^{1}H, ^{13}C, and ^{15}N Nuclear Magnetic Resonance Studies on the Tautomerism of the Schiff's Bases of 3-Acetyl-6-methyl-2*H*-pyran-2,4(3*H*)-dione and 3,5-Diacetyltetrahydropyran-2,4,6-trione

By **Sau-Fun Tan, Kok-Peng Ang,* and H. L. Jayachandran,** Chemistry Department, National University of Singapore, Singapore
Alan J. Jones and William R. Begg, The National NMR Centre, The Australian National University, Canberra Australia

The ^{1}H and ^{13}C n.m.r. spectra of 3-acetyl-6-methyl-2*H*-pyran-2,4(3*H*)-dione (I) and 3,5-diacetyltetrahydropyran-2,4,6-trione (III) and their Schiff's bases were studied in $CDCl_3$ over a range of temperatures for elucidation of possible tautomerism. Whereas compound (I) appears to exist in only one form, at least two forms have been detected for compound (III). The Schiff's bases exist predominantly in keto-amine forms and the rotational barrier due to substantial double bond character of the exocyclic carbon to carbon bonds allows ready detection of rotamers. Structures of the predominant rotamers are deduced from the ^{1}H and ^{13}C spectra and the assignments of NH proton signals are based on the relative strengths of the intramolecular hydrogen-bonds. The chemical shifts of NH protons correlate linearly with the pK_a of the amine precursors. The ^{15}N spectra of some ^{15}N-enriched Schiff's bases were obtained in $CDCl_3$ and in $(CD_3)_2SO$ and the considerable downfield shifts of the ^{15}N resonances, compared with those of typical amides, are indicative of extensive electron delocalisation.

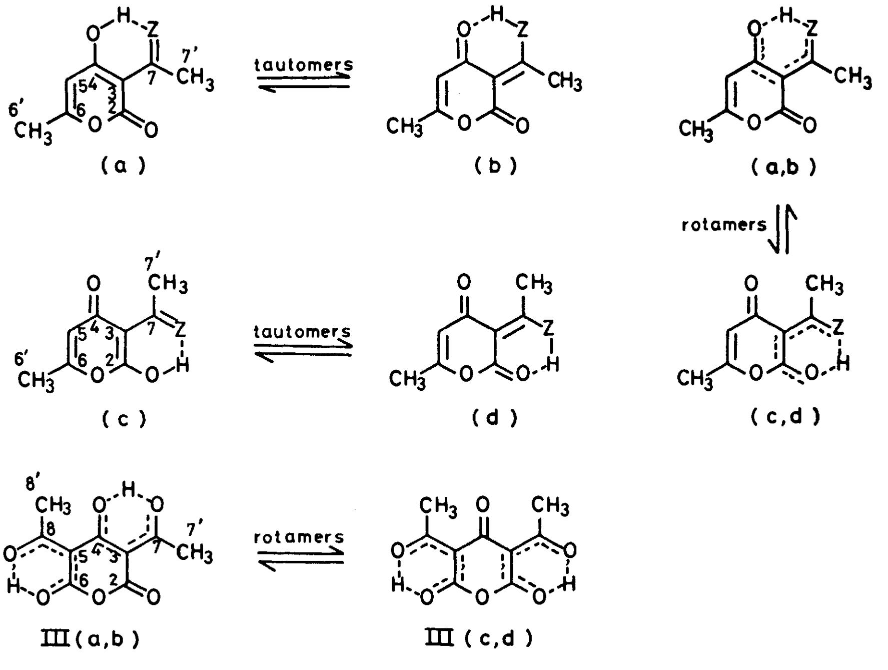
EXTENSIVE studies have been made by Forsen, Nilsson, and their co-workers[1-3] on the tautomerism of β-triketones. Using ^{1}H and ^{13}C n.m.r. spectroscopy, Yamaguchi and his co-workers[4-6] studied the tautomerism of some five-membered heterocyclic tricarbonyl compounds, namely tenuazonic acid analogues and their Schiff's bases, and demonstrated the existence of both 'internal' and 'external' tautomers. The 'external' tautomers are, in fact, rotamers.

3-Acetyl-6-methyl-2*H*-pyran-2,4(3*H*)-dione (I) and 3,5-diacetyltetrahydropyran-2,4,6-trione (III) may be regarded as six-membered heterocyclic β-tricarbonyl and β-pentacarbonyl systems. The possible existence of similar tautomers and rotamers for these compounds and their Schiff's bases has now been examined by ^{1}H, ^{13}C, and ^{15}N n.m.r. spectroscopy.

RESULTS AND DISCUSSION

^{1}H *N.m.r. Spectra of* 3-*Acetyl*-6-*methyl*-2H-*pyran*-2,4(3H)-*dione* (I) *and its Schiff's Bases* (IIA—H).—Although 3-acetyltetronic acid and its Schiff's bases have been shown to exist as mixtures of tautomeric forms,[4,5] compound (I) has been assigned a unique structure (Ia) and its Schiff's base a unique structure (IIb).[7,8] For (I), prototropic exchanges between two oxygen atoms is fast on the n.m.r. time-scale. Because of extensive electron delocalisation in the conjugated chelate ring, the tautomeric pair (Ia and b) may be described as resonance

(I) Z = O
(IIA) Z = NMe
(IIB) Z = $NCH_2C_6H_5$
(IIC) Z = NC_6H_5
(IID) Z = NC_6H_4OMe-*p*
(IIE) Z = NC_6H_4Cl-*p*
(IIF) Z = NC_6H_4Me-*p*
(IIG) Z = NC_6H_4Br-*p*
(IIH) Z = NC_6H_4COMe-*p*



hybrid (Ia,b). The resulting very strong intramolecular hydrogen-bond is evidenced by the very low-field OH resonance and the lower acidity of (I) compared with that of 4-hydroxy-6-methyl-2-pyrone (VI).[9]

The preference of the Schiff bases for the keto-amine to the enol-imine structure is confirmed by the observation of NH–R coupling in the alkyl Schiff's bases (IIA and B) and ^{15}N–H coupling in ^{15}N-enriched samples of (IIA and C). This could be partly due to the stronger NH $\cdots$ O bond relative to N $\cdots$ HO bond.[10] However, the magnitude of the coupling constant J_{NH}, in the region of 83—85 Hz, suggests that (II) may be intermediate in character between the Schiff's bases of salicylaldehyde–acetophenone and those of acetylacetone [10] and may be comparable to the Schiff's bases of 2-hydroxy-1-naphthaldehyde [11] as far as keto-amine $\rightleftharpoons$ enol-imine tautomerism is concerned.

Lowering the temperature to 223 K failed to reveal the presence of the minor rotamer (Ic,d). However, from the low-temperature spectra of the Schiff's bases, the

TABLE 1

^{1}H N.m.r. data of compound (I) and its Schiff's bases (II)

Compound	T/K	Chemical shifts (p.p.m.)				Approximate ratio of rotamers
		CH_3	NH	OH	Others	
(I)	308	2.28 (C-6) 2.62 (side chain)		16.68	6.0 (C-5)	
	223	2.30 2.65		16.72	6.0	
(IIA)	308	2.1 (C-6) 2.63 (side chain) 3.16 (N-Me) (d, J 4.75 Hz)	14.0		5.66 (C-5)	
	233	2.12 2.66 3.18	14.05 (bq) 12.0		5.68	23 : 1
(IIA) (^{15}N-enriched)	233	2.15 2.67 (d, $^3J_{NH}$ 2.5 Hz) 3.28 (dd, J 4.75, $^2J_{NH}$ 1 Hz)	14.05 (dq, J 4.75, $^1J_{NH}$ 86 Hz)		5.7	
(IIB)	308	2.06 (C-6) 2.63 (side chain)	14.55 (b)		4.63 (N-CH_2–) (d, J 5.25 Hz) 5.58 (C-5)	
(IIC)	308	2.18 (C-6) 2.60 (side chain)	15.82		5.75 (C-5) 7.30 (phenyl)	
	273	2.18 2.60	15.80 13.48		5.72 7.30	40 : 1
	233	2.18 2.60	15.80 13.48		5.72 7.30	60 : 1
(IIC) (^{15}N-enriched)	308	2.18 (C-6) 2.62 (d, J 2.25 Hz) (side chain)	15.82 (d, $^1J_{NH}$ 84 Hz)		5.78 (C-5) 7.28 (phenyl)	
	233	2.16 2.60 (d, J 2 Hz)	15.8 (d, $^1J_{NH}$ 84 Hz)		5.78 7.30	
(IID)	308	2.15 (C-6) 2.58 (side chain) 3.83 (O-Me)	15.62 13.30 (vb)		5.72 (C-5) 7.15 (aryl)	24 : 1
	233	2.16 2.58 3.85	15.62 13.38		5.75 7.10	40 : 1
(IIE)	308	2.14 (C-6) 2.58 side chain)	15.88 13.40		5.68 (C-5) 7.30 (aryl)	27 : 1
	233	2.15 2.58	15.86 13.45		5.72 7.30	43 : 1
(IIF)	308	2.14 (C-6) 2.38 2.58 (side chain)	15.74		5.72 (C-5) 7—7.4 (aryl)	
(IIG)	308	2.15 (C-6) 2.58 (side chain)	15.90 13.4 (b)		5.72 (C-5) 7—7.7 (aryl)	24 : 1
(IIH)	308	2.17 (C-6) 2.64	16.14 13.6 (b)		5.78 (C-5) 7.2—8.1 (aryl)	30 : 1

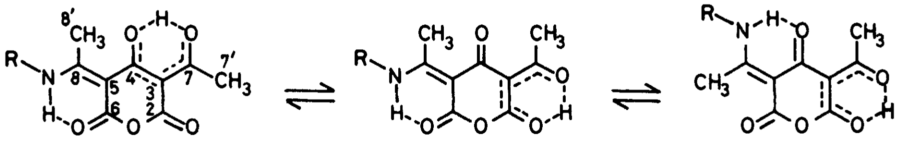
b = broad, d = doublet, sh = sharp, t = triplet, bq = broad quartet, dd = double doublet, dq = double quartet. For compounds (I), (IIA), (IIC), (IID), and (IIE), spectra obtained at intermediate temperatures do not show substantial changes in chemical shifts while tautomeric ratios of compounds (IIA—E) follow the trend indicated in the other temperature extremes.

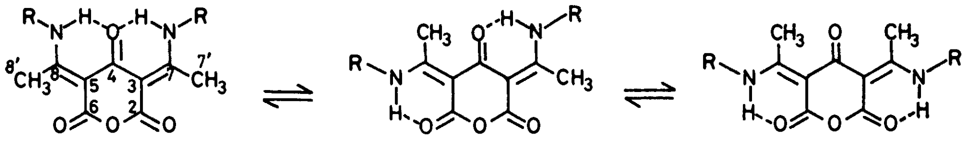
corresponding minor rotamer (IIc,d) could be detected. In addition to the main NH signal at δ 14.0—16.1, the spectrum of each of the Schiff's bases (IIA—H) shows a smaller signal at δ 12.0—13.5 which becomes progressively more distinct as the temperature is lowered (Table 1). The difference in the chemical shifts shows that the NH is chelated more strongly to a ketone carbonyl in the major rotamer (IIa,b) than to an ester carbonyl in the minor rotamer (IIc,d).[12,13]

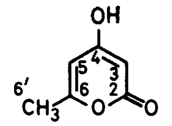
^{1}H *N.m.r. Spectra of* 3,5-*Diacetyltetrahydropyran*-2,4,6-*trione* (III), *its Mono-Schiff's Bases* (IV A—L), *and Bis-Schiff's bases* (VA—K).—Compound (III) is a strong dibasic acid.[9] Among the many theoretically possible tautomers and rotamers, only the bis-enolic forms need be considered. From an i.r. study, the α-pyrone structure (IIIa,b) is preferred in the solid state, although the presence of some γ-pyrone form (IIIc,d) in $CHCl_3$ solution cannot be excluded. Cyclic anhydride absorptions are absent both in the solid state and in the solution spectra.

The unsymmetrical structure (IIIa,b) is supported by the ^{1}H n.m.r. spectrum (Table 2) which shows two different methyl signals of equal intensity and two hydroxy-signals. The sharp enolic peak at δ 19.08 is assigned to the more strongly chelated OH at C-4 while the broader one at δ 16.05 to the more acidic [9] and more readily exchangeable OH [14] at C-6. Addition of a drop of D_2O causes the latter to disappear within 5 min while the former takes more than 15 min to vanish. The existence of a minor rotamer is detectable even in the spectrum obtained at 305 K but more clearly at lower temperatures. There are only two minor signals at δ 2.76 and 16.55, for the methyl and enolic protons respectively, compared with four main ones. The reduced number of these smaller signals suggests a symmetrical structure such as (IIIc,d) for this rotamer.

A; R = Me
B; R = $CH_2C_6H_5$
C; R = C_6H_5
D; R = C_6H_4OMe-p
E; R = C_6H_4Cl-p
F; R = C_6H_4Me-p
G; R = C_6H_4Br-p
H; R = $C_6H_4COMe-p$
J; R = $C_6H_4NO_2-p$
K; R = C_6H_4Cl-o
L; R = C_6H_4Br-o
M; R = α-naphthyl
N; R = C_6H_4OMe-o


(IVa,b) (IVc,d) (IVe,f)


(Va) (Vb) (Vc)


(VI)

The ^{1}H n.m.r. spectrum of each of the mono-Schiff's bases (IVA—L) (Table 2) shows two slightly different methyl signals, a very low-field OH signal around δ 19 and a broad NH signal around δ 12.4—13.8. The chemical shift of the enolic proton is close to the value of the lowest-field peak of the parent compound (III) and is therefore assigned to the OH at C-4. The NH proton couples strongly with α-protons in the alkyl bases (IVA and B) as well as with ^{15}N in the ^{15}N-enriched samples of (IVA and C), showing predominance of keto-amine forms. It is noted that the NH resonance is at higher field than in Schiff's bases (II). This could be explained by structure (IVa,b) where the hydrogen-bond with the carbonyl at C-6 may be expected to be weaker than that between NH and C-4 carbonyl in (IIa,b).

Lowering the temperature not only causes slight changes in chemical shifts but also reveals a weaker OH peak at δ 18.5—18.7, indicating the presence of a minor rotamer, probably (IVc,d). Although no new NH peak could be observed, the broadness and weakness of any minor NH signal may make it difficult to detect so that the possibility of other structures such as (IVe,f) could not be entirely ruled out.

The predominance of keto-amine character in the bis-Schiff's bases (VA—K) is again demonstrated by strong coupling between the NH protons and α-protons of adjacent alkyl groups in (VA and B) as well as by large ^{15}N-H coupling constants observed with ^{15}N-enriched samples of (VA and C). This predominance of the keto-amine form implies substantial double-bond character in the exocyclic carbon–carbon bonds,[15] thus increasing the barrier to rotation.[16] The separate existence of rotamers may be more readily observable than in the parent compound (III).

The ^{1}H spectrum of each bis-Schiff's base (Table 2) clearly shows three NH absorptions, a strong central one flanked unsymmetrically by two equally weak ones. The unequal intensities and uneven spacing of these three peaks preclude their origin as attributable to ^{14}N quadrupolar coupling. Using ^{15}N-enriched samples of (VA and C), each of these signals is split into a doublet. It is probable that the large signal is produced by both NH protons of a major rotamer with the symmetrical structure while the two smaller signals are produced by different NH protons of an unsymmetrical minor rotamer. If the relative strengths of intramolecular hydrogen-bonding may be used as a guide to the relative chemical shifts, then the lowest-field resonance, which is close

TABLE 2

^{1}H N.m.r. data of compound (III), its mono-Schiff's bases (IV), and bis-Schiff's bases (V)

		Chemical shifts (p.p.m.)				Approximate ratio of rotamers
Compound	T/K	CH_3	NH	OH	Others	
(III)	308	2.68				
		2.74		16.40 (b)		5.5 : 1
		2.76		19.08 (sh)		
	273	2.69		16.44		
		2.75		16.30 (b)		4 : 1
		2.78		19.20 (sh)		
	233	2.70		16.28		
		2.76		16.55		5 : 1
		2.80		19.34		
(IVA)	308	2.65				
		2.70	12.16	18.96		
		3.24 (N-Me) (d, J 5 Hz)				
(IVB)	308	2.62			4.76 (N-CH_2-)	
		2.72	12.44	18.85	(d, J 5.4 Hz)	
					7.36 (aryl)	
	223	2.62	12.46	19.15	4.72	4 : 1
		2.70		18.75	7.36	
(IVC)	308	2.64	13.66	18.95	7.35 (aryl)	
		2.66				
	233	2.68	13.65	19.20	7.40	4.5 : 1
		2.69		18.60		
(IVC)	308	2.66	13.66	19.00	7.4 (aryl)	
(^{15}N-enriched)		(d, J 3.25 Hz)	(d, $^{1}J_{NH}$ 87.5 Hz)			
	233	2.68	13.70	19.25	7.4	4.5 : 1
		(d, J 3.2 Hz)	(d, $^{1}J_{NH}$ 88.5 Hz)	18.62		
(IVD)	308	2.62	13.52	19.00 (b)	7.2	
		2.68				
		3.85				
	233	2.62	13.54	19.18	7.2	8 : 1
		2.68		18.68		
		3.85				
(IVE)	308	2.62	13.6	19.05	7.1—7.6 (aryl)	
		2.66				
(IVF)	308	2.40	13.54	18.90	7.2 (aryl)	
		2.62				
(IVG)	308	2.62	13.60	19.05	7.1—7.6 (aryl)	
		2.66				
(IVH)	308	2.64	13.80	19.15	7.3—8.1 (aryl)	
		2.68				
(IVJ)	308	2.70	14.00	19.20	7.4—8.5 (aryl)	
(IVK)	308	2.60	13.62	19.18 (b)	7.4 (aryl)	
		2.65				
	233	2.60	13.60	19.25	7.4	3 : 1
		2.68		18.52		
(IVL)	308	2.58	13.55	19.15	7.4	
		2.65				
	233	2.58	13.58	19.28	7.4	
		2.65		18.54		3.3 : 1
(VA)	308	2.63	13.20 (b)			
		3.12 (N-Me) (d, J 4.75 Hz)				
	233	2.63	13.20			2.3 : 1
		3.20 (d, J 4.8 Hz)	11.80			
			13.90			
(VA)	308	2.58	13.1 (vb)			
(^{15}N-enriched)		2.62 (d, $^{3}J_{NH}$ 2.5 Hz)	(d, $^{1}J_{NH}$ 87 Hz)			
		3.10 (N-Me) (dd, J 4.75, $^{2}J_{NH}$ 1.25 Hz)				

TABLE 2 (*continued*)

Compound	T/K	Chemical shifts (p.p.m.) CH$_3$	NH	OH	Others	Approximate ratio of rotamers
(VA) (^{15}N-enriched)	233	2.59	13.10 (d, $^1J_{NH}$ 87 Hz)			
		2.61 (d, $^3J_{NH}$ 2.5 Hz)	11.80 (d, $^1J_{NH}$ 90 Hz)			2.25 : 1
		3.12 (N-Me) (dd, J 4.8, $^2J_{NH}$ 1.5 Hz)	13.78 (d, $^1J_{NH}$ 84 Hz)			
(VB)	308	2.64	13.4 (b)		4.64 (N-CH$_2$–) (d, J 5.5 Hz) 7.30 (aryl)	
	233	2.62	13.48 (t)		4.65 (d, J 5.5 Hz)	4.0 : 1
			12.20		7.35	
			14.25			
(VC)	308	2.60	14.69		7.3	
			13.42			2 : 1
			15.64			
	233	2.56	14.78		7.3	
			13.42			3.7 : 1
			15.64			
(VC) (^{15}N-enriched)	308	2.58 (d, $^3J_{NH}$ 2 Hz)	14.68 (d, $^1J_{NH}$ 85.5 Hz)		7.3 (aryl)	
			13.42 (d, $^1J_{NH}$ 85 Hz)			2 : 1
			15.58 (d, $^1J_{NH}$ 85 Hz)			
	233	2.62 (d, $^3J_{NH}$ 2 Hz)	14.78 (d, $^1J_{NH}$ 85.5 Hz)		7.3	
			13.45 (d, $^1J_{NH}$ 87 Hz)			4.5 : 1
			15.64 (d, $^1J_{NH}$ 85.5 Hz)			
(VD)	308	2.58	14.52		7.00 (aryl)	
		3.82 (O-Me)	13.28			2.2 : 1
			15.40			
	233	2.58	14.62		7.05	3.3 : 1
		3.85	13.30			
			15.41			
(VE)	308	2.60	14.62		7.1—7.4 (aryl)	
			13.35			2.2 : 1
			15.60			
(VF)	308	2.38	14.60		7.2 (aryl)	
		2.59	13.35			2.2 : 1
			15.50			
(VG)	308	2.58	14.60		7.1—7.6 (aryl)	
			13.34			3.3 : 1
			15.60			
(VH)	308	2.62	14.80		7.8—8.1 (aryl)	
		2.66	13.60			2.7 : 1
			15.85			
(VM)	308	2.56	14.95		7.3—8.0 (naphthyl)	
			13.65			2 : 1
			15.90			
	233	2.58	15.05		7.8	
			13.65			6 : 1
			15.90			
(VN)	308	2.54	14.42		7.2 (aryl)	
		3.84	13.12			2.2 : 1
			15.31			
	233	2.55	14.46		7.2	
		3.88	13.20			6.5 : 1
			15.35			

Spectra of compounds (III), (IVA), (IVB), (IVC), (IVD), (IVK), and (IVL) obtained at intermediate temperatures show minor changes in chemical shifts and tautomeric ratios. For compounds (VA), (VB), (VC), (VD), (VM), and (VN), the spectra obtained at intermediate temperatures show changes in chemical shifts and tautomeric ratios which follow the trend indicated at the other temperature extremes.

to those found for Schiff's bases (II), may be assigned to the NH proton most strongly chelated to the C-4 carbonyl and the highest-field NH resonance, which is close to those found for Schiff's bases (IV), to the proton least strongly chelated to the C-6 carbonyl of a structure such as (Vb). The intense central NH peak of intermediate chemical shift could be attributed to the two similar NH protons of structure (Va) where they are both chelated to the C-4 carbonyl. The other symmetrical structure (Vc) is considered less probable as its NH protons may be expected to be less strongly hydrogen-bonded to carbonyls at C-2 and -6 and therefore to resonate at higher field. With a reduction in the temperature, these signals sharpen and shift slightly. Calculations based on relative intensities indicate a ratio of major : minor rotamers varying between 2 : 1 and 7 : 1 depending on the substituent group at nitrogen and the temperature. This ratio appears to increase with lowering of temperature for the aromatic bis-Schiff's bases but no similar trend can be detected for the mono-Schiff's bases. Addition of a drop of trifluoroacetic acid at 253 K causes the three NH signals to coalesce. As vinylogous amides, these Schiff's bases probably protonate at the oxygen atom,[17] reducing considerably the double-bond character of the exocyclic carbon-to-carbon bond and consequently lowering the rotational barrier between the various forms. Rapid equilibration leads to merging of the signals.

It is found that *ortho*-substituents in the aniline moiety, [(IVK and L), (VM and N)], produce no significant changes in the ratios of the rotamers. Small but inconsistent changes are observed for the NH chemical shifts. Hence it appears that steric effects due to the *ortho*-groups on the conjugated chelate ring are insignificant. This is not unexpected if the benzene ring is non-coplanar with the rest of the molecule, as is the case in benzylidene anils.[18]

TABLE 3

^{13}C chemical shifts (p.p.m.) and ^{13}C–H coupling constants[a] of the major tautomers

Carbon assignment	(I)[c]	(IIA)$_{298}$	(IIA)$_{213}$	(IIC)$_{298}$	(IIC)$_{213}$	(III)[d]$_{298}$	(III)[d]$_{213}$	(IVA)[e]$_{298}$
C-2	161.18 (s)	163.8 (b)	164.0	166.3 (w)	163.7 (s)	169.1	168.7	
C-3	99.92 (bm)	99.6 (w)	96.3	97.8 (w)	97.0 (bm)	95.8	95.4	
C-4	181.17 (5.3, 1.8)	184.6 (b)	184.4	184.95	184.8 (s)	184.0	183.5	
C-5	101.46 (172.9, 3.7)	107.5 (b)	107.4	107.2	107.2 (169)	97.7	97.1	
C-6	169.18 (6.3)	162.6 (b)	162.6	163.4	163.5 (6.0)	157.3	157.5	
C-7	205.23 (5.5)	177.0 (s)	177.0	175.4 (11.1)[b]	175.3 (bs)	203.5	204.1	
C-8						196.8	197.0	
C-6′	20.69 (120.0, 2.7)	19.8	20.1	20.3	20.9 (129)			
C-7′	29.97 (129.6)	17.8	18.4	19.9	20.2 (129)	28.0	29.0	28.0 (b)
C-8′						25.2	25.9	18.5 (w)
N-CH$_3$		30.8	31.0					31.2
Ph-*o*				129.6	129.5			
Ph-*m*				125.5	125.5			
Ph-*p*				128.1	128.1			
Ph-α				136.4	135.7			

Carbon assignment	(IVA)[e]$_{213}$	(IVC)$_{298}$	(IVC)[f]$_{213}$	(VA)$_{298}$	(VA)[g]$_{213}$	(VC)[h]$_{298}$	(VC)[h]$_{213}$	(VI)$_{296}$
C-2	165.0	165.9 (b)	165.0	162.2 (vb)	162.4	161.8	162.0 (s)	167.74 (s)
C-3	95.7	96.9 (b)	96.0	93.1	92.2	94.0	93.2 (bs)	89.26 (dd) (168, 3.6)
C-4	183.5	185.6 (vb)	184.0	186.3 (vb)	186.6	186.9	186.5 (s)	172.13 (t) (1.7)
C-5	89.0	90.8 (b)	89.9	93.1	92.2	94.0	93.3 (bs)	101.6 (dq) (170, 3.5)
C-6	160.0	159.5	159.6	162.2 (vb)	162.4	161.8 (w)	162.0 (s)	163.61 (q) (6·4)
C-7	203.2	202.7 (vb)	203.3	175.3 (b)	175.3	173.7 (11.1)[b]	173.5 (8.3) (m)	
C-8	175.1	174.1 (b)	173.7	175.3 (b)	175.3	173.7 (11.1)[b]	173.5	
C-6′								19.79 (dq) (130.0, 2.7)
C-7′	29.5	28.1 (vb)	29.5	17.9	18.5	20.6	21.2 (130.8)	
C-8′	19.1	20.8 (s)	21.4	17.9	18.5	20.6	21.2	
N-CH$_3$	31.6			30.5	30.9			
Ph-*o*		129.9	129.9			129.6	129.5	
Ph-*m*		125.9	125.7			125.8	125.6	
Ph-*p*		128.9	129.0			127.9	127.9	
Ph-α		135.5	135.1			136.6 (16.5)[b]	135.9	

[a] $^1J_{CH}$ and $^2J_{CH}$ values are in parentheses. [b] $^1J_{NC}$ in ^{15}N-enriched samples. [c] Previously determined[23] though assigned incorrectly. [d] Minor lines at 198.8, 25.7 (298 K), and 199.1, 189.0, 158.9, 97.5, and 26.1 p.p.m. (213 K). [e] No resonances observed after 77 000 pulses due to rapid equilibrium at 298 K. Only weak lines at 160 and 89 p.p.m. at 213 K. Concentration low due to lack of solubility. [f] Minor lines at 198.4, 186.7, 183.6, 175.3, 97.3, and 26.4 p.p.m. [g] Minor lines at 184.8, 175.7, 174.5, 162.0, 92.9, 30.6, and 18.3 p.p.m. [h] Minor lines at 185.0, 172.9, 165.9, 162.0, 159.0, 158.4, 136.1, 135.6, 127.8, 125.6, 94.1, 93,8, 77.3, and 21.0 p.p.m.

^{13}C *N.m.r. Spectra*.—The ^{13}C chemical shifts and some long-range coupling constant data for the compounds (I), (III) and their Schiff's bases (IIA,C), (IVA,C), and (VA,C) and for 4-hydroxy-6-methyl-2-pyrone (VI) are summarised in Table 3. Fully coupled spectra, determined at 213 K, were used to confirm some of the assignments. For example, in (IIC), the quintet at δ 163.5 (*J* 6.0 Hz) is assigned to C-6 and the doublet at δ 107.2 (*J* 169 Hz) to C-5. The resonance at δ 163.7 which lies in the range of ester carbonyls and other α-pyrone carbonyls[19] can be assigned to the lactone carbonyl at C-2, while the lowest-field signal at δ 184.8, which is close to the chemical shift of α,β-unsaturated ketones [20a] and γ-pyrone carbonyl carbons,[21] is assigned to the ketone carbonyl at C-4. Heteronuclear coupling, J_{CN}, in ^{15}N-enriched compounds helped to confirm the assignment of δ 175.3 to C-7 in (IIC) and δ 173.7 and 136.6 to C-7/8 and the phenyl α-carbon in (VC). Apart from the methyl and phenyl signals, the remaining peak at δ 97.0 in (IIC) must be assigned to C-3. This high-field shift was observed by Yamaguchi in the tetramic acid analogues and was attributed to the high electron density at the analogous site in these compounds.[6] In compounds (III) and (IV), the peak at δ 183.5 is assigned to C-4, which is deshielded by the OH group [19,22] as well as by the adjacent acetyl substituents,[20b] and is in agreement with the chemical shift of C-4 in compound (I) (δ 181.2).[23]

Evidence for tautomeric equilibria and the predominance of a specific tautomer or rotamer is readily obtained from the ^{13}C spectra, which provide complimentary information to the deductions made from the ^{1}H specta. Thus, the broad (vb) or (b), or low intensity resonance (w) (see Table 3) in the spectra of (IIA), (IVA), (IVC), and (VA) at 298 K indicate that there is rapid equilibrium on the ^{13}C n.m.r. time scale between the tautomeric populations with perhaps one major tautomer preferred. In all cases, sharp lines are observed at 213 K representing one or two tautomers and/or rotamers. Generally, as expected, the equilibria are slow for the phenyl relative to the methylamine compounds. The proposed symmetry of the structure of the major rotamer of (VA,C) is confirmed by the observation of only three pyrone ring carbon lines in a 2 : 2 : 1 ratio. The existence of distinct minor rotamers of the Schiff's bases (IVA, C) and (VA and C) is also revealed by low-intensity lines in their respective spectra at 213 K [also at 298 K for (VC)] although minor rotamers of (IIA and C) do not exhibit distinct resonances probably because of their low concentrations even at 213 K. The observation of only four or five low-intensity lines in the ^{13}C spectrum of compound (III) at 213 K is consistent with the postulate of a symmetrical minor rotamer. The assignments of the resonances of the minor rotamers is made by analogy to the major forms. Variations in T_1 relaxation times and consequent uncertainties in spectral-line intensities preclude deduction of tautomeric populations but crude estimates of minor : major ratios are 1 : 6, 1 : 4, and 1 : 4.5 for compounds (IVC), (VA), and (VC), respectively, at 213 K.

It is instructive to compare the ^{13}C chemical shifts of the compounds studied in this series. The α- and β-deshielding effects commonly associated with substituents are grossly modified by the presence of intramolecular hydrogen-bonding. Thus, in comparing compound (I) with 4-hydroxy-6-methyl-2-pyrone (VI) (Table 3) the usual α- and β-downfield shifts induced by an acetyl substituent are modified, in particular at C-2, which shifts upfield by 6.5 p.p.m. This effect must arise from a net gain of electron density at C-2 in (I) resulting from hydrogen-bonding of the OH and acetyl functions at C-4 and -3. In compounds (I), (III), and (IVA,C) the low-field shifts (δ 202—205) of the carbonyl carbon at C-7 are similar to that in *o*-hydroxyacetophenone (δ 204.4) and are clearly indicative of strong hydrogen-bonding.[24] In addition, the high electron density at C-3 (C-5) in the series of Schiff's bases (II), (IV), and (V) is indicated by the high-field shift of this carbon (δ 93—97). It is also noteworthy that the carbon atom adjacent to C-3 or C-5 (C-7 or C-8) in this series shifts only moderately in the range δ 173.7—177. In fact the minor variations in the difference in shifts between C-3 and -7 reflect the polarisability of this highly olefinic double bond. In (IIA and C) Δδ is 80.4 and 77.6 p.p.m. indicating that delocalisation of the lone pair of electrons on the nitrogen in the methyl compound is greater than in the phenyl system, as expected.[25]

^{15}N *N.m.r. Spectra*.—The ^{15}N chemical shifts of the Schiff's bases (II), (IV), and (V) may be expected to fall somewhere between those of typical amides and enamines. However, the experimental values, determined in most cases in two solvents (Table 4), show significantly greater deshielding than those of typical amides,[26a] reflecting the more extensive delocalisation of the nitrogen lone pair in these conjugated chelate systems and the greater contribution of dipolar structures. Differences in the ^{15}N chemical shifts in the phenyl- compared to the methyl substituted nitrogen, typically 22 p.p.m., result from the shielding effect of *N*-methyl and deshielding effect of *N*-phenyl groups.[26a] The J_{NH} values ranging from 83 to 91 Hz are typical of *sp*^{2}-hybridised nitrogen,[27] and similar to those for vinylogous amides.[28]

TABLE 4

^{15}N chemical shifts (in p.p.m. relative to ammonia) of Schiff's bases

Compound	In $CDCl_3$	In [$^2H_6$]DMSO [a]	$^1J_{NH}$/Hz	Tautomer ratio [b]
(IIA)	139.64		89.1	
(IIC)	162.05	160	83.3	
(IVA)	139.18	149.48	88.4	
(IVC)	160.65		91.6	
(VA)	129.90	135.25	88.5	4 : 1
	131.80	138.4	85.5	1 : 1
(VC)	153.19	154.11	85.2	5 : 1
	156.7	157.32		1 : 1

[a] Values for [$^2H_6$]DMSO titrated to pH 2; pH increase gave greater proportion of major tautomer. [b] Ratios determined for acid solution in [$^2H_6$]DMSO.

Hydrogen-bonding has been shown to produce small downfield shifts on ^{15}N resonances,[29] a trend similar to that observed for the NH proton shifts. Thus the difference of 1.8 p.p.m. in the NH proton shifts in compounds (IIC) and (IVC) may be correlated with the difference in the relative strength of the hydrogen-bond. The ^{15}N shifts of these compounds differ by only 1.4 p.p.m. However, whereas the NH proton shifts of (IIA) and (IVA) differ by 2.1 p.p.m., their ^{15}N shifts differ only by 0.5 p.p.m. Moreover, although the NH shifts for (V) are intermediate between those of (II) and (IV), the ^{15}N shift for (V) is at substantially higher field (9—10 p.p.m.). Clearly there are more influences on the ^{15}N shifts than intramolecular hydrogen-bonding and this is reflected also by the marked difference in chemical shifts observed in the two solvent systems used, in particular, in comparing the *N*-methyl [(IVA), (VA)] and *N*-phenyl [(IIC),(VC)] shifts.

TABLE 5

Chemical shifts of NH protons of the Schiff's bases and the pK_a values of the corresponding amines (R-NH_2)

Amine substituent R	Amine basicity (pK_a in water) *	Chemical shifts (p.p.m.) of the NH proton of Schiff's bases at 308 K (II)	(IV)	(V)
R = Me	10.66	14.00	12.16	13.20
R = CH_2Ph	9.34	14.55	12.44	13.40
R = Ph	4.60	15.82	13.66	14.65
R = *p*-$OMeC_6H_4$	5.31	15.62	13.52	14.52
R = *p*-ClC_6H_4	3.98	15.88	13.60	14.62
R = *p*-$CH_3C_6H_4$	5.10	15.74	13.54	14.60
R = *p*-BrC_6H_4	3.86	15.90	13.60	14.60
R = *p*-$CH_3COC_6H_4$	2.75	16.14	13.80	14.80
R = *p*-$NO_2C_6H_4$	1.02		14.00	

* A. Albert and E. P. Serjeant, 'The Determination of Ionization Constants,' Chapman and Hall, London, 1971.

In compounds (VA and C) the presence of minor rotamers is most readily demonstrated in the ^{15}N spectra and differences in the ratio of these rotamers, to favour the major form, were induced on changing the pH from acid to neutral in the case of compound (VC).

Correlation of the Chemical Shifts of NH Protons of the Schiff's Bases with pK_a *of the Amine Precursors*.—Comparisons of the chemical shifts of the NH protons among members of each of the three series of Schiff's bases (II), (IV), and (V) reveals a correlation with the basicities of the amines from which they are derived (Table 5). In the Schiff's base formed from a more strongly basic amine, the NH proton is more strongly bonded to nitrogen and therefore forms a less symmetrical and weaker hydrogen-bond with the carbonyl oxygen. This is reflected by the higher-field NH resonance signal. A linear plot of NH chemical shifts against pK_a values of the amines for each series of Schiff's bases (Figure) is obtained.

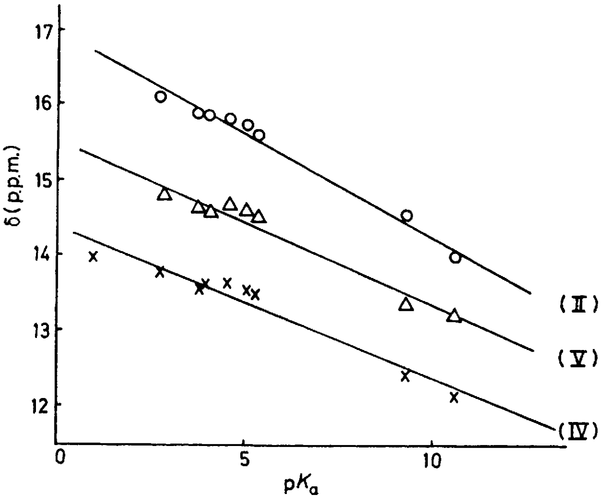


FIGURE Chemical shifts of NH protons of Schiff's bases (IIA—H), (IVA—J), and (VA—H) *versus* pK_a values of the respective amine precursors

EXPERIMENTAL

The ^1H n.m.r. spectra were obtained for $CDCl_3$ solutions at various temperatures, using a Perkin-Elmer R32 spectrometer at 90 MHz. The ^{13}C spectra were determined in $CDCl_3$ solutions at 67.89 MHz in the Fourier mode on a Bruker HFX-270 spectrometer while the ^{15}N spectra were recorded with ^{15}N-enriched samples in $CDCl_3$ or $(CD_3)_2SO$ solutions using the same instrument and according to methods described previously.[30] The ^1H and ^{13}C chemical shifts were recorded relative to tetramethylsilane as the internal reference and the ^{15}N chemical shifts relative to an external nitrate ion reference (5M-$NH_4{}^{15}NO_3$ in 2M-nitric acid–D_2O) and converted to ammonia scale by the use of the factor 375.59.[26b] I.r. spectra were recorded on a Unicam SP 1000 spectrometer.

TABLE 6

M.p.s and microanalytical data

Schiff's base	M.p. (°C)	Microanalyses (%)				
			C	H	N	Cl/Br
(IVA)	210—212	Found	53.2	5.05	6.35	
	(from benzene)	$C_{10}H_{11}NO_5$ requires	53.35	4.9	6.2	
(IVG)	205—207	Found	49.3	3.3	3.7	22.2
	(from ethanol)	$C_{15}H_{12}BrNO_5$ requires	49.2	3.3	3.85	21.85
(IVH)	236—239	Found	62.05	4.6	4.15	
	(from benzene)	$C_{17}H_{15}NO_6$ requires	62.0	4.55	4.25	
(IVL)	159—161	Found	49.2	3.55	4.15	22.0
	(from ethanol)	$C_{15}H_{12}BrNO_5$ requires	49.2	3.3	3.85	21.85
(VA)	220—222	Found	55.5	5.95	11.95	
	(from ethanol)	$C_{11}H_{14}N_2O_4$ requires	55.45	5.9	11.75	
(VE)	209—211	Found	58.35	3.7	6.4	16.55
	(from chloroform–ethanol)	$C_{21}H_{16}Cl_2N_2O_4$ requires	58.45	3.7	6.5	16.45
(VG)	210	Found	48.55	3.15	5.3	30.9
	(from chloroform–ethanol)	$C_{21}H_{16}Br_2N_2O_4$ requires	48.45	3.1	5.4	30.75
(VH)	212	Found	67.0	5.0	6.0	
	(from chloroform–ethanol)	$C_{25}H_{22}N_2O_6$ requires	67.25	4.95	6.3	
(VM)	225—227	Found	75.05	5.05	5.8	
	(from ethanol)	$C_{29}H_{22}N_2O_4$ requires	75.3	4.75	6.05	
(VN)	176—178	Found	65.6	5.4	6.6	
	(from ethanol)	$C_{23}H_{22}N_2O_6$ requires	65.4	5.2	6.6	

Materials.—Compound (I) was commercially available (Merck) and used after recrystallization from ethanol. Compound (III) and the Schiff's bases (II), (IV), and (V) were prepared and purified according to reported procedures.[31] The ^{15}N-enriched Schiff's bases were prepared on a microscale by using [^{15}N]aniline or [^{15}N]methylamine hydrochloride, supplied by BOC Limited, Prochem. The new Schiff's bases were prepared by similar methods and their m.p.s and microanalyses are given in Table 6.

[1/279 *Received*, 18*th February*, 1981]

REFERENCES

[1] S. Forsen and M. Nilsson, ' The Chemistry of the Carbonyl Group,' ed. J. Zabicky, Wiley, London, 1970, vol. 2, p. 157.

[2] S. Forsen, F. Merenyi, and M. Nilsson, *Acta Chem. Scand.*, 1967, **21**, 620.

[3] S. Forsen and M. Nilsson, *Acta Chem. Scand.*, 1959, **13**, 1383; S. Forsen, F. Merenyi, and M. Nilsson, *ibid.*, 1964, **18**, 1208.

[4] T. Yamaguchi, K. Saito, T. Tsujimoto, and H. Yuki, *J. Heterocycl. Chem.*, 1976, **13**, 533.

[5] T. Yamaguchi, K. Saito, T. Tsujimoto, and H. Yuki, *Bull. Chem. Soc. Jpn.*, 1976, **49**, 1161.

[6] K. Saito and T. Yamaguchi, *J. Chem. Soc., Perkin Trans. 2*, 1979, 1605.

[7] F. .Filira, M. Acampora, V. Giormani, M. Rothstein, and F. Dangeli, *Gazz. Chim. Ital.*, 1977, **107**, 479.

[8] P. Caramella and A. Queri, *Chim. Ind. (Milan)*, 1971, **53**, 556.

[9] K. P. Ang and S. F. Tan, *J. Chem. Soc., Perkin Trans. 2*, 1979, 1525.

[10] N. M. D. Brown and D. C. Nonhebel, *Tetrahedron*, 1968, **24**, 5655.

[11] (*a*) G. O. Dudek and R. H. Holm, *J. Am. Chem. Soc.*, 1961, **83**, 3914; (*b*) G. O. Dudek, *ibid.*, 1963, **85**, 694.

[12] C. H. McMullen and C. J. M. Stirling, *J. Chem. Soc. B*, 1966, 1217.

[13] (*a*) R. W. Hey and P. P. Williams, *J. Chem. Soc.*, 1964, 2270; (*b*) A. L. Porte, H. S. Gutowsky, and I. Moyer Hunsberger, *J. Am. Chem. Soc.*, 1960, **82**, 5057.

[14] D. C. Nonhebel, *Tetrahedron*, 1968, **24**, 1869.

[15] G. O. Dudek and G. P. Volpp, *J. Am. Chem. Soc.*, 1963, **85**, 2697.

[16] L. M. Jackman in ' Dynamic Nuclear Magnetic Resonance Spectroscopy,' eds. L. M. Jackman and F. A. Cotton, Academic Press, London, 1975, pp. 218—226.

[17] J. V. Greenhill, *Chem. Soc. Rev.*, 1977, 77, and references therein.

[18] L. E. Khoo, *Spectrochim. Acta*, 1979, **35A**, 993.

[19] W. V. Turner and W. H. Pirkle, *J. Org. Chem.*, 1974, **39**, 1935.

[20] G. C. Levy and G. L. Nelson, ' Carbon-13 NMR for Organic Chemists,' Wiley, New York, 1972, (*a*) p. 114; (*b*) p. 67.

[21] I. W. J. Still, N. Plavac, D. M. McKinnon, and M. S. Chauhan, *Can. J. Chem.*, 1976, **54**, 280.

[22] C. A. Kingsbury, M. Cliffton, and J. H. Looker, *J. Org. Chem.*, 1976, **41**, 2777.

[23] J. P. Jacobsen, T. Reffstrup, and P. M. Boll, *Acta Chem, Scand.*, 1977, **B31**, 761.

[24] J. B. Stothers and P. C. Lauterbur, *Can. J. Chem.*, 1964, **42**, 1563.

[25] W. Schwotzer and W. V. Philipsborn, *Helv. Chim. Acta*, 1977, **60**, 1501.

[26] G. C. Levy and R. L. Lichter, ' Nitrogen-15 NMR Spectroscopy,' Wiley, New York, 1979, (*a*) pp. 59—62; (*b*) p. 32.

[27] G. Binsch, J. B. Lambert, B. W. Roberts, and J. D. Roberts, *J. Chem. Soc.*, 1964, **86**, 5564.

[28] G. O. Dudek and E. P. Dudek, *J. Am. Chem. Soc.*, 1966, **88**, 2407.

[29] L. Paolillo and E. D. Becker, *Org. Magn. Reson.*, 1970, **2**, 168.

[30] A. J. Jones, H. McNab, and P. Hanisch, *Aust. J. Chem.*, 1978, **31**, 1005.

[31] A. K. Kiang, S. F. Tan, and W. S. Wong, *J. Chem. Soc. C*, 1971, 2721.