nmr ($CDCl_3$) τ 2.05 (d, 1 H, J = 2.5 Hz, thiophene), 2.63 (s, 5 H, C_6H_5), 2.88 (q, 1 H, thiophene), 3.67 (d, 1 H, J = 1.0 Hz, methine).

Anal. Calcd for $C_{12}H_8O_2S$: C, 66.64; H, 3.73; S, 14.83. Found: C, 66.87; H, 3.55; S, 14.79.

Registry No.—**1**, 33527-26-3; **2**, 33527-20-7; **14**, 36540-46-2; **15**, 36540-47-3; **19**, 36540-48-4; **20**, 36540-49-5; **26**, 36540-50-8; **27**, 36540-51-9; **28**, 36540-52-0; aluminum chloride, 7446-70-0; benzene, 71-43-2.

1,2,4-Triazoles. XXXII. Syntheses and Correlation of Proton Magnetic Resonance Spectral Characteristics with Molecular Orbital Parameters of Derivatives of the *s*-Triazolo[4,3-*a*]quinoline and *s*-Triazolo[3,4-*a*]isoquinoline Ring Systems[1]

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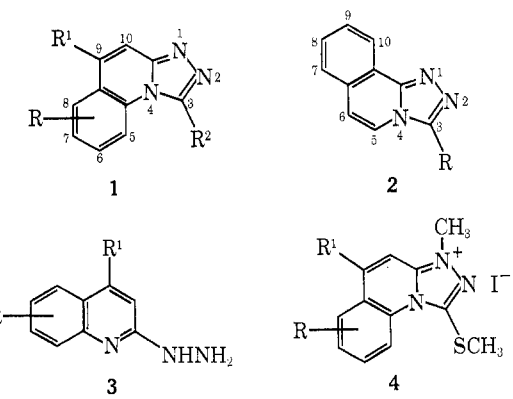
The syntheses and proton magnetic resonance (pmr) spectral data at 60 MHz for several members of the title ring systems are described. Confirmation of the spectral assignments was obtained by examination of several of the products at 100 MHz. Of particular interest are correlations observed between chemical shifts and electron densities calculated by the FEHT method. Ultraviolet absorption data for these ring systems are also described.

In a continuation of our interests in the chemistry of the *s*-triazole ring system, we have extended our study of the *s*-triazolo[4,3-*a*]pyridine and *s*-triazolo[1,5-*a*]pyridine systems[2] to include two benzo-fused derivatives, the *s*-triazolo[4,3-*a*]quinoline (**1**) and the *s*-triazolo[3,4-*a*]isoquinoline (**2**) ring systems. The influence of the fused benzene ring on the spectral and chemical properties of these ring systems is of interest as is the nature of the electron delocalization throughout these systems. The empirical correlation between chemical shifts and calculated π-electron densities in the benzenoid series[3] suggested the study of the ring systems from these viewpoints. The presence of heteroatoms in these nonalternant heterocycles requires the use of SCF[3-6] methods for the calculation of the electron densities. This method, in contrast to the simple Hückel approach, has been shown[3] to provide useful correlations of the above type. To aid in the interpretation of the pmr spectra, suitable methyl-substituted products were synthesized by the procedures described below.

Synthetic Procedures.—Reports of the synthesis of *s*-triazolo[4,3-*a*]quinoline[7] and of 9-methyl-*s*-triazolo[4,3-*a*]quinoline-3-thiol[8] appeared as early as 1900. Oxidative ring closure of various aromatic aldehyde 2-quinolyl hydrazones with ferric chloride or nitrobenzene was shown[9a] to be an effective route to 3-substituted derivatives, and the introduction of substituents into the 3 position analogous to those reported for the *s*-triazolo[4,3-*a*]pyridine system[10] was also described.[9b]



Standard procedures developed for other ring systems[10] were used for the synthesis of the *s*-triazolo[4,3-*a*]quinoline derivatives described in Table I. The intermediate 2-quinolylhydrazines used in the cyclization reactions were prepared in good yields from the appropriate methyl-substituted quinoline *via* the 1-methyl-2-quinolones and 2-chloroquinolines.[11] These hydrazines, with or without substituents in either the benzene or the pyridine rings, readily cyclized with aliphatic acids to the desired products except as described below. Cyanogen bromide and carbon disulfide were found to be quite effective in forming the 3-amino (**1**, $R^2 = NH_2$) and 3-mercapto (**1**, $R^2 = SH$) derivatives. 8-Methyl-2-quinolylhydrazine was found to be extremely resistant to cyclization with either formic acid or acetic acid, the *N*-formyl and *N*-acetyl

(1) Support of this work by Public Health Service Research Grant CA 08495-01, National Cancer Institute, and by the University of Kentucky Computing Center, is gratefully acknowledged.

(2) K. T. Potts, H. R. Burton, T. H. Crawford, and S. W. Thomas, *J. Org. Chem.*, **31**, 3522 (1966), and references cited therein.

(3) G. G. Hall, A. Hardisson, and L. M. Jackman, *Tetrahedron, Suppl. 2*, **19**, 101 (1963), and references cited therein.

(4) A. Streitwieser, Jr., "Molecular Orbital Calculations for Organic Chemistry," Wiley, New York, N. Y., 1962, Chapter 16, and references cited therein.

(5) M. J. S. Dewar and G. J. Gleicher, *J. Chem. Phys.*, **44**, 759 (1966).

(6) C. A. Girard and S. L. Smith, Abstracts, 156th National Meeting of the American Chemical Society, Atlantic City, N. J., Sept 1968, ORGN 188; C. A. Girard, "Some Empirical Investigations on a Fock Modified Extended Hückel Molecular Orbital Method," Ph.D. Dissertation, M. I. King Library, University of Kentucky, Lexington, Ky., 1972.

(7) W. Marckwald and E. Meyer, *Ber.*, **33**, 1885 (1900).

(8) W. Marckwald and M. Chain, *ibid.*, **33**, 1895 (1900).

(9) (a) S. Naqui and V. R. Srinivasan, *Indian J. Chem.*, **3**, 162 (1965); (b) G. S. Sidhu, S. Naqui, and D. S. Iyengar, *J. Heterocycl. Chem.*, **3**, 158 (1966); (c) see also H. Reimlinger, J. J. M. Vandewalle, and W. R. F. Lingier, *Chem. Ber.*, **103**, 1960 (1970).

(10) K. T. Potts and H. R. Burton, *J. Org. Chem.*, **31**, 251 (1966); K. T. Potts, H. R. Burton, and S. K. Roy, *ibid.*, **31**, 256 (1966).

(11) W. H. Perkins and R. Bobinson, *J. Chem. Soc.*, 1978 (1913).

Table I[e]

Some s-Triazolo[4,3-a]quinolines (1)[e]

Registry no.	R	R1	R2	Mp, °C	Uv data (CH_3OH), λ_{max} (log ϵ)
235-06-3	H	H	H	170–171[a]	245[b] (3.72), 278 (3.71), 297 (3.71), 307 (3.93), 318 (3.98)
35359-22-9	H	H	CH_3	168–169	203 (4.63), 211 (4.65), 215 (4.64), 228[b] (4.46), 238[b] (4.31), 290 (4.11), 301 (3.92), 314 (3.87)
35359-23-0	H	H	SH	274	276 (3.99), 312[b] (4.07), 322 (4.05)
35359-24-1	H	H	SCH_3	117–119[c]	248 (3.74), 258 (3.78), 303 (4.09), 316 (4.08)
35359-25-2	H	CH_3	H	227–228	210[b] (4.39), 230 (4.61), 243[b] (4.06), 267 (3.82), 274[b] (3.73), 313[b] (3.73), 325 (3.87), 338 (3.66)
35359-26-3	H	CH_3	CH_3	195	212 (4.53), 216 (4.53), 225[b] (4.38), 231[b] (4.36), 243 (4.14), 253 (3.99), 281[b] (3.93), 292 (3.82), 302 (3.93), 316 (3.82)
35359-27-4	H	CH_3	SH	280[d]	212 (5.05), 270[b] (4.59), 278 (4.72), 321 (4.25).
35359-28-5	7-CH_3	H	H	192–193	216 (4.43), 230[b] (4.50), 235 (4.53), 250 (4.04), 280 (4.02), 291 (4.02), 308 (3.71), 325 (3.68)
35359-29-6	7-CH_3	H	CH_3	160–161	213 (4.56), 217 (4.57), 227 (4.53), 233 (4.53), 251[b] (4.06), 263 (3.73), 269[b] (3.82), 283 (4.03), 293 (4.03), 306[b] (3.82), 320 (3.68)
35359-30-9	7-CH_3	H	NH_2	245 dec	215 (4.60), 251 (4.15), 260[b] (4.04), 297[b] (3.90), 328 (4.04)
35359-31-0	7-CH_3	H	SH	294–296 dec	211 (4.62), 220 (4.67), 273[b] (4.30), 282 (4.47), 305 (3.85), 318 (3.85)
35359-32-1	6-CH_3	H	H	190–191	211–215 (4.45), 226 (4.35), 231[b] (4.33), 280[b] (4.00), 288 (4.04), 313[b] (3.40)
440-54-0	H			119–120	235 (4.30), 238 (4.30), 262 (3.84), 271[b] (3.48), 304 (3.35), 317 (3.30)
7639-56-7	CH_3			168	240 (4.59), 247 (4.59), 265 (3.77), 275[b] (3.70), 306 (3.26), 320 (3.14)
27210-14-6	NH_2			268–270 dec	209 (4.70), 250[b] (4.58), 259 (4.69), 304 (3.66)

[a] Lit.[6] mp 175°. [b] Shoulder. [c] We thank Dr. S. Naqui for the preparation of this compound. [d] Lit.[7] mp 280°. [e] Satisfactory analytical values (±0.4% for C, H, N) were reported for all new compounds in table: Ed.

compounds, respectively, being obtained. The *N*-formyl compound was readily cyclized to the desired 5-methyl-*s*-triazolo[4,3-*a*]quinoline by heating about its melting point for 6 hr; however, the *N*-acetyl compound (ν_{CO} 1665 cm^{-1}) did not cyclize under similar conditions. This is most likely due to the large steric interaction of the methyl groups at positions 3 and 5 of the fused ring system, which is clearly shown by suitable models. A similar steric interaction was observed in the formation of 3,5-disubstituted *s*-triazolo[4,3-*a*]pyridines,[10] but in the present case the overlap of the two methyl groups is so great that ring closure is prevented.

The *s*-triazolo[4,3-*a*]quinoline-3-thiols, when treated with methyl iodide and base, readily formed the anticipated 3-methylthio compounds; with excess methyl iodide the corresponding 1-methyl-3-methylthio-*s*-triazolo[4,3-*a*]quinolinium iodides (**4**) were obtained. That further reaction of the 3-methylthio compounds with methyl iodide occurred so readily is understandable on comparison of the π-electron densities at N-1 for this ring system with those of *s*-triazolo[4,3-*a*]-pyridine.[10] The alternative route to these 1-substituted products was also successful in this system. Thus 1-methyl-1-(4-methyl-2-quinolyl)hydrazine, prepared from 2-chloro-4-methylquinoline and methyl hydrazine, when treated with cyanogen bromide gave 1,9-dimethyl-3-amino-*s*-triazolo[4,3-*a*]quinolinium bromide.

In the *s*-triazolo[3,4-*a*]isoquinoline system (**2**) only the 3-phenyl derivative had been prepared previously.[9a,c] Our present work shows that cyclization of 1-isoquinolylhydrazine with aliphatic acids is a convenient route to the 3-alkyl derivatives and that the 3-amino compound is also readily available by cyclization with cyanogen bromide. The limitation to the synthesis of derivatives of this ring system lies in the involved processes needed to obtain the appropriate 1-isoquinolylhydrazines.

Proton Magnetic Resonance Spectra.—Observed chemical shifts and coupling constants for the compounds described above are listed in Table II. In general, the spectra of the *s*-triazolo[4,3-*a*]quinolines consist of an isolated signal near 9.20 ppm and a complex aggregation of peaks between 7.40 and 8.20 ppm relative to internal TMS. The isolated signal near 9.20 ppm can be unambiguously assigned to H_3, since it disappears upon substitution at that position. The remaining complex pattern arises from five or six (depending on the degree of substitution) closely spaced, strongly coupled protons and cannot be readily analyzed on a first-order basis. Examination of the spectra

TABLE II

Substituents			Chemical shifts[a] of protons at positions							Coupling constants, Hz
R	R^1	R^2	3	5	6	7	8	9	10	
Pmr Parameters for Some *s*-Triazolo[4,3-*a*]quinolines (1)										
H	H	H	9.25 ± 0.01	8.02 ± 0.03	7.69 ± 0.05	7.53 ± 0.05	7.80 ± 0.03	7.60 ± 0.03	7.68 ± 0.03	$J_{5,6}$ = 7.8; $J_{6,7}$ = 7.5; $J_{7,8}$ = 7.5; $J_{5,7}$ = 1.3; $J_{6,8}$ = 1.8; $J_{9,10}$ = 9.5; $J_{9,10}$ = 1.2
H	H	CH_3[b]	*2.15 ± 0.01*	8.22 ± 0.03	7.65 ± 0.05	7.55 ± 0.05	7.80 ± 0.03	7.48 ± 0.03	7.60 ± 0.03	
H	CH_3	H	9.16 ± 0.01	7.95 ± 0.05	7.62 ± 0.05	7.53 ± 0.05	7.78 ± 0.05	*2.59 ± 0.01*	7.45 ± 0.03	$J_{5,6}$ = 7.9; $J_{6,8}$ = 1.6; $J_{9,10}$ = 9.1; $J_{9,10}$ = 1.2
7-CH_3	H	H	9.20 ± 0.01	7.86 ± 0.03	7.48 ± 0.05	*2.53 ± 0.01*	7.57 ± 0.03	7.53 ± 0.03	7.64 ± 0.03	
H	CH_3	CH_3	*2.04 ± 0.01*	8.13 ± 0.05	7.65 ± 0.05	7.55 ± 0.05	7.85 ± 0.05	*2.59 ± 0.01*	7.44 ± 0.01	$J_{9,10}$ = 9.2
5-CH_3	H	H	9.54 ± 0.01	*2.95 ± 0.01*	7.46 ± 0.08	7.46 ± 0.08	7.46 ± 0.08	7.57 ± 0.05	7.70 ± 0.01	
Pmr Parameters for Some *s*-Triazolo[3,4-*a*]isoquinolines (2)										
H	H	H	8.75 ± 0.01	7.88 ± 0.01	7.11 ± 0.01	7.63 ± 0.10	7.63 ± 0.10	7.63 ± 0.10	8.70 ± 0.03	$J_{5,6}$ = 7.0
H	H	CH_3	*2.75 ± 0.01*	7.64 ± 0.03	7.07 ± 0.01	7.55 ± 0.10	7.55 ± 0.10	7.55 ± 0.10	8.67 ± 0.03	$J_{5,6}$ = 7.1; $J_{6,10}$ = 0.5

[a] Chemical shifts (extrapolated to infinite dilution) are given in parts per million downfield from internal TMS. [b] Methyl proton absorptions italicized.

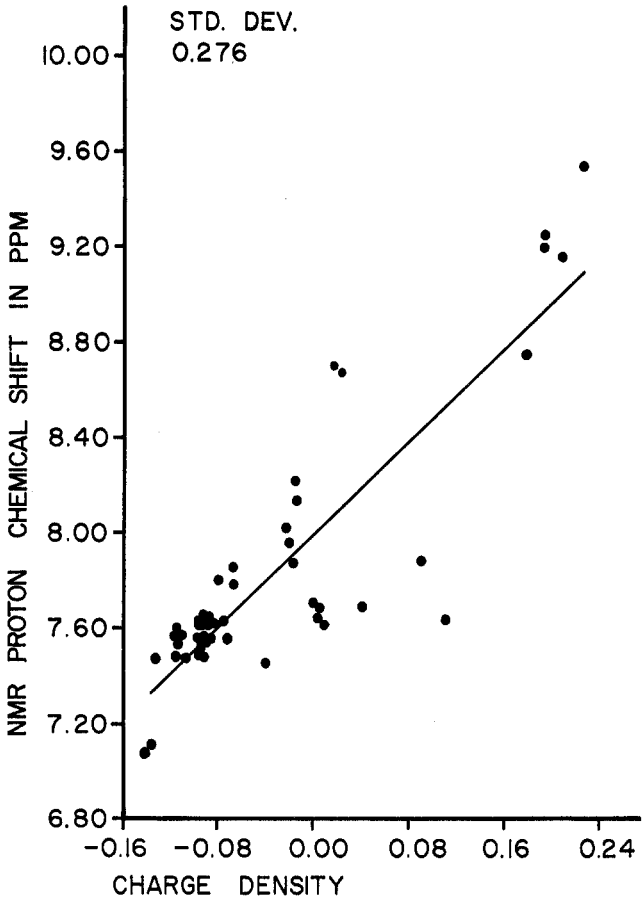


Figure 1.—Plot of proton chemical shift (extrapolated to infinite dilution) *vs.* proton environmental charge density.

from various methyl-substituted compounds and utilization of spin decoupling techniques lead to a satisfactory analysis of these spectra and provided chemical shift data sufficiently accurate for the purposes of this investigation. Assignments were confirmed by examination of the 100-MHz spectra of *s*-triazolo[4,3-*a*]quinoline and its 7-methyl and 3,9-dimethyl derivatives.

The spectra of two *s*-triazolo[3,4-*a*]isoquinolines were analyzed in a similar manner.

Chemical shifts of the methyl groups and ring protons are in accord with expectations[2] with one exception, the unusually low-field signal (8.70 ppm) for H_{10} in the isoquinoline series. Position 10 does have a low charge density (*vide infra*), but this is not low enough to explain the observed shift. Chloroform is known to hydrogen bond strongly to N_1, but specific solvent effects do not provide a suitable rationalization, since the dilution shift of H_{10} is quite similar to that of other protons in the molecule. (In the concentration range investigated, all dilution shifts were 5 Hz or less.) Ring current effects do not appear to be important, since an analogous shift is not observed for H_5 in the quinoline series where it has a similar geometrical relationship to the *s*-triazole ring. Possibly, the unusual downfield shift of H_{10} in the isoquinolines reflects the local anisotropy of the N_1–N_2 bond. Alternatively, the nonbonding electron pair on N_1 might repel the bonding electrons in C–H bond at position 10, thus producing the requisite deshielding of H_{10}.

TABLE III
ASSUMED BOND LENGTHS AND BOND ANGLES USED IN THE CALCULATIONS

Bond	Bond length, Å	Bond angles
C_{10a}–N_1 (I)	1.360	Five-membered rings, 108°
C_{10b}–N_1 (II)	1.360	Six-membered rings, 120°
N_1–N_2	1.270	
N_2–C_3	1.360	
C_3–N_4	1.390	
All other bonds	1.397	

Theoretical.—Fock-EHT (FEHT) self-consistent field (SCF) calculations were carried out according to procedures described elsewhere.[6] All input parameters were identical with those used previously for a variety of nitrogen heterocycles, including *s*-triazolo[4,3-*a*]pyridines. The specific bond lengths and bond angles used in the calculations are shown in Table III.

Results

In Figure 1 the proton environmental charge (equal to the sum of the charge densities on the hydrogen concerned and the σ and π densities on the adjacent carbon[12]) are plotted against the experimentally deter-

(12) Tables of calculated charge densities will appear following these pages in the microfilm edition of this volume of the journal. Single copies may be obtained from the Business Operations Office, Books and Journals Division, American Chemical Society, 1155 Sixteenth St., N.W., Washington, D. C. 20036, by referring to code number JOC-72-4410. Remit check or money order for $3.00 for photocopy or $2.00 for microfiche.

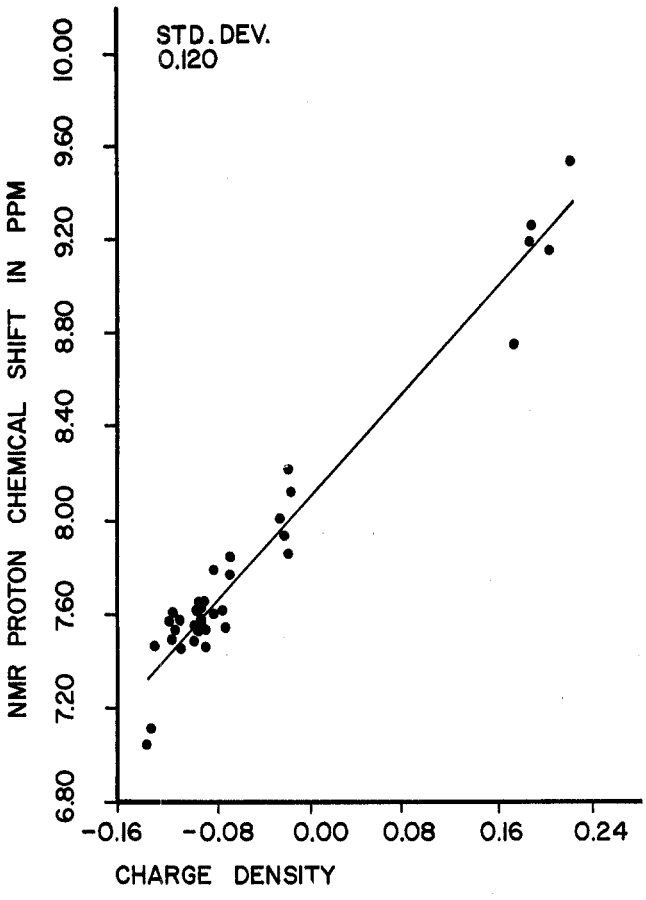


Figure 2.—Plot of proton chemical shift (at infinite dilution) *vs.* proton environmental charge density for protons in the benzenoid portions of the triazoloquinolines (S.D. = 0.120 ppm).

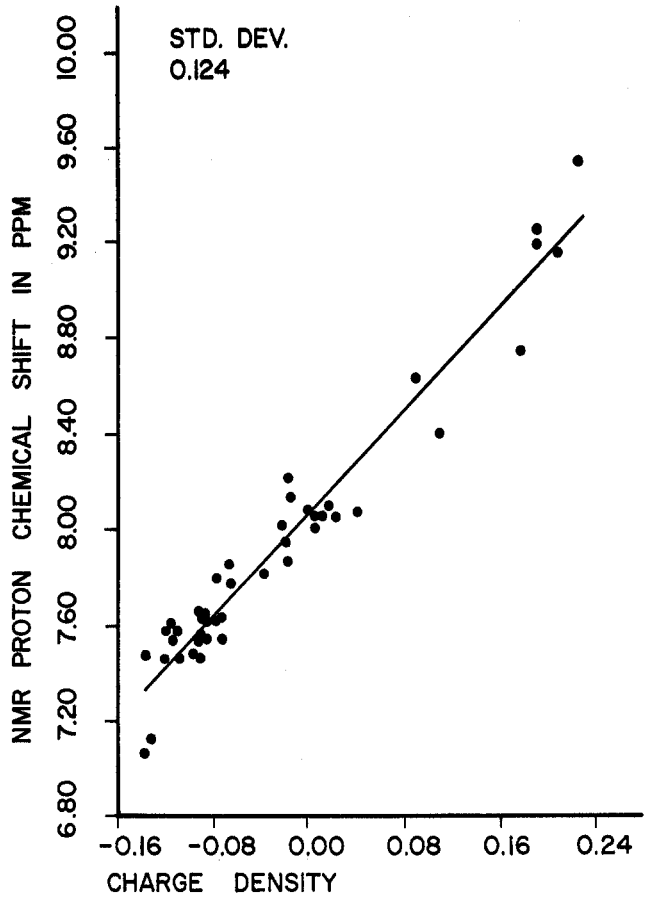


Figure 3.—Plot of corrected proton chemical shifts (at infinite dilution) *vs.* proton environmental charge density (S.D. = 0.124 ppm).

mined chemical shifts (S.D. = 0.276 ppm). The result is noticeably better than plots *vs.* proton, carbon σ, or carbon π densities alone. The empirical correlation between proton environmental charge density (PECD) and chemical shifts in the benzenoid portions of the molecules is excellent, as shown in Figure 2 (S.D. = 0.120 ppm). Application of corrections for anisotropy effects to H_{10} in all compounds and to H_5 in the iso series of 0.375 and 0.75 ppm, respectively, results in excellent empirical agreement (Figure 3, S.D. = 0.124). The resulting slope of 5.40 ppm/electron observed for these results is appreciably smaller than those observed previously (7–10 ppm/electron), but in excellent agreement with the values predicted theoretically (4–7 ppm/electron).[13,14]

The improved correlation resulting from the use of environmental charge density rather than simple π density probably is due to the polarizing effect of heteroatoms on the σ electron system in heterocycles, which is likely to produce significantly different σ densities at various sites, particularly near the heteroatoms. This is, of course, in contrast to carbocyclic systems where the carbon σ densities vary little if at all, and the variations in π density are the controlling factor.

(13) A. H. Gawer and B. P. Dailey, *J. Chem. Phys.*, **42**, 2658 (1965), and references cited therein.

(14) G. Fraenkel, R. E. Carter, A. McLachlan, and J. H. Richards, *J. Amer. Chem. Soc.*, **84**, 4623 (1960).

Conclusions

The calculated results presented here are subject to all the uncertainties and criticisms inherent in any empirical or semiempirical MO treatment. Within the empirical framework the data support two significant conclusions. First, the chemical shift of a proton attached to an aromatic system, particularly complex heteroaromatics, usefully reflects the ground state σ and π electron density at the adjacent carbon. Second, the inclusion of the carbon σ electron density changes is desirable when considering the ground state charge distribution and resulting character of heteroaromatic compounds. Finally, it is noteworthy that the charge densities calculated by the FEHT method for these compounds yield proton chemical shift correlations which fit the same empirical expressions as do correlations for olefins, carbocyclic aromatics, and simple heterocyclic aromatics using a single set of input parameters and the appropriate geometry.[15]

Experimental Section[16]

The reaction conditions described below were found to be the most satisfactory for the preparation of the various chloroquinolines. 2-Chloro-6-methylquinoline[17] and 1-chloroisoquinoline[18]

(15) C. A. Girard and S. L. Smith, unpublished observations.

(16) All evaporations were done under reduced pressure using a Rotavap apparatus. Melting points were determined in capillaries and infrared spectra were measured on a Perkin-Elmer Model 421 infrared spectrophotometer. The ultraviolet absorption data were obtained using a Beckman DK2 spectrophotometer and microanalyses were carried out by Galbraith Laboratories, Inc., Knoxville, Tenn.

(17) F. H. Hamer, *J. Chem. Soc.*, 209 (1928).

(18) B. Elpern and C. S. Hamilton, *J. Amer. Chem. Soc.*, **68**, 1436 (1946).

have been described previously and 2-chloro-4-methylquinoline was obtained commercially.

1,8-Dimethyl-2-quinoline.—Dimethyl sulfate (126.0 g) was added dropwise to 8-methylquinoline (143.0 g) with constant stirring. The reaction mixture solidified and was then heated on a steam bath for 0.5 hr. The methosulfate was dissolved in water (200 ml) and cooled to 0°, and solutions of sodium hydroxide (200 g) in water (300 ml) and potassium ferricyanide (700 g) in water (1300 ml) were added simultaneously, keeping the temperature of the mixture below 7°. The product was left overnight at room temperature and then extracted with chloroform. The chloroform extract was washed, dried (Na_2SO_4), and distilled, yielding a dark solid that, on distillation under reduced pressure, gave a light-colored oil, bp 210–215° (25 mm), that soon crystallized. It was recrystallized from benzene, forming colorless needles, yield 104.0 g, mp 96–97°.

Anal. Calcd for $C_{11}H_{11}NO$: C, 76.3; H, 6.35; N, 8.1. Found: C, 76.4; H, 6.6; N, 8.1.

2-Chloro-8-methylquinoline.—1,8-Dimethyl-2-quinolone (40.0 g) was heated under reflux with phosphorus oxychloride (40.0 g) and phosphorus pentachloride (75.0 g) for 5 hr. The excess oxychloride was removed under reduced pressure and the residue was poured into ice water. The reaction mixture was basified with potassium hydroxide solution (pH 9–10) and then thoroughly extracted with benzene. The organic layer was washed, dried (Na_2SO_4), and concentrated; the dark residue distilled under reduced pressure, bp 210–220° (20–30 mm), yielding a solid that crystallized from benzene as short, colorless needles, yield 8.0 g, mp 55–56°.

Anal. Calcd for $C_{10}H_8ClN$: C, 67.6; H, 4.5; N, 7.9. Found: C, 67.5; H, 4.7; N, 8.2.

The picrate crystallized from alcohol as yellow needles, mp 133–135°.

Anal. Calcd for $C_{16}H_{11}ClN_4O_7$: N, 13.8. Found: N, 13.85.

The procedure found most satisfactory for the preparation of the hydrazines is illustrated below. 1-Hydrazinoisoquinoline has been described previously.[19]

2-Hydrazino-6-methylquinoline.—2-Chloro-7-methylquinoline (20.0 g) was refluxed with 95% hydrazine hydrate (50 ml) in ethanol (100 ml) for 2 hr. The excess hydrazine and alcohol were removed under reduced pressure and the residue was treated with cold water, basified with sodium hydroxide solution, and extracted with ether. The ethereal extract was washed, dried (Na_2SO_4), and distilled, giving a solid residue that crystallized from benzene (charcoal) as colorless needles, yield 15.0 g (75%), mp 151° dec.

Anal. Calcd for $C_{10}H_{11}N_3$: C, 69.4; H, 6.35; N, 24.3. Found: C, 69.6; H, 6.4; N, 24.15.

In a similar fashion, 2-hydrazino-4-methylquinoline crystallized from benzene as colorless needles, yield 90%, mp 144–145°.

Anal. Calcd for $C_{10}H_{11}N_3$: C, 69.4; H, 6.35; N, 24 3. Found: C, 69.4; H, 6.5; N, 24.3.

2-Hydrazino-8-methylquinoline formed colorless needles (75%) from benzene, mp 122°.

Anal. Calcd for $C_{10}H_{11}N_3$: C, 69.4; H, 6.35; N, 24.3. Found: C, 69.7; H, 6.4; N, 24.3.

***s*-Triazolo[4,3-*a*]quinolines and *s*-Triazolo[3,4-*a*]isoquinolines.**—The general procedures used for the preparation of the compounds described in Table I are illustrated below.

7-Methyl-*s*-triazolo[4,3-*a*]quinoline.—2-Hydrazino-6-methylquinoline (2.0 g) was heated under reflux with 98% formic acid (5 ml) for 1 hr. The excess formic acid was then removed under reduced pressure and the residue was treated with ice-cold water (50 ml). Basification with sodium hydroxide, followed by extraction with chloroform, yielded a solid that, when recrystallized from benzene, separated as colorless needles, yield 2.0 g (95%), mp 192–193°.

3-Amino-7-methyl-*s*-triazolo[4,3-*a*]quinoline.—2-Hydrazino-6-methylquinoline (2.12 g) was dissolved in methanol (125 ml), and cyanogen bromide (1.3 g) was added carefully in the cold. After 3 hr of reflux, the excess methanol was removed under reduced pressure and the residue was treated with water and basified. The solid that separated was collected and washed with water. It crystallized from ethanol as fine, colorless needles, yield 2.0 g (87%), mp 245° dec.

7-Methyl-*s*-triazolo[4,3-*a*]quinoline-3-thiol.—2-Hydrazino-6-methylquinoline (5.2 g) in chloroform (150 ml) was refluxed with carbon disulfide (7.0 g) for 8 hr. Chloroform was then distilled off and the resulting product was recrystallized from methanol (charcoal) from which it separated as golden yellow needles, yield 4.5 g (70%), mp 294–296° dec.

1,7-Dimethyl-3-methylthio-*s*-triazolo[4,3-*a*]quinolinium Iodide.—7-Methyl-*s*-triazolo[4,3-*a*]quinoline-3-thiol (0.5 g) was dissolved in 10% sodium hydroxide solution (10 ml) and methyl iodide (1 ml) was added to it with vigorous shaking. The mixture was then left standing overnight when a solid separated. This was filtered, washed with water, and recrystallized from ethanol, from which it separated as colorless needles: yield 0.5 g; mp 247–248° dec; $\lambda_{max}^{CH_3OH}$ 222 nm (log 4.51), 244 sh (3.86), 252 (4.39), 296 sh (3.85), 310 (3.98), 326 (3.92), 338 sh (3.85).

Anal. Calcd for $C_{13}H_{14}IN_3S$: C, 42.0; H, 3.8; N, 11.3. Found: C, 42.1; H, 3.8; N, 11.1.

Similarly 1,9-dimethyl-3-methylthio-*s*-triazolo[4,3-*a*]quinolinium iodide was prepared from 9-methyl-*s*-triazolo[4,3-*a*]quinoline-3-thiol. It crystallized from alcohol, forming fine, colorless needles: yield 75%; mp 299–300° dec; $\lambda_{max}^{CH_3OH}$ 218 nm (log 4.78), 215 (4.41), 219 sh (4.03), 302 (4.16), 332 (4.20).

Anal. Calcd for $C_{13}H_{14}IN_3S$: C, 42.0; H, 3.8; N, 11.2. Found: C, 41.5; H, 4.3; N, 10.9.

1-Methyl-1-(4-methyl-2-quinolyl) Hydrazine.—2-Chloro-4-methylquinoline (8.0 g) was dissolved in methanol (100 ml), and methyl hydrazine (6.0 g) was added to it slowly in the cold. The mixture was then refluxed for 1 hr. The excess reagents were removed under reduced pressure and the residue (5.0 g) was poured into water. The precipitate was filtered, washed, and recrystallized from benzene–petroleum ether (bp 30–60°) from which the product separated as colorless needles, mp 53–54°. It was characterized as the picrate, which formed yellow needles from ethanol, mp 170° dec.

Anal. Calcd for $C_{17}H_{16}N_6O_7$: C, 49.0; H, 3.9. Found: C, 49.5; H, 4.2.

3-Amino-1,9-dimethyl-*s*-triazolo[4,3-*a*]quinolinium Bromide.—1-Methyl-1-(4-methyl-2-quinolyl) hydrazine (1.9 g) in methanol (20 ml) was treated with cyanogen bromide (1.1 g) in the cold and the resulting mixture was refluxed for 3 hr. Methanol was then removed under reduced pressure and the residue was recrystallized several times from alcohol, forming fine, colorless needles: mp 299–300° dec; $\lambda_{max}^{CH_3OH}$ 214 nm (log ϵ 4.47), 242 (4.13), 291 sh (3.80), 303 (3.90), 328 (3.98).

Anal. Calcd for $C_{12}H_{13}BrN_4$: C, 49.1; H, 4.4; N, 19.1. Found: C, 48.9; H, 4.6; N, 18.9.

Reaction of 8-Methyl-2-quinolylhydrazine with Acetic Acid.—The above hydrazine (3.5 g) was refluxed with acetic acid (6 ml) for 5 hr. After evaporation to dryness, water was added and the reaction mixture was neutralized. The product that separated crystallized from methanol–benzene as white flakes: mp 203–204°; ir (Nujol) main bands 3268, 1653, 1613, 1342, 1267, 1006, 848, 800, 763 cm^{-1}.

Anal. Calcd for $C_{12}H_{13}N_3O$: C, 67.0; H, 6.0; N, 19.5. Found: C, 67.2; H, 6.0; N, 19.3.

Pmr Spectra.—Samples were prepared at several concentrations in deuteriochloroform containing TMS, degassed by the freeze–thaw technique, and sealed under vacuum. Spectra were determined on a Varian HA-60-IL spectrometer operating in the frequency sweep mode (probe temperature ~25°) and were calibrated by counting peak positions directly. Reported chemical shifts were obtained by extrapolation to infinite dilution. Computer analyses of portions of the spectra were accomplished using NMRIT, NMREN,[20] and LAOCOON III.[21] Spin-decoupling experiments were performed with Hewlett-Packard audio oscillators (Models 200CD and 201CD). Calculations were carried out as described previously[6] using IBM 7040 and 360/50 computers.

Registry No.—1,8-Dimethyl-2-quinolone, 35359-35-4; 2-chloro-8-methylquinoline, 4225-85-8; 2-chloro-8-methylquinoline picrate, 35359-37-6; 2-hydrazino-6-methylquinoline, 35359-38-7; 2-hydrazino-4-methylquinoline, 21703-52-6; 2-hydrazino-8-methylquinoline, 35359-40-1; 1,7-dimethyl-3-methylthio-*s*-triazolo[4,3-*a*]-quinolinium iodide, 35359-41-2; 1,9-dimethyl-3-methylthio-*s*-triazolo[4,3-*a*]quinolinium iodide, 35356-62-8; 1-methyl-1-(4-methyl-2-quinolyl) hydrazine, 35356-63-9;

(19) CIBA Ltd., British Patent 710,047 (June 2, 1954); *Chem. Abstr.*, **49**, 7606 (1955).

(20) J. D. Swalen and C. A. Reilly, *J. Chem. Phys.*, **37**, 21 (1962).

(21) LAOCOON III is an improved version of LAOCOON II: S. Castellano and A. A. Bothner-By, *J. Chem. Phys.*, **41**, 3863 (1964).

1-methyl-1-(4-methyl-2-quinolyl) hydrazine picrate, 35356-64-0; 3-amino-1,9-dimethyl-s-triazolo[4,3-a]-quinolinium bromide, 35356-65-1; compound of mp 203–204°, 35427-27-1.

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The Mechanism of the Benzidine Rearrangement. II.[1,2] The Rearrangement of N-Acetylhydrazobenzene

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In concentrated perchloric acid–sodium perchlorate solutions, N-acetylhydrazobenzene undergoes an intramolecular rearrangement to N-acetylbenzidine. The rate of rearrangement has a first-order dependency on the Hammett acidity, H_0, and is subject to a small solvent isotope effect, $k_{H_2O}/k_{D_2O} = 1.27$. A small but reproducible substrate isotope effect is observed on the rate of rearrangement of the ring perdeuterated material, $k_H/k_D = 1.07$. On the basis of these observations it is concluded that the rearrangement is clearly a manifestation of the benzidine rearrangement, that the mechanism of rearrangement involves a single proton transfer in an equilibrium established prior to the rate-limiting process, and that both the solvent deuterium isotope effect and the substrate deuterium isotope are secondary isotope effects. Arguments are given in favor of a pathway involving a rate-limiting heterolysis of the nitrogen–nitrogen σ bond following the preequilibrium proton transfer. The electron-withdrawing, inductive effect of the N-acetyl substituent is envisaged to usurp the catalytic role of the second proton in the acid-catalyzed rearrangement of hydrazobenzene. The driving force for bond heterolysis and rearrangement is a cumulation of the repulsion between the N-acetyl group and the protonated N′-amino nitrogen, and incipient bonding of a π-complex type. The reaction of N-acetylhydrazobenzene to give benzidine (and presumably diphenyline) in dilute acid solutions probably proceeds *via* slow hydrolysis to hydrazobenzene, followed by rapid rearrangement to the observed product(s).

The research described in this series on the mechanism of the benzidine rearrangement was incepted with the intention of investigating the nature of the transient bonding forces responsible for imparting *intra*molecularity to the transformation. Accordingly, structural analogs of hydrazobenzene have been prepared and investigated with the expectation that the mode of rearrangement of these compounds will provide evidence which will aid in defining the energetics of the rate-limiting and the product-forming stages of the reactions.

The first paper in this series[1] reports evidence for the formation of N-acetyl-O,N-diphenylhydroxylamine as a transient intermediate in the reaction of N-acetyl-N-phenylhydroxylamine with diphenyliodonium hydroxide. The N-acetyl-O,N-diphenylhydroxylamine thus produced was found to undergo a spontaneous, intramolecular rearrangement to 4′-hydroxy-4-acetamidobiphenyl and traces of 2′-hydroxy-4-acetamidobiphenyl. The spontaneity of this benzidine-like rearrangement in the absence of acid catalysis was rationalized as resulting from the combination of the electron-withdrawing effect of the N-acetyl substituent with the greater electronegativity of the O-phenyl oxygen as compared to nitrogen, which together simulate the electronic characteristics of the diprotonated hydrazobenzene cation.

In this paper there is described a mechanistic study of the acid-catalyzed rearrangement of N-acetylhydrazobenzene which was carried out with the intention of examining the possibility that the N-acetyl function can act as an internal general acid catalyst in such processes generally.

Experimental Section

Melting and boiling points are uncorrected. Pmr spectra were recorded with a Varian A-60 spectrometer and ir spectra with a Perkin-Elmer 21 spectrometer.

Instrumentation.—All kinetic measurements were performed with a Zeiss PMQ-II spectrophotometer equipped with a thermostated cell compartment and cell holder. The mass spectrometer analyses were carried out on an Atlas CH-4 mass spectrometer, by recording the cracking pattern and the detail in the molecular weight region at low ionization potentials.

Materials.—The concentrated perchloric acid (70–72%) and sodium perchlorate (analytical grade) used were the commercially available materials, as were deuterium oxide, sulfuric acid-d_2 (99.6 atom % D), and benzene-d_6 (99.5 atom % D). Perchloric acid-d_1 and nitric acid-d_1 were prepared from the corresponding anhydrous sodium salts according to the procedures described for the isotopically normal materials.[4]

N-Acetylhydrazobenzene was prepared after the method of Goldschmidt and Euler. The crude product was recrystallized from chloroform, mp 162–163° (reported[5] mp 159°).

2,3,4,5,6,2′,3′,4′,5′,6′-Decadeuterio-N-acetylhydrazobenzene was prepared by the nitration of benzene-d_6 with nitric acid-d_1 and sulfuric acid-d_2 followed by reduction of the resulting nitrobenzene-d_5 (99.5 atom % deuterium content by nmr) with zinc dust in alcoholic sodium hydroxide and acylation with acetic anhydride.[5] Each step was carried out according to the usual procedures employed for the isotopically normal materials. The resulting ring perdeuterio-N-acetylhydrazobenzene, mp 162–163°, gave pmr and ir spectra which indicated a high degree of ring deuterium content.

The Acid-Catalyzed Reaction of N-Acetylhydrazobenzene in Ethanol–Water Solution.—N-Acetylhydrazobenzene, 1.00 g (4.43 mmol), dissolved in 75 ml of ethanol and 10 ml of concentrated hydrochloric acid, gave, after standing at room temperature for 24 hr, a white, crystalline precipitate. This material was collected by vacuum filtration, redissolved in water, and neu-

(1) This work was done in partial fulfillment of the requirements for the Ph.D. degree by Michael F. Dunn. First paper in this series: J. R. Cox, Jr., and M. F. Dunn, *Tetrahedron Lett.*, 985 (1963).

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(4) G. Brauer, Ed., "Handbook of Preparative Inorganic Chemistry," 2nd ed, Academic Press, New York, N. Y., 1963, pp 318, 491.

(5) S. Goldschmidt and K. Euler, *Chem. Ber.*, **55**, 616 (1922).