conversions) and alkyl radicals intermediate in the Hofman–Löffler–Freitag rearrangement have been successfully used in the homolytic alkylation of protonated heteroaromatic bases,[4] this last reaction must be very fast. Actually the value[5] of the rate constant for the chlorine transfer (eq 1) in Hofman–Löffler–Freitag rearrangement is higher than $10^4$ L $mol^{-1}$ $s^{-1}$ at 30 °C and the attack of the radical I to protonated heteroaromatic bases successfully competes with the very fast reaction of eq 1.

$$\underset{\text{I}}{RN^+H_2(CH_2)_3\dot{C}H_2} + R_2N^+HCl \rightarrow RN^+H_2(CH_2)_3CH_2Cl + R_2N^{+\cdot}H \quad (1)$$

Moreover, the homolytic alkylation of protonated heteroaromatic bases also takes place in the presence of cupric salts,[10] which oxidize the alkyl radicals with a high rate (the rate constants[6,7] for the oxidation of primary alkyl radicals by $Cu(OAc)_2$ and $CuCl_2$ were estimated respectively as $1.2 \times 10^6$ and $1.1 \times 10^9$ L $mol^{-1}$ $s^{-1}$ at 25 °C). The knowledge of the absolute rate constants of the homolytic aromatic alkylation

**Scheme I**



is therefore of fundamental importance for understanding the synthetic success of the homolytic alkylation in the heteroaromatic series and the very little interest of the same reaction in the homocyclic aromatic series.

## Results and Discussion

The main kinetic model used to determine the absolute rate constants in the reactions of primary alkyl radicals and protonated heteroaromatic bases ($ArH_2^+$) is shown in Scheme I.

This model is particularly useful for the following reasons:

(1) The cyclization of the 5-hexenyl radical to yield the cyclopentylmethyl radical is one of the best studied[8] free-radical reactions from the kinetic point of view so that the value of $k_c$, determined with a variety of methods, is quite accurate.

(2) Recently, Ingold and co-workers[9] reported the temperature dependence of $k_c$; that allows one to work with a large range of temperatures.

(3) The value of $k_c$ is quite independent of the solvent[8,9] and the complication due to different experimental conditions is eliminated.

(4) The cyclization of the primary alkyl radical II gives rise to the primary alkyl radical III so that we can reasonably assume that II and III react with the same rates (in particular $k_a = k_a'$ and $k_{ox} = k_{ox}'$).

(5) The reaction of Scheme I is very clean; the yields based on ArH are >90% (V and VII are the only heteroaromatic compounds of the reaction). The yields based on the acyl peroxide are >70% if a small amount of copper(I) salt is used. This behavior makes valid the kinetic model also in the unlikely hypothesis that $k_a$ and $k_{ox}$ are significantly different from $k_a'$ and $k_{ox}'$ because the cyclization of the 5-hexenyl radical and the addition to the heteroaromatic bases are irreversible processes under these conditions.

The kinetic equation 2 is obtained from Scheme I by the steady-state assumption for radical III:

$$\frac{d[III]}{dt} = k_c[II] - k_a'[III][ArH_2^+] - k_{ox}''[Cu^{2+}][III] = 0 \quad (2)$$

$$\frac{[II]}{[III]} = \frac{k_a'[ArH_2^+] + k_{ox}''[Cu^{2+}]}{k_c}$$

$$\frac{d[VII]}{dt} = k_a[II][ArH_2^+]$$

$$\frac{D[V]}{dt} = k_a'[III][ArH_2^+]$$

$$\frac{d[VII]}{d[V]} = \frac{k_a}{k_c}[ArH_2^+] + \frac{k_{ox}}{k_c}[Cu^{2+}]$$

Under our conditions (very low concentration of copper(II) salt and high yield of aromatic alkylation) the second term is negligible, and the kinetic equation 3 is obtained for low conversions (subscript i = initial, f = final). It was experimentally confirmed.

$$\frac{[VII]_f}{[V]_f} = \frac{k_a}{k_c}[ArH_2^+]_i \quad (3)$$

The irreversibility of the cyclization reaction was well evidenced[8,9] and was further confirmed in the aromatic alkylation with dicyclopentylacetyl peroxide; by either thermal or catalytic decomposition of the peroxide, only the cyclopentylmethyl derivatives were obtained without any formation of the hexenyl derivatives. This reaction was therefore utilized to prepare pure samples of cyclopentylmethyl derivatives for the quantitative analyses.

In order to prove the irreversibility of the primary alkyl radicals addition to protonated heteroaromatic bases, we carried out the reaction with or without cupric salt. In the presence of cupric salt, the intermediate radical adducts IV are very rapidly oxidized:

$$RArH_2^{+\cdot} + Cu^{2+} \xrightarrow{k_{ox}} RArH^+ + Cu^+ + H^+ \quad (4a)$$

The process of Scheme I is characterized by an effective redox chain and the reaction may be carried out also at low temperature with a catalytic amount of copper(I) salt.

In the absence of cupric salt the radical adduct rearomatization is mainly determined by a chain process[10] characterized by the induced decomposition of the acyl peroxide (eq 4b); a higher temperature is required in this case.

$$RArH_2^{+\cdot} + RCOOOCOR \rightarrow RArH^+ + R\cdot + CO_2 + RCOOH \quad (4b)$$

If the addition of the alkyl radical to the heteroaromatic base were reversible in the absence of cupric salt we should have expected a higher ratio [V]/[VII] because the cyclization of II into III is certainly irreversible and reaction 4a is faster than reaction 4b.

In agreement with the irreversibility of the process, we obtain the same results in the presence or absence of $Cu^{2+}$ at the same temperatures (60–80 °C) with quinoxaline and 4-methylquinoline. Moreover, the reversibility of the addition should be considerably affected by an increase in the temperature favoring the cyclization products; that is not the case, as will be shown later. On the contrary, with the less reactive 4-methylpyridine the ratio [VII]/[V] at 79 °C is somewhat lower in the absence of $Cu^{2+}$, suggesting a certain degree of reversibility which increases the cyclopentylmethylation. This result suggests too that some of the values of relative rates previously[3] obtained in homolytic aromatic alkylation by the competitive method have to be reexamined on the grounds of a possible reversibility, especially when stabilized radicals are involved and the radical source is not enough of an oxidant (i.e., the use of *t*-BuO-OBu-*t* in the homolytic aromatic cyclohexylation[11]) to rearomatize the radical adducts rapidly (eq 4 and 5) and to make the whole process irreversible. Nucleophilic

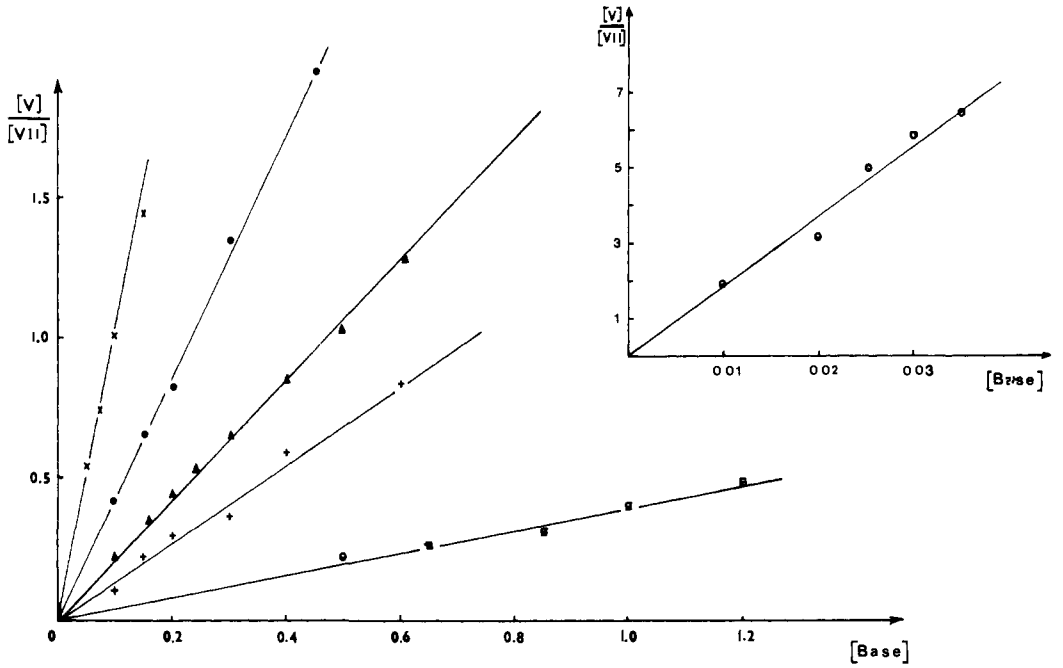



**Figure 1.** Base concentration dependence of the ratio VII/V in $Cu^{I}$-catalyzed alkylation of same protonated heteroaromatic bases by di-*n*-heptyl peroxide (25 °C, $Cu^{I} = 1.6 \times 10^{-3}$ M, peroxide $1\ 10^{-2}$ M, $H_2SO_4$ 1 M, $CH_3COOH:H_2O(1:1)$): □, 4-methylpyridine; ▲, 4-methylquinoline; x, benzothiazole; +, 4-acetylpyridine; ●, 4-cyanopyridine; ○, quinoxaline.

**Table I.** Rates and Relative Arrhenius Parameters for the Addition of Primary Radicals to Some Protonated Heteroaromatic Bases

| Base | $k_a$ (25 °C)[a] | $E_c - E_a$, kcal | Log $A_c/A_a$ | $E_a$,[b] kcal | Log $A_a$[b] |
|---|---|---|---|---|---|
| 4-Methylpyridine | $4.1 \times 10^4$ | 1.95 | 1.6 | 6.85 | 9.2 |
| 4-Acetylpyridine | $1.3 \times 10^5$ | | | | |
| 4-Cyanopyridine | $2.5 \times 10^5$ | 2.90 | 1.5 | 4.9 | 9.3 |
| 4-Methylquinoline | $2.2 \times 10^5$ | 2.60 | 1.6 | 5.2 | 9.2 |
| Benzothiazole | $9.9 \times 10^5$ | | | | |
| Quinoxaline | $1.8 \times 10^7$ | 5.00 | 1.5 | 2.8 | 9.3 |

[a] Determined assuming $k_c = 1 \times 10^5$ L mol$^{-1}$ s$^{-1}$. [b] Determined assuming $k_c$ from ref 9.

carbon-centered free radicals, such as acyl and benzyl, which form weaker bonds than alkyl radicals, show in fact features of reversibility in the addition to olefins and aromatics.[12]

In agreement with the simplification of eq 2 into eq 3, the plots of [VII]/[V] against $[ArH_2^+]$ afford straight lines passing through the origin, Figure 1. The values $k_a/k_c$ evaluated from the slopes enable us to calculate $k_a$ for several heteroaromatic bases, knowing the value $k_c$[9] [log $(k_c/s^{-1}) = 10.7 - 7.8/\theta$, where $\theta = 2.3RT$ kcal/mol]. The results at 25 °C are summarized in Table I.

Arrhenius plots give excellent straight lines for several heteroaromatic compounds in the temperature range of 15–80 °C (Figure 2). Arrhenius parameters are also given in Table I. All frequency factors are of the expected similar order of magnitude, whereas the activation energies considerably decrease as the electron deficiency of the heteroaromatic compound increases, supporting once again a large contribution of the polar form VIII to the transition state, owing to the nucleophilic character of the alkyl radicals (R·).[3]

$$[ArH_2^+R\cdot] \leftrightarrow [ArH_2\cdot R^+]$$
VIII

All the structural factors which stabilize the polar forms VIII favor an electron transfer, decrease the activation energy, and determine the reactivity and the selectivity of the process. Since the alkylation rate constant of protonated quinoxaline is very high (Table I), this process can compete even with very fast reactions of the alkyl radicals, such as the ligand-transfer oxidation by cupric chloride (eq 5), whose rate constant (1.1 ×

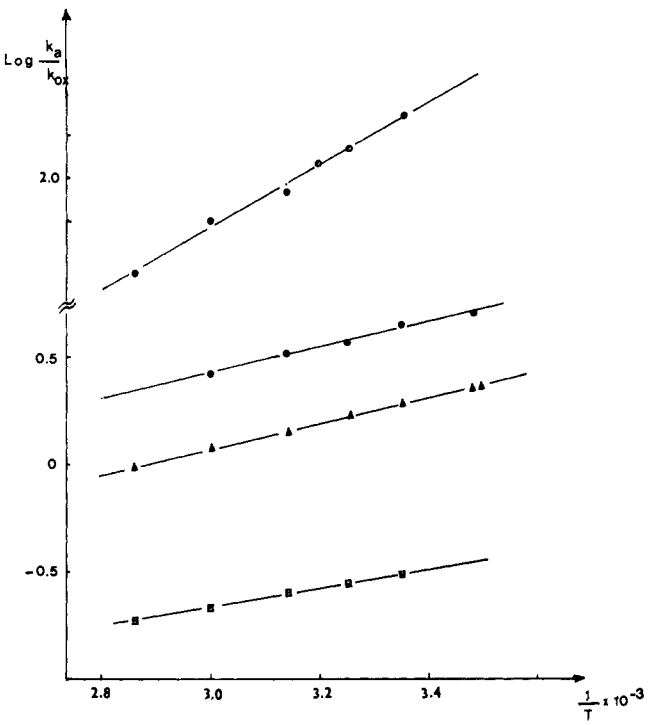



**Figure 2.** Temperature dependence of the ratio $k_a/k_c$ in alkylation of same heteroaromatic bases by di-*n*-heptyl peroxide: □, 4-methylpyridine; ▲, 4-methylquinoline; ●, 4-cyanopyridine; ○, quinoxaline.

**Table II.** Orientation (%), Partial Rate Factors ($f$), and Relative Reactivities ($K_H^{OCH_3}$) in Homolytic Alkylation of Anisole

| Radical | $o$ % ($f_o$) | $m$ % ($f_m$) | $p$ % ($f_p$) | $K_H^{OCH_3}$ |
|---|---|---|---|---|
| Methyl[14] | 74 | 15 | 11 | |
| $n$-Butyl[a] | 75 (6.52) | 16.7 (1.45) | 8.3 (1.44) | 2.9 |
| *b* | 72.7 (7.8) | 19.4 (2.1) | 7.9 (1.7) | 3.6 |
| Cyclohexyl[11] | 67 (4.6) | 28 (1.9) | 5 (0.69) | 2.3 |

[a] Thermolysis of divaleroyl peroxide at 78 °C. [b] Thermolysis of divaleroyl peroxide + $Cu^{2+}$ at 79 °C.

$10^9$ L mol$^{-1}$ s$^{-1}$ at 25 °C) is close to the diffusion-controlled limit.[7] On these grounds we could use a different kinetic treatment, based on the redox chains shown in Scheme II.

**Scheme II**

$$(n\text{-}C_7H_{15}COO)_2 + Cu^+ \longrightarrow n\text{-}C_7H_{15}\cdot + CO_2 + Cu^{2+} + n\text{-}C_7H_{15}COO^-$$

$$n\text{-}C_7H_{15}\cdot + CuCl^+ \xrightarrow{k_t} n\text{-}C_7H_{15}Cl + Cu^+ \quad (5)$$

IX

$$n\text{-}C_7H_{15}\cdot + \text{(protonated quinoxaline)} \xrightarrow{k_a} \text{(adduct)} \quad (6)$$

$$\text{(adduct)} \leftrightarrow \text{(adduct)} + CuCl^+ \longrightarrow \text{(product)} + Cu^+ + HCl$$

X

The reaction of Scheme II is also very clean; only octanoic acid and the compounds IX and X are formed. The kinetic chains are long enough to allow the use of a small amount of copper salt and both the interactions 5 and 6 are irreversible. The final yields of IX and X are therefore related to quinoxaline and cupric salt concentrations according to

$$\frac{[IX]_f}{[X]_f} = \frac{k_t}{k_a}\frac{[Cu^{2+}]_i}{[\text{quinoxaline}]_i} \quad (7)$$

As cupric chloride is a composite of individual species in solution[7] ($CuCl^+$, $CuCl_2$, $CuCl_2^-$, and $CuCl_4^{2-}$), it was important to use experimental conditions very similar to those used for the determination of $k_t$. The chlorine ion was therefore supplied by lithium chloride in acetic acid solution. The value of $k_a$ obtained in this way ($3.1 \times 10^7$ L mol$^{-1}$ s$^{-1}$ at 25 °C) is in reasonable agreement with the value $1.8 \times 10^7$ L mol$^{-1}$ s$^{-1}$ of Table I considering the high rates involved and the slightly different conditions.

This result further supports the irreversibility of the addition of primary alkyl radicals to quinoxaline; namely, if the addition were reversible, we should have expected an "apparent" value of $k_a$ lower than the corresponding value of Table I because of the very high value of $k_t$ ($1.1 \times 10^9$ L mol$^{-1}$ s$^{-1}$ at 25 °C) and the sure irreversibility of reaction 5.

In order to understand the dramatic difference of behavior of the homolytic alkylation in homocyclic aromatics[3] it was necessary to know the absolute rate constants in this series too. Nevertheless, the kinetic models used with the heteroaromatic bases proved to be fruitless. In fact the reactions, also in the presence of small amounts of cupric salts (acetate, chloride, thiocyanate), did not lead to aromatic attack in a significant amount for kinetic treatment, but mainly led to the oxidation of the alkyl radicals by electron-transfer or ligand-transfer processes, which are much faster reactions than the addition of the alkyl radicals to the benzene ring. On the other hand the use of 6-heptenoyl peroxide did not work because under all conditions, no hexenylation of the benzene ring was observed, but only cyclopentylmethylation. That means that the cyclization reaction is much faster than the addition of the alkyl radical to the benzene ring and makes this model impracticable too.

We therefore chose the competitive method to determine the relative rates between the least reactive heteroaromatic base of Table I (4-methylpyridine) and homocyclic aromatics by assuming that also in the homocyclic aromatic series the homolytic alkylation is irreversible in the presence of cupric salt or that the effects of reversibility are minimized anyhow by the high rate of reaction 8.

$$\text{(R, H)} + Cu^{2+} \longrightarrow \text{(R)} + Cu^+ + H^+ \quad (8)$$

Valeroyl peroxide in the presence and absence of cupric acetate was used to determine the relative rates of protonated 4-methylpyridine, anisole, and benzene toward $n$-butyl radical. The former was respectively 78 and 281 times more reactive than anisole and benzene at 79 °C in the presence of cupric salt and 113 and 330 in the absence of $Cu^{2+}$. The direct competition in the presence of cupric salt gives very poor yields of aromatic alkylation because 1-butene, arising from the oxidation of the $n$-butyl radical, is by far the main product of the reaction, but it is clean enough to show that anisole is 3.6 times more reactive than benzene; in the absence of $Cu^{2+}$ anisole was 2.9 times more reactive than benzene in direct competition. These values agree very well with those (3.6 and 2.92) indirectly derived from the competition of benzene, anisole, and 4-methylpyridine. The differences of relative rates in the presence and absence of $Cu^{2+}$ can be considered the result of the reversibility of the process, which also affects to some extent the isomer distribution (Table II). If we assume that the effects of reversibility can be neglected in the presence of $Cu^{2+}$ owing to the very fast reaction 8, we estimate respectively for benzene and anisole the rate constants $3.8 \times 10^2$ and $1.3 \times 10^3$ L mol$^{-1}$ s$^{-1}$ at 79 °C. This order of magnitude agrees with our previous results obtained in the alkylation of benzene by $n$-nonyl radical;[10] in fact 1-phenylnonane and 5-phenylnonane were the only alkylation products obtained in 30:1 ratio indicating that the intramolecular hydrogen abstraction, for which rate constants of $10^{-1}$–$10$ s$^{-1}$ were estimated[13] in gas phase, competes with the addition to the benzene ring.

In addition to the low substrate selectivity, a low positional selectivity characterizes the alkylation in homocyclic aromatic series and contrasts with the high positional and substrate selectivity obtained with protonated heteroaromatic bases. This low selectivity is in agreement with previous results obtained in homolytic methylation[14] and cyclohexylation[11] of benzene derivatives (Table II), even if, in our opinion, especially the data of cyclohexylation should be reexamined bearing in mind the probable reversibility. It is interesting that in all cases

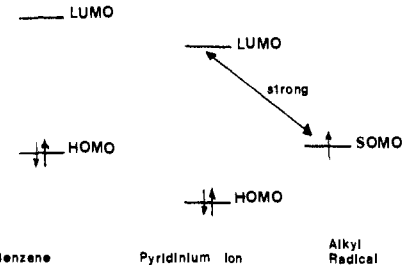



Figure 3.

anisole is more reactive than benzene; on the contrary with the same radicals 4-methoxypyridine is much less reactive than pyridine;[3] the same substituent therefore has opposite effects depending on the nature of the aromatic ring. This behavior can be included in the general explanation based on polar effects[3] and can be also considered, as will be discussed later on, in terms of frontier orbital theory.

Unprotonated 4-methylpyridine was only 3.95 times more reactive than benzene toward *n*-butyl radical by the competitive method at 78 °C; perhaps this value is even slightly higher than the actual one because a certain amount of valeric acid is formed during the decomposition of the peroxide and the protonation of 4-methylpyridine takes place to a small extent. This value, however, clearly shows once again the great activating effect that the protonation determines on the reactivity of heteroaromatic bases with nucleophilic free radicals. The partial rate factors and the rate constants at 79 °C of benzene, anisole, unprotonated 4-methylpyridine, and some protonated heteroaromatic bases are summarized in Table III.

These results clearly explain the dramatic difference of synthetic interest between homocyclic aromatics and protonated heteroaromatic bases. In fact, they indicate that, for structural reasons, the homolytic alkylation does not give clean substitutions in the homocyclic aromatic series, at least with significant conversions of the aromatic substrates. The hydrogen abstraction rates from C–H bonds of alkyl groups by primary alkyl radicals[15] are of the same order of magnitude as the addition to the benzene ring. That is also confirmed by the results obtained with methyl radicals and alkylbenzenes:[14] isopropylbenzene reacts only at the side chain, whereas ethylbenzene and toluene give respectively 97 and 96% of methane and small quantities of nuclear attack. Moreover, the very low positional and substrate selectivity contributes to further decrease the synthetic interest in the homocyclic aromatic series leading to complex mixtures of reaction products.

On the contrary, the great synthetic interest of the homolytic alkylation of protonated heteroaromatic bases is strictly related to the high rates of the addition reactions, which overcome other possible side reactions of the alkyl radicals, such as hydrogen abstraction, and at the same time determine a very high positional and substrate selectivity.

The influence of polar effects was shown to be the main cause of this behavior. It was previously[3c] suggested that a transition state similar to a charge-transfer complex is involved, and that the degree of charge development in the transition state depends on the donor character of the radical and the acceptor character of the aromatic ring according to VIII (a complete electron transfer being the limit case). Chemical[16] and ESR spectroscopic[17] evidences have actually supported a complete electron transfer in the cases of strongly nucleophilic radicals, such as PhĊ(OH)Ph, and protonated heteroaromatic bases. The factors affecting the degree of charge development in the transition state (the radical and aromatic substrate polarities, bond energies, electronic configurations of the radicals, etc.) were recently[33] discussed; certainly solvation effects cannot be ignored in a transition state like VIII,

**Table III.** Partial Rate Factors of Position 2 and Absolute Rates ($k_a$) in Homolytic Alkylation by Primary Alkyl Radicals at 79 °C in Acidic Medium

| Substrate | Partial rate factor | $k_a$, L mol$^{-1}$ s$^{-1}$ |
|---|---|---|
| Benzene | 1 | $3.8 \times 10^2$ |
| Anisole | 7.8 | $1.3 \times 10^3$ |
| 4-Methylpyridine[a] | 11.8 | |
| 4-Methylpyridine | $8.4 \times 10^2$ | $1.1 \times 10^5$ |
| 4-Cyanopyridine | $1.4 \times 10^4$ | $1.8 \times 10^6$ |
| 4-Methylquinoline | $4.5 \times 10^3$ | $5.7 \times 10^5$ |
| Quinoxaline | $2.1 \times 10^5$ | $2.7 \times 10^7$ |

[a] Unprotonated base.

but the used kinetic models are not versatile enough for such a study. It was also suggested that a measure of these polarities (donor character of the radical and acceptor character of the aromatic substrate) can be offered by the corresponding ionization potentials.[3,18] The phenomenon can also be explained in terms of frontier orbitals theory.[19] This explanation does not differ in substantial aspects from that based on polar effects, because the HOMOs and SOMOs energies are roughly given by the ionization potentials of the substrate and the free radical. Benzene derivatives have in fact considerably higher HOMO and LUMO energies than protonated heteroaromatic bases. Thus with nucleophilic alkyl radicals, characterized by relatively high-energy SOMO, the important frontier orbital will be the LUMO of the protonated heteroaromatic base; the strong interactions of SOMO and LUMO determine the high reactivity and selectivity. With benzene derivatives we can expect relatively weak interactions between the SOMO of the alkyl radical and the LUMO and HOMO of the aromatic substrate determining a lower reactivity and selectivity (Figure 3). *This behavior, however, represents a failure of the reactivity–selectivity principle.* The classical high reactivity–low selectivity relationship is reversed: in heteroaromatic series a high positional and substrate selectivity is associated with high rate constants; in benzene series much lower rate constants characterize very low positional and substrate selectivities. The same conclusion is obtained by comparing the rates and the selectivities of the homolytic aromatic arylation with the homolytic alkylation. A very low positional and substrate selectivity is in fact the most qualifying characteristic of the homolytic aromatic arylation, even with protonated heteroaromatic bases.[20] It was recently suggested[21] that the nonselectivity of phenyl radical attack on aromatic molecules is reflected in the high rate constants, which have been estimated[22] at 80 °C for benzene in the range of $10^3$–$10^4$ L mol$^{-1}$ s$^{-1}$ (the very low substrate selectivity indicates that the rate constants are not considerably different also in the heteroaromatic series). Even if we consider only the heterocyclic series once again the reactivity–selectivity principle is therefore reversed; alkyl radicals are more reactive and much more selective than aryl radicals.

The validity of the reactivity–selectivity principle has recently been cast into doubt by an increasing number of papers[23] concerning ionic reactions, in which the expected inverse relationship was not observed. As concerns free-radical reactions our suggestion is that the *reactivity–selectivity principle cannot hold when polar effects play a preeminent role in determining the reaction rates.* This statement can be derived from the Evans–Polanyi rule, but, *until recently*, significant examples of this behavior in free-radical addition reactions have not been reported and anyway they have not been interpreted according to this statement. Other recent results can be now included, in our opinion, in this picture. The homolytic acylation of protonated heteroaromatic bases is another very selective process of great synthetic interest;[3] also in this case the high

**Table IV.** $\pi$-Electron Density of Mono- and Diprotonated Quinoxaline by NMR Analysis and INDO Calculation[28]

| | Position | $q$(NMR) | $q$(INDO) |
|---|---|---|---|
| Monoprotonated quinoxaline | 2 | *0.874* | *0.853* |
| | 3 | 0.918 | 1.022 |
| | 5 | 0.940 | 0.965 |
| | 6 | 0.922 | 0.968 |
| | 7 | 0.914 | 0.907 |
| | 8 | 0.958 | 1.036 |
| Diprotonated quinoxaline | 2-3 | *0.873* | *0.897* |
| | 5-8 | 0.932 | 1.003 |
| | 6-7 | *0.883* | *0.870* |

selectivity is associated with high reactivity. In fact the absolute rate constants evaluated for benzothiazole[24] and quinoxaline[12] are respectively $7.1 \times 10^5$ and $3.6 \times 10^6$ L mol$^{-1}$ s$^{-1}$ at 5 °C. As the addition of acyl radicals to heteroaromatic rings has features of reversibility[12] these data must be considered minima values, but in any case they are higher than the rates of very unselective reactions, such as homolytic aromatic arylation and homolytic alkylation in the benzene series (no homolytic acylation occurs with benzene derivatives). It may be a surprise that the rate of phenyl radical addition to a heteroaromatic ring is lower than those of alkyl and acyl radicals if the difference of the strengths of the bonds formed by these radicals[25] is considered (i.e., the strengths of the bonds Ph-H, $RCH_2$-H, and RCO-H are respectively 112, 98, and 87 kcal/mol). The fact is explained by the strong polar effects observed with alkyl and acyl radicals, which overcome the less favorable energetics compared with phenylation.

Other examples of failure of the RSP are provided by the addition of free radicals to olefins. Secondary alkyl radicals are generally less reactive and more selective than primary alkyl radicals in agreement with the RSP because the energetics is less favorable. However, this behavior is reversed in the addition reaction to electron-deficient olefins (acrylic monomers), owing to important contribution of polar effects; secondary alkyl radicals are always more selective, but they are also more reactive than primary alkyl radicals owing to their higher nucleophilic character.[26] Work is in progress to determine absolute rate constants in the homolytic aromatic alkylation also with secondary and tertiary alkyl radicals.

Always due to polar effects, in the addition to fluorinated olefins, trifluoromethyl radical is the most reactive but also the most selective[27] in the series $\cdot CH_3$, $\cdot CH_2F$, $\cdot CHF_2$, and $\cdot CF_3$.

A final aspect needs to be discussed. The dramatic difference in behavior of the homocyclic and heterocyclic aromatics toward alkyl radicals could not be merely the result of the aromatic ring's electron deficiency with the consequent different extent of polar effects, but should reflect different mechanisms in the two series and the comparison should be less significant. Recent results of ours, however, confirm that the electron deficiency of the aromatic ring is actually the cause of the increased reactivity and selectivity. As a protonated heteroaromatic ring is much more reactive than the benzene ring, the homolytic alkylation occurs exclusively in the heterocyclic ring of polycyclic compounds[3] (quinoline, isoquinoline, acridine, benzothiazole, benzimidazole, etc.). Monoprotonated quinoxaline follows this general behavior and only the pyrazine ring is attacked with high rate (Table I). As regards diprotonated quinoxaline, the 6 position is as reactive as the 2 position. In this last case we do not have so far the absolute rate constants of the homolytic alkylation, because it was impossible to use the same kinetic model in a very strong acidic medium.

However, we have qualitative evidences that diprotonated quinoxaline reacts even faster with alkyl radicals than the monoprotonated one. In fact, when we generate alkyl radicals

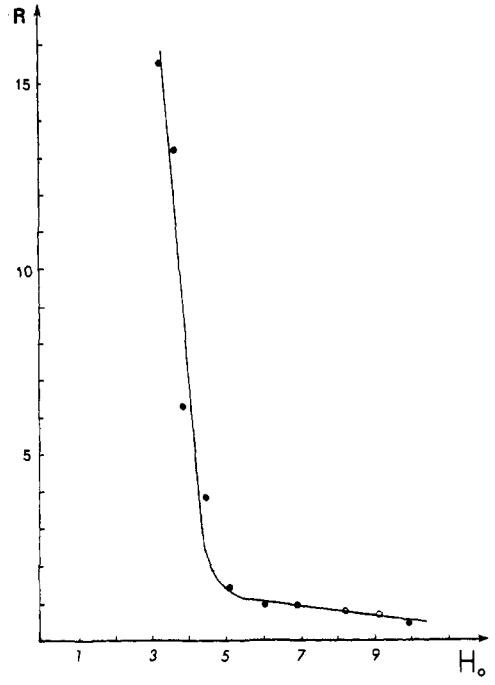



**Figure 4.** Plot of the ratio ($R$) of the isomers 2- and 6-cyclohexylquinoxaline vs. Hammett acidity function for the system $CH_3COOH/H_2SO_4$.

by intra- or intermolecular reaction by $N$-chloro amines,[4] under acidic condition, the attack to the diprotonated quinoxaline competes more effectively either with halogen transfer from protonated $N$-chloro amines (eq 1) or with other protonated heteroaromatic bases. The effect of the medium acidity on the ratios of 2 and 6 isomers in the cyclohexylation of quinoxaline by cyclohexane or $N$-chlorodimethylamine is shown in Figure 4.

We[3] have previously observed good correlations between the relative rates of the homolytic alkylation of the 2 position in protonated 4-substituted pyridines and the chemical shifts of the proton in position 2, suggesting that the main factor controlling both the free-radical reactivity and the relative shielding of the hydrogen nuclei is the electron density in position 2 of the molecules.

The experimental and calculated electron densities at different carbon atoms of mono- and diprotonated quinoxaline are reported in Table IV.

The data of Figure 4 and Table IV show that the positional selectivity of diprotonated quinoxaline toward nucleophilic radicals is correlated with the electronic density of the same positions. This correlation explains well the increased reactivity of the 6 position and once again suggests that the preeminent influence of the polar effects determines mainly the great difference in behavior between homocyclic and protonated heterocyclic aromatics toward nucleophilic carbon-centered radicals. These aspects could support the suggestion of a referee that a complexation due to SUMO-LUMO interaction (possibly a C-T complex) is followed by homolytic attack governed by local charge density; this last interaction would determine the positional selectivity whereas the C-T complex formation would determine the substrate selectivity.

## Experimental Section

**General Methods.** Melting and boiling points are uncorrected. NMR spectra were run in $CCl_4$ ($Me_4Si$ as internal standard) using a Varian A-100 (or A-60) spectrometer. Mass spectra were obtained on a Hitachi Perkin-Elmer RMU-6D mass spectrometer at 70 eV using an all-glass inlet system at 200 °C. GLC analyses were performed on a Hewlett-Packard 5850 chromatograph using the following columns: 20 ft × 1/8 in. 2% XE-60 on Chromosorb G-AW-

**Table V.** Alkylation Rates of Protonated Heteroaromatic Bases by Di-6-heptenoyl Peroxide[a]

| Base | M | Products, mol % VII | V | VII/V | $k_a/k_c$ |
|---|---|---|---|---|---|
| 4-Methylpyridine[b] | 0.50 | 14 | 64 | 0.22 | 0.44 |
| | 0.65 | 16 | 64 | 0.25 | 0.39 |
| | 0.83 | 20 | 65 | 0.31 | 0.37 |
| | 1.00 | 23 | 56 | 0.41 | 0.41 |
| | 1.20 | 25 | 51 | 0.49 | 0.43 |
| Benzothiazole[c] | 0.050 | 28 | 51 | 0.55 | 11.0 |
| | 0.075 | 35 | 46 | 0.76 | 10.1 |
| | 0.100 | 41 | 41 | 1.00 | 10.0 |
| | 0.150 | 51 | 36 | 1.42 | 9.5 |
| 4-Cyanopyridine[c] | 0.10 | 25 | 60 | 0.42 | 4.16 |
| | 0.15 | 33 | 51 | 0.65 | 4.34 |
| | 0.20 | 38 | 46 | 0.83 | 4.15 |
| | 0.30 | 50 | 37 | 1.35 | 4.50 |
| | 0.45 | 53 | 27 | 1.96 | 4.36 |
| | 0.50 | 61 | 27 | 2.26 | 4.52 |
| 4-Methylquinoline[c] | 0.10 | 17 | 65 | 0.25 | 2.50 |
| | 0.17 | 20 | 56 | 0.36 | 2.12 |
| | 0.20 | 26 | 59 | 0.44 | 2.20 |
| | 0.24 | 28 | 52 | 0.54 | 2.25 |
| | 0.30 | 31 | 47 | 0.60 | 2.00 |
| | 0.40 | 40 | 48 | 0.84 | 2.20 |
| | 0.50 | 45 | 44 | 1.02 | 2.00 |
| | 0.60 | 52 | 40 | 1.30 | 2.18 |
| 4-Acetylpyridine[c] | 0.10 | 7 | 70 | 0.10 | 1.00 |
| | 0.15 | 15 | 67 | 0.22 | 1.49 |
| | 0.20 | 18 | 62 | 0.29 | 1.45 |
| | 0.30 | 21 | 62 | 0.34 | 1.13 |
| | 0.40 | 29 | 49 | 0.59 | 1.47 |
| | 0.60 | 34 | 41 | 0.83 | 1.38 |
| Quinoxaline[d] | 0.035 | 72 | 11 | 6.53 | 186 |
| | 0.030 | 71 | 12 | 5.92 | 197 |
| | 0.025 | 75 | 15 | 5.00 | 200 |
| | 0.020 | 64 | 20 | 3.20 | 160 |
| | 0.010 | 55 | 29 | 1.90 | 190 |

[a] All the reactions were run at 25 °C in $CH_3COOH$–$H_2O$ (1:1). [b] Peroxide ($10^{-2}$ M); CuOAc (1.6 $10^{-3}$ M); $H_2SO_4$ (2 M). [c] Peroxide ($10^{-2}$ M); CuOAc (1.6 $10^{-3}$ M); $H_2SO_4$ (1 M). [d] Peroxide ($10^{-3}$ M); CuOAc ($5 \times 10^{-4}$ M); $H_2SO_4$ (1 M).

**Table VI.** Temperature Dependences of the Ratio VII/V in the Alkylation Reactions of Protonated Heteroaromatic Bases by Di-6-heptenoyl Peroxide[a]

| Base | Temp, °C | Products, mol % VII | V | VII/V | $k_a/k_c$ |
|---|---|---|---|---|---|
| 4-Methylquinoline[b] | 10.5 | 35 | 50 | 0.64 | 2.30 |
| | 13.5 | 32 | 48 | 0.67 | 2.23 |
| | 26.0 | 31 | 47 | 0.60 | 2.00 |
| | 35.0 | 28 | 53 | 0.53 | 1.68 |
| | 46.0 | 25 | 58 | 0.43 | 1.44 |
| | 60.0 | 22 | 61 | 0.36 | 1.20 |
| | 80.0 | 14 | 58 | 0.24 | 0.80 |
| 4-Methylpyridine[c] | 25.0 | 15 | 60 | 0.253 | 0.25 |
| | 36.0 | 18 | 75 | 0.233 | 0.23 |
| | 46.0 | 13 | 68 | 0.192 | 0.19 |
| | 60.0 | 13 | 70 | 0.186 | 0.18 |
| | 29.0 | 11 | 72 | 0.153 | 0.15 |
| Quinoxaline[d] | 25.0 | 71 | 13 | 5.46 | 198 |
| | 36.0 | 68 | 17 | 4.00 | 132 |
| | 40.0 | 66 | 20 | 3.30 | 110 |
| | 45.5 | 56 | 23 | 2.44 | 82 |
| | 61.0 | 51 | 27 | 1.89 | 63 |
| | 80.5 | 43 | 34 | 1.17 | 38 |
| 4-Cyanopyridine[b] | 14.0 | 51 | 34 | 1.50 | 5.25 |
| | 25.0 | 46 | 36 | 1.28 | 4.26 |
| | 36.0 | 48 | 44 | 1.09 | 3.63 |
| | 45.5 | 40 | 42 | 0.95 | 3.16 |
| | 60.0 | 34 | 42 | 0.81 | 2.69 |

[a] All the reactions were run in $CH_3COOH$–$H_2O$ (1:1). [b] Heteroaromatic base (0.3 M); $H_2SO_4$ (1 M); peroxide ($10^{-2}$ M); CuOAc ($1.6 \times 10^{-3}$ M). [c] 4-Methylpyridine (0.83 M); $H_2SO_4$ (2 M); peroxide (0.1 M); CuOAc ($10^{-2}$ M). [d] Quinoxaline (0.03 M); $H_2SO_4$ (1 M); peroxide ($2 \times 10^{-3}$ M); CuOAc ($5 \times 10^{-4}$ M).

DMCS; 15 ft × 1/5 in. 10% U.C.C. W on Chromosorb W AW-DMCS. Isomer distribution was determined with a 6 ft × 1/5 in. 10% DEGS on Chromosorb W-AW-DMCS. The retention times of all products agreed with those obtained by GLC analysis of independently synthesized samples.

**Materials.** 4-Methylquinoline, 4-methylpyridine, and 4-acetylpyridine were dried over KOH and distilled. 4-Cyanopyridine and quinoxaline were sublimed. Benzothiazole was purified by crystallization at −10 °C and distillation. Acetic acid and acetonitrile were refluxed over $P_2O_5$ and distilled. Benzene was distilled twice over Na. Benzonitrile and anisole were distilled before use. The isomeric *o*-, *m*-, and *p*-butylanisole were prepared using standard procedure. 6-Heptenoic acid (mp 25–26 °C, bp 80 °C (1 mmHg)) was prepared according to the literature[29] starting from 1,2,6-hexanetriol, and purified[30] through 6,7-dibromoheptanoic acid. The 6-heptenoic acid was regenerated with zinc dust. Cyclopentylacetic acid (bp 125 °C (23 mm)) was prepared by catalytic reduction of 2-cyclopentenylacetic acid (bp 95 °C (2.5 mm)).

The diacyl peroxides were obtained by the standard method,[31] adding the acyl chlorides in ether to a cooled (−10 °C) solution of ether, pyridine, and $H_2O_2$. 6-Heptenoyl, cyclopentylacetyl, *n*-octanoyl, and *n*-valeroyl peroxides, pure at 98–99% (by iodometric titration), were stored at −30 °C. Copper(I) acetate was prepared as the acetonitrile complex by stirring 1.6 g ($8 \times 10^{-3}$ mol) of $Cu(OAc)_2 \cdot 5H_2O$ with an excess of copper powder in 100 mL of degassed $CH_3CN$–$CH_3COOH$ (6:4) mixture under a slight pressure of $N_2$. The solution was standardized against $Ce(SO_4)_2$ (0.1 N).

**Alkylation of Heteroaromatic Bases by Diacyl Peroxides. General Preparative Procedure for 5-Hexenyl and Cyclopentylmethyl Derivatives.** The heteroaromatic base (0.02 mol) and concentrated $H_2SO_4$ (0.04 mol) were dissolved in 50 mL of degassed mixture $CH_3CN$–$CH_3COOH$ (60:40) under $N_2$; 5 mL of a standardized solution of Cu(I) (0.016 M) was added at room temperature. The peroxide (0.014 mol), dissolved in 10 mL of acetonitrile, was added to the stirred solution. $CO_2$ immediately evolved and the solution was stirred until the development of $CO_2$ ceased.

The solvents were removed under reduced pressure, and the residue was dissolved in 30 mL of a stirred and cooled mixture of 30% NaOH, $NH_4Cl$, and ether. The ether was separated and the basic solution was extracted twice with ether. After removal of the solvent the residue was chromatographed over $SiO_2$ or distilled. The overall yields range from 60 to 90% based on the peroxide and 80–95% based on the heteroaromatic base. In all cases the reactions were very clean; with the 6-heptenoyl peroxide the 5-hexenyl and the cyclopentylmethyl derivatives were formed in different ratios determined by the reactivity of the heteroaromatic base (see kinetics results); with cyclopentylacetyl peroxide only the cyclopentylmethyl derivatives were obtained. All the alkyl derivatives of the heteroaromatic bases were isolated as pure samples by preparative GLC (15-ft column packed with 10% U.C.C).

2-(5-Hexenyl)-4-methylpyridine: IR $\nu_{max}$ 915 $cm^{-1}$(vinyl); $^1H$ NMR $\delta$ 8.2 (1 H, d, $H_6$), 6.8 (1 H, d, $H_5$), 6.8 (1 H, s, $H_3$), 6.17–5.60 (m, 1 vinyl H), 5.07–4.68 (m, 2 vinyl H), 2.9 (1 H, t, $-CH_2Ar$), 2.24 (3 H, s, $CH_3$), 2.0 (m, 2 H, $CH_2CH=$), 1.4–1.9 (m, 4 H); MS *m/e* 175 ($M'^+$), 134, *103*, 93, 92, 39. Anal. Calcd for $C_{12}H_{17}N$: C, 82.23; H, 9.78; N, 7.99. Found: C, 82.21; H, 9.27; N, 8.00.

2-Cyclopentylmethyl-4 methylpyridine: NMR $\delta$ 8.24 (1 H, d, $H_6$), 6.7 (1 H, d, $H_6$), 6.8 (1 H, s, $H_3$), 2.66 (2 H, d, $CH_2CH$), 2.1–2.4 (1 H, m, –CH), 2.24 (3 H, s, $CH_3$), 1.4–1.9 (8 H, m, $CH_2$); MS *m/e* 175 ($M^{+\cdot}$), 146, 132, *103*, 93, 77, 39. Anal. Calcd for $C_{12}H_{17}N$: C, 82.23; H, 9.78; N, 7.99. Found: C, 82.2; H, 9.8; N, 7.9.

2-(5-Hexenyl)-4-acetylpyridine: IR 915 $cm^{-1}$; NMR $\delta$ 8.54 (1 H, d, $H_6$), 7.40 (1 H, d, $H_5$), 7.43 (1 H, s, $H_3$), 6.15–5.60 (m, 1 vinyl H), 5.1–4.7 (m, 2 vinyl H), 2.7 (2 H, t, $CH_2Ar$), 2.1 (2 H, td, $CH_2CH=$), 2.5 (3 H, s, $COCH_3$), 1.4–1.9 (4 H, m); MS *m/e* 203 ($M^{+\cdot}$), 162, 148, *135*, 77, 57, 43. Anal. Calcd for $C_{13}H_{17}NO$: C, 76.81; H, 8.43; N, 6.89. Found: C, 76.74; H, 8.27; N, 6.72.

2-Cyclopentylmethyl-4-acetylpyridine: NMR $\delta$ 8.6 (1 H, d, $H_6$), 7.4 (1 H, d, $H_5$), 7.4 (1 H, d, $H_3$), 2.80 (2 H, d, $CH_2CH$), 2.5 (3 H,

**Table VII**

| Substrates (molar ratio) | $k_a$ (with $Cu^{2+}$) | $k_a$ (without $Cu^{2+}$) |
|---|---|---|
| Anisole/benzene (2:1) (1:1) | 3.6 ± 0.1 | 2.9 ± 0.1 |
| Methylpyridine/anisole (1:15) (1:25) | 78 ± 5 | 113 ± 6 |
| Methylpyridine/benzene (1:25) (1:40) | 281 ± 20 | 330 ± 30 |

s, $COCH_3$), 2.1–2.4 (1 H, m, -CH), 1.4–1.9 (8 H, m); MS *m/e* 203 ($M^{+\cdot}$), 174, 160, 148, *135*, 93, 43. Anal. Calcd for $C_{13}H_{17}NO$: C, 76.81; H, 8.43; N, 6.89. Found: C, 76.71; H, 8.49; N, 6.98.

2-(5-Hexenyl)-4-cyanopyridine: IR 915 $cm^{-1}$; NMR $\delta$ 8.7 (1 H, d, $H_6$), 7.3 (1 H, d, $H_5$), 7.4 (1 H, s, $H_3$), 6.2–5.6 (1 H, m, vinyl H), 5.1–4.7 (m, 2 vinyl H), 2.8 (2 H, t, $CH_2Ar$), 2.1 (2 H, td, $CH_2CH$=), 1.4–1.9 (4 H, m); MS *m/e* 188 ($M^{+\cdot}$), 147, *120*, 105, 93. Anal. Calcd for $C_{12}H_{14}N_2$: C, 77.38; H, 7.58; N, 15.04. Found: C, 77.5; H, 7.5; N, 15.1.

2-Cyclopentylmethyl-4-cyanopyridine: NMR $\delta$ 8.6 (1 H, d, $H_6$), 7.3 (1 H, d, $H_5$), 7.4 (1 H, s, $H_3$), 2.82 (2 H, d, $CH_2CH$), 2.2–2.5 (1 H, m, -CH), 1.4–1.9 (8 H, m); MS *m/e* 188 ($M^{+\cdot}$), 159, 145, 133, *120*, 106, 93. Anal. Calcd for $C_{12}H_{14}N_2$: C, 77.38; H, 7.58; N, 15.04. Found: C, 77.46; H, 7.69; N, 15.14.

2-(5-Hexenyl)-4-methylquinoline: a sample isolated by preparative GLC (10% UCC, 200 °C) showed IR 915 $cm^{-1}$ (vinyl); NMR $\delta$ 7.15 (1 H, s, $H_3$), 7.4–8.1 (4 H, m, aromatics), 6.2–5.6 (1 H, m, vinyl), 5.1–4.7 (m, 2 vinyl H), 2.94 (2 H, t, $CH_2Ar$), 2.60 (3 H, s, $CH_3$), 2.4–2.0 (2 H, m, $CH_2CH$=), 1.4–2.1 (4 H, m); MS *m/e* 225 ($M^{+\cdot}$), 184, 170, *157*, 115, 93. Anal. Calcd for $C_{16}H_{19}N$: C, 85.28; H, 8.50; N, 6.22. Found: C, 85.40; H, 8.25; N, 6.31.

2-(Cyclopentylmethyl)-4-methylquinoline: NMR $\delta$ 7.2 (1 H, s, $H_3$), 7.4–8.1 (4 H, m, Ar), 2.9 (2 H, d, $CH_2CH$), 2.58 (3 H, s, $CH_3$), 2.3–2.5 (1 H, m, CH); MS *m/e* 225 ($M^{+\cdot}$), 196, 184, 182, 170, *157*, 142, 115. Anal. Calcd for $C_{16}H_{19}N$: C, 85.28; H, 8.50; N, 6.22. Found: C, 85.3; H, 8.6; N, 6.3.

2-(5-Hexenyl)benzothiazole: a sample isolated by preparative GLC (10% UCC, 190 °C) showed IR 915 $cm^{-1}$ (vinyl); NMR $\delta$ 7.5–8.0 (4 H, m, Ar), 6.2–5.5 (1 H, m, vinyl), 5.1–4.7 (m, 2 vinyl H), 2.8 (2 H, t, $CH_2Ar$), 2.4–2.1 (2 H, m, $CH_2CH$=), 1.4–2.1 (4 H, m); MS *m/e* 217 ($M^{+\cdot}$), 176, 162, *148*, 147, 109, 91, 76. Anal. Calcd for $C_{13}H_{15}NS$: C, 71.38; H, 6.95; N, 6.44. Found: C, 71.3; H, 7.0; N, 6.5.

2-Cyclopentylmethylbenzothiazole: NMR $\delta$ 7.5–8.0 (4 H, m, Ar), 2.9 (2 H, d, $CH_2CH$), 2.2–2.5 (1 H, m, CH), 1.4–1.9 (8 H, m); MS *m/e* 217 ($M^{+\cdot}$), 188, 174, 160, *148*, 93, 91, 55. Anal. Calcd for $C_{13}H_{15}NS$: C, 71.38; H, 6.95; N = 6/44/ Found: C, 71.5; H, 7.0; N, 6.4.

2-(5-Hexenyl)quinoxaline: a sample isolated by preparative GLC (UCC, 200 °C) showed IR $\nu_{max}$ 915 $cm^{-1}$ (vinyl); NMR $\delta$ 8.50 (1 H, s, $H_3$), 7.60–8.20 (4 H, m, $H_{5,6,7,8}$), 6.2–5.6 (1 H, m, vinyl), 5.1–4.7 (2 H, m, vinyl), 2.80 (2 H, t, $CH_2Ar$), 1.5–2.2 (6 H, m); MS *m/e* 212 ($M^{+\cdot}$), 171, 157, *144*, 93, 91, 55. Anal. Calcd for $C_{14}H_{16}N_2$: C, 79.21; H, 7.60; N, 13.20. Found: C, 79.1; H, 7.5; H, 13.2.

2-Cyclopentylmethylquinoxaline: NMR $\delta$ 8.51 (1 H, s, $H_3$), 7.60–8.20 (4 H, m, aromatics), 2.95 (2 H, t, $CH_2CH$), 1.4–1.9 (8 H, m); MS *m/e* 212 ($M^{+}$-), 183, 169, *144*, 93, 55. Anal. Calcd for $C_{14}H_{16}N_2$: C, 79.21; H, 7.60; N, 13.20. Found: C, 79.2; H, 7.50; N, 13.11.

**Kinetics. General Procedure.** The following standard solutions were prepared: (1) heteroaromatic base (0.01–1.2 M) in $H_2SO_4$ (0.6–2 M), $CH_3COOH$–$H_2O$ (1:1); (2) diacyl peroxide (0.01 M) in acetic acid; (3) copper(I) acetate (1.6–$10^{-3}$ M) in $CH_3CN$–$CH_3COOH$ (6:4). These solutions were placed in a thermostatic bath and flushed with $N_2$ for 10 min. Then to 10 mL of the solution (1) were added first 1 mL of the solution (2) and then 1 mL of the solution (3). The mixture was kept on thermostatic bath for 2 h under $N_2$, then cooled at 0 °C, basified with 10% NaOH solution, extracted three times with 5 mL of ether, and dried on $Na_2SO_4$. After addition of an internal standard, the joined ethereal extracts were analyzed by GLC. In Tables V and VI are reported the resulting values of VII/V ratios concerning the influence of the concentrations and of the temperature. All data are an average result of two independent reactions.

**Alkylation of Quinoxaline by Di-*n*-octanoyl Peroxide in the Presence of $CuCl_2$.** A standard solution was prepared as follows: quinoxaline (0.6 M), $H_2SO_4$ (1.2 M), $CuCl_2$ ($6 \times 10^{-3}$ M), and LiCl ($5 \times 10^{-2}$ M) in $CH_3COOH$–$H_2O$ (1:1). To 50 mL of this standard solution, flushed with $N_2$ at 25 °C in a thermostatic bath, was added 1 mL of a solution of di-*n*-octanoyl peroxide (0.3 M) in acetic acid and the decomposition of the peroxide was initiated for addition of 6 mL of a solution of copper(I) acetate ($1.6 \times 10^{-3}$ M). The reaction was kept for 2 h at 25 °C. Then *n*-octyl chloride and *n*-butylquinoxaline were added as internal standards. The resulting mixture was basified at 0 °C and extracted twice with pentane. The analyses were performed on a 10% U.C.C. column at 90 °C for *n*-heptyl chloride (1) and at 220 °C for *n*-heptylquinoxaline (2). A value of 0.32 for the molar ratio (1):(2) is the average result of three independent runs.

**Competitive Experiments.** As source of *n*-butyl radical was used di-*n*-valeroyl peroxide. The peroxide ($1 \times 10^{-3}$ M) was added to a solution of two substracts for a total of 0.11 mol, acetic acid (12 mL) and trifluoroacetic acid (1 mL).

When $Cu(OAc)_2$ ($0.12 \times 10^{-3}$ M) was added to the solution, the yield in butyl derivatives was much lower and it has been necessary to increase the quantity of peroxide ($5.6 \times 10^{-3}$ M). The mixture was kept at 79 °C for 2.5 h under $N_2$, then cooled at 0 °C, basified with 30% NaOH solution, extracted three times with ether, and dried on $Na_2SO_4$. The ethereal solutions were analyzed by GLC using either 10% U.C.C. or 10% DEGS columns. Two runs were conducted for each system and an average result was taken for the two runs. The substrates molar ratio, the resulting values of relative rate ($K$) with or without $Cu^{2+}$, and the accuracy in determining each value are reported in Table VII.

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# Analysis of the Swain–Moseley–Bown Equation and Comparison of the Results with Nucleophilicities Derived from Halonium Ion Reactions

**Paul E. Peterson,* D. Warren Vidrine, Francis J. Waller, P. M. Henrichs, Steve Magaha, and Bruce Stevens**

*Contribution from the Department of Chemistry, University of South Carolina, Columbia, South Carolina 29208, and the Department of Chemistry, St. Louis University, St. Louis, Missouri 63156.* *Received March 21, 1977*

**Abstract:** In 1956 Swain, Moseley, and Bown correlated the rates of solvolysis of a variety of alkyl and acyl derivatives through the equation $\log k/k_0 = c_1d_1 + c_2d_2$. The equation has now been transformed to the form $\log k/k_0 = sN + mY$, where the solvent parameter $Y$ is a measure of ionizing power and $N$ appears to represent either nucleophilicity or electrophilicity. Compounds whose reactions are sensitive to electrophilicity exhibit negative sensitivity parameters, $s$. The reaction of pentamethyleneiodonium hexafluoroantimonate (**1**) with aqueous solutions of nucleophiles or pairs of nucleophiles generated a nucleophilicity scale encompassing both anionic and uncharged nucleophiles. The scale shows a linear correlation with that generated by reactions of methyl iodide. It is inferred that the charge type of both nucleophiles and substrates is unimportant for $S_N2$ reactions in $H_2O$.

Recently there have been some substantial advances in our understanding of the role of nucleophilicity in organic reactions. The work of Ritchie and co-workers has shown that various reactants, including particularly triarylmethyl cations, tropylium ions, and diazonium ions, obey the rate law[1]

$$\log k - \log k_0 = N^+ \qquad (1)$$

The difference in the logarithms of the rate constants for reactions of a substrate with a nucleophilic system (e.g., $N_3^-$ in $CH_3OH$) and for reaction with a standard system ($H_2O$ nucleophile in $H_2O$ solvent) is a constant, $N^+$, which represents the difference in nucleophilicity of the two systems. Compounds with a high range of reactivity were shown to exhibit the same sensitivity to differences in nucleophilicity. Furthermore, the $N^+$ scale differs from the nucleophilicity scales generated from rates of $S_N2$ reactions. Recently the first step of the hydrolysis reactions of esters and related compounds has been shown to follow eq 1, provided certain assumptions hold for the other processes which govern the overall rate.[2] It is possible that the $N^+$ nucleophilicities represent an important component of $S_N2$ nucleophilicities, but considerable mystery surrounds the situation.

On another front, the nucleophilic component of the rates of solvolytic reactions of methyl, primary, and secondary substrates (e.g., isopropyl tosylate) have been identified and quantitatively characterized.[3,4] This work grew, in part, from the experimental observation in Schleyer's group[5] that 2-adamantyl derivatives do not respond to an increase in the nucleophilicity of the solvent in the way that isopropyl derivatives do. In our own group a comparable study grew from the observation[6] that the high reactivity of now isolable halonium ion salts made them suitable for determining the nucleophilicity of carboxylic acids in a constant solvent, $SO_2$.

Both Schleyer's group[3] and ours[4] proposed sets of compound and solvent parameters for equations of the type

$$\log k_A - \log k_B = sN_A^B + mY_A^B \qquad (2)$$

Here $k_A$ and $k_B$ are rate constants for reaction in solvents A and B, $N_A^B$ is the change in solvent nucleophilicity, $Y_A^B$ is the change in solvent ionizing power, and $s$ (1 in Schleyer's paper) and $n$ are sensitivity parameters characteristic of the compound. In still another treatment[3a] the solvent response of solvolytic rates is regarded as occupying a spectrum the extremes of which are represented by the reaction of methyl and adamantyl derivatives.

Curiously a successful treatment of solvolytic rates involving an equation comparable to eq 2 was used by Swain, Moseley, and Bown approximately 22 years ago,[7] but it has not been extended as new solvents and compounds were explored. The correlation of Swain, Moseley, and Bown also involves two solvent parameters, $d_1$ and $d_2$, and two compound parameters, $c_1$ and $c_2$.

$$\log k - \log k_0 = c_1d_1 + c_2d_2 \qquad (3)$$

The rate constant, $k_0$, refers to the reaction in the standard solvent, 80% ethanol, also chosen as the solvent of zero $Y$ value in the Winstein-Grunwald-Jones equation,[8]

$$\log k - \log k_0 = mY \qquad (4)$$

As Streitwieser[9] and others have pointed out, the choice of parameters for *tert*-butyl chloride, $c_1 \equiv 1$ and $d_1 = 1$, has made the Swain-Moseley-Bown parameters of "no theoretical significance". Various authors of textbooks recorded them,[10] but no meaningful interpretation ever was found. In 1972 we reported in preliminary form a resolution of this dilemma which