Reference Data

^1H and ^{13}C NMR Studies of some *O*-Carbamoyloximes

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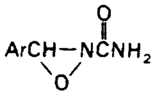
The ^1H and ^{13}C NMR spectra were assigned for a series of *O*-carbamoyloximes of *ortho*- and *para*-substituted benzaldehyde. These compounds exist exclusively in the *E* configuration. The aromatic protons and carbons show correlations with the appropriate substituent-induced shifts and with Hammett parameters.

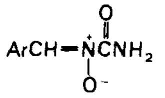
KEY WORDS O-Carbamoyloximes ^1H and ^{13}C NMR Hammett parameters

INTRODUCTION

At the beginning of the century, it was reported[1] that an aqueous suspension of an aromatic aldehyde, on treatment with hydroxylamine hydrochloride and potassium cyanate, afforded a compound of molecular formula $ArC_2H_3N_2O_2$, which was believed to have an oxaziridine structure (I):

$$ArCHO + NH_2OH \cdot HCl + KNCO \rightarrow ArC_2H_3N_2O_2$$


I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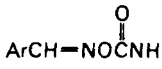
III

The structure class was later modified[2] to that of a nitrone (II), but was recently proved[3,4] by x-ray crystal analysis to have an alternative structure (III), an *O*-carbamoyloxime possessing the *E* configuration. We have synthesized several *ortho*- and *para*-substituted benzaldehyde *O*-carbamoyloximes and studied their ^1H and ^{13}C NMR spectra in order to investigate the correlations of chemical shifts with Hammett σ values and with substituent-induced chemical shifts. Closely related studies on other $XC_6H_4C{=}N$ systems have been reported.[5]

EXPERIMENTAL

The *O*-carbamoyloximes were prepared following the literature procedure.[1] In a typical run, a mixture of hydroxylamine hydrochloride (25 mmol), potassium cyanate (29 mmol) and aldehyde (15 mmol) in water (5 ml) was stirred at 0 °C for 4 h. The proton NMR spectrum of the crude products always revealed the presence of *O*-carbamoyloxime and (*E*)-oxime (approximate ratio 60:40), together with some unreacted aldehyde. The *O*-carbamoyloxime was obtained as white needles after crystallization from ethanol. Several other experimental conditions failed to synthesize the elusive nitrone (II).

p-Hydroxybenzaldehyde *O*-carbamoyloxime, m.p. 155–156 °C (decomp.) (Found: C, 53.65; H, 4.63; N, 15.41. $C_8H_8N_2O_3$ requires C, 53.33; H, 4.47; N, 15.55%).

o-Chlorobenzaldehyde *O*-carbamoyloxime, m.p. 121–122 °C (Found: C, 48.08; H, 3.69; N, 14.33. $C_8H_7N_2O_2Cl$ requires C, 48.38; H, 3.55; N, 14.11%).

The following melting points were obtained: benzaldehyde *O*-carbamoyloxime, 124–125 °C (lit.[1] m.p. 124 °C); *p*-dimethylaminobenzaldehyde *O*-carbamoyloxime, 167–167.5 °C (decomp.) (lit.[1] m.p. 164–165 °C); *p*-methylbenzaldehyde *O*-carbamoyloxime, 143–144 °C (lit.[1] m.p. 142 °C); *p*-methoxybenzaldehyde *O*-carbamoyloxime, 128–129 °C (lit.[1] m.p. 133 °C); *p*-nitrobenzaldehyde *O*-carbamoyloxime, 168–170 °C (lit.[1] m.p. 160 °C); and *o*-hydroxybenzaldehyde *O*-carbamoyloxime, 101–102 °C (lit.[1] m.p. 102–105 °C).

All spectra were recorded at 80.13 MHz (^1H) and at 20.15 MHz (^{13}C) on a Bruker AC 80 Fourier transform NMR spectrometer at the ambient probe temperature (*ca.* 35 °C). The compounds were studied as 5–10 mol-% solutions in $CDCl_3$, acetone-d_6 and DMSO-d_6 with internal TMS as reference. The ^{13}C acquisition parameters were as follows: spectral width, 5000 Hz; data points, 16K; pulse width, 2 μs (90° = 4.7 μs); number of transients, 5000. Spectra for some of the highly polar compounds were not recorded in deuteriochloroform owing to their low solubility.

RESULTS AND DISCUSSION

The proton chemical shifts are given in Table 1, and spectra indicate the presence of only one isomer in all the compounds studied. An x-ray study[5] of *p*-bromobenzaldehyde *O*-carbamoyloxime showed it to be in the *E* configuration, and this is assumed to be the case in the present compounds.

Table 2 shows the correlations observed for the chemical shifts of H-α with Hammett σ_{para},[7] H-2,6 with Z_{meta}[8] and H-3,5 with Z_{ortho}[8] of the *para* substituents. The largest deviation is noted for the 4-nitro compound. From the linear relationships it is possible to derive the substituent-induced shifts for the *O*-carbamoyloxime group ($NH_2COON{=}CH{-}$) as +0.75 (Z_{ortho}) and +0.05 (Z_{meta}).

The H-α resonances in *O*-carbamoyloximes are 0.3–0.4 ppm to lower field than those in the corresponding oximes[3] owing to the electron-withdrawing property of the $CONH_2$ group. The H-α resonances in the *Z* isomers of oximes are in the range 7.3–7.6 ppm, whereas those of all the compounds studied here are in the range 8.2–8.8 ppm; this confirms our compounds are in the *E* configuration. We were unable to detect any *Z* isomer in the *O*-carbamoyloximes.

The chemical shift of H-α is sensitive to the substituent, the geometry around the C=N bond and the solvent.[8] When the solvent is changed from $CDCl_3$ to DMSO-d_6, the H-α proton signal moves downfield by about 0.3 ppm compared with the ring proton signals, owing to the anisotropy of the S—O bond. The phenolic proton in **7** absorbs at 10.20 ppm (similarly to **4**), indicating only weak or no hydrogen bonding between the OH and the imine nitrogen. This is to be expected as the sp^2-hybridized nitrogens are poor electron-pair donors.

Carbon spectra

Assignment of the ^{13}C NMR signals (Table 3) was achieved by the usual methods for multiplicity under off-resonance conditions (and using DEPT in few cases) and using known substituent-induced chemical shifts (SCS). Some assignments were assisted by SFORD spectra. The SCS of the aromatic carbons due to the *O*-carbamoyloxime substituent are *ipso* +1.5, *ortho* −0.4, *meta* +0.5 and *para* +3.2; the corresponding SCS for the oxime are +1.3, −1.5, +0.2 and +1.4, respectively. This shows that the lone pair on the oxygen is less involved in the ring in the compounds under study compared with the corresponding oximes owing to the presence of the $CONH_2$ group.

Table 2 also shows that good correlations are observed for the chemical shifts of C-4 with Z_{ipso} (SCS at the *ipso* carbon of the 4-substituent), C-1 and C-α with σ_{para} of the 4-substituents. The C=N carbon chemical shift in *para*-substituted *C*-phenylimines has been shown[5] to correlate well with the inductive/field parameter, σ_I, but only poorly with

Table 1. ^1H NMR chemical shifts of $RC_6H_4\overset{\alpha}{C}H{=}NO\overset{\overset{O}{\|}}{C}NH_2$

Compound	R	H-α	H-2,6	H-3,5	NH_2	Other	Solvent
1	H	8.37	7.62	7.35–7.55[a]	5.98	—	$CDCl_3$
		8.48	7.92	7.33–7.55[a]	6.70	—	Acetone-d_6
		8.58	7.86	7.33–7.65[a]	7.15		DMSO-d_6
2	4-CH_3	8.30	7.55	7.25	6.15	2.40(CH_3)	$CDCl_3$
		8.42	7.68	7.28	6.60	2.36(CH_3)	Acetone-d_6
		8.58	7.78	7.36	7.35	2.41(CH_3)	DMSO-d_6
3	4-OCH_3	8.25	7.60	6.92	6.15	3.82(OCH_3)	$CDCl_3$
		8.40	7.75	7.05	6.60	3.87(OCH_3)	Acetone-d_6
		8.55	7.82	7.08	7.25	3.84(OCH_3)	DMSO-d_6
4	4-OH	8.35	7.65	6.93	6.70	9.00(OH)	Acetone-d_6
		8.48	7.72	6.95	7.20	10.12(OH)	DMSO-d_6
5	4-NMe_2	8.42	7.75	6.92	6.58	3.22(NMe_2)	Acetone-d_6
		8.40	7.68	6.72	7.08	3.05(NMe_2)	DMSO-d_6
6	4-NO_2	8.78	8.38	8.18	7.30	—	DMSO-d_6
7	2-OH	8.72	7.88[b]	6.70–7.50[a]	7.15	10.20(OH)	DMSO-d_6
		8.75	7.88[b]	7.15–7.48[a]	6.05	—	$CDCl_3$
8	2-Cl	8.75	8.08[b]	7.35–7.65	6.60	—	Acetone-d_6
		8.78	8.18[b]	7.42–7.68[a]	7.25	—	DMSO-d_6

[a] H-3,4,5.
[b] H-6.

Table 2. Correlation of chemical shifts with substituent parameters[a]

Nucleus	Parameter	*a*	*b*	*r*
H-α	σ_{para}	8.59	0.256	0.985
H-2,6	Z_{meta}	8.00	1.05	0.920
H-3,5	Z_{ortho}	7.30	0.95	0.986
C-α	σ_{para}	152.8	−2.24	0.965
C-1	σ_{para}	128.7	18.7	0.990
C-2,6	Z_{meta}	128.5	1.93	0.878
C-3,5	Z_{ortho}	130.6	1.13	0.981
C-4	Z_{ipso}	133.5	0.924	0.985

[a] *a* and *b* are the coefficients of the equation $\delta = a + b\sigma$ and $\delta = a + bZ_i$; *r* = correlation coefficient.

Table 3. ^{13}C NMR chemical shifts of $RC_6H_4\overset{\alpha}{C}H{=}NO\overset{\overset{O}{\|}}{C}NH_2$

R	C-α	CO	C-1	C-2	C-3	C-4	C-5	C-6	Other	Solvent
H	153.9	156.3	130.0	128.1	129.1	131.7	128.1	129.0	—	$CDCl_3$
	154.1	156.4	132.1	129.0	129.7	132.3	129.0	129.7	—	Acetone-d_6
	153.3	155.3	130.6	128.0	128.8	131.2	128.0	128.8	—	DMSO-d_6
4-CH_3	153.8	156.5	127.0	128.1	129.8	142.4	129.8	128.1	21.6(Me)	$CDCl_3$
	154.0	156.4	127.3	129.0	130.4	142.5	130.4	129.0	21.5(Me)	Acetone-d_6
	153.0	155.2	126.2	127.9	129.3	141.1	129.3	127.9	21.9(Me)	DMSO-d_6
4-OCH_3	153.5	156.8	122.5	129.9	114.6	162.6	114.6	129.9	55.5(OMe)	$CDCl_3$
	152.8	155.5	122.8	129.7	114.3	161.7	114.3	129.7	55.2(OMe)	DMSO-d_6
4-OH	153.8	157.0	123.1	130.9	116.8	161.4	116.8	130.9	—	Acetone-d_6
	152.9	155.5	121.2	129.8	115.6	160.2	115.6	129.8	—	DMSO-d_6
4-NMe_2	154.1	156.8	118.8	130.9	113.1	153.0	113.1	130.9	40.8(NMe_2)	Acetone-d_6
	153.1	155.6	117.0	129.6	111.5	152.1	111.5	129.6	40.4(NMe_2)	DMSO-d_6
4-NO_2	150.1	153.7	143.4	131.2	127.7	151.5	127.7	131.2	—	DMSO-d_6
2-OH	153.0	154.6	118.2	158.4	117.4	133.3	120.5	131.4	—	Acetone-d_6
	151.8	154.1	122.1	160.0	119.9	134.2	123.1	132.0	—	DMSO-d_6
2-Cl	151.1	156.0	128.1	135.2	128.1	132.6	127.2	130.7	—	$CDCl_3$
	150.6	155.5	127.5	135.5	129.1	133.5	128.4	131.0	—	Acetone-d_6
	148.0	152.8	130.2	132.1	128.7	130.9	127.3	129.6	—	DMSO-d_6

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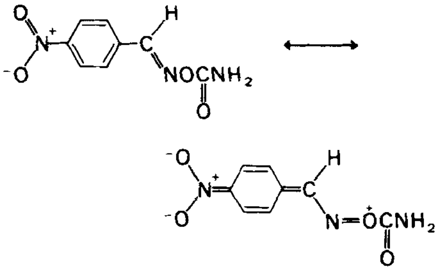
σ_{para}. A poor correlation exists for C-2,6 with Z_{meta}. In addition to the electronic effects, these carbons are presumably being affected by their proximity to the bulky carbamoyloxime group. Of the five *para*-substituents, the NO_2 group seems to exhibit the largest differences in electronic distribution compared with the other four groups, which are all electron releasing. This may be due to a strong contribution from the following resonance structures when a nitro group is present:



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^{13}C NMR Spectra of Some 4-Substituted *N*-Acetonyl-*N*,*N*-dimethyl-*N*-phenacylammonium Bromides

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The ^{13}C NMR signals for some 4-substituted *N*-acetonyl-*N*,*N*-dimethyl-*N*-phenacylammonium bromides were assigned. The HETERCOSY and COLOC sequences allow an unambiguous distinction between the very similar signals of the methylene carbons. The chemical shifts observed for the aromatic ring carbons are in close agreement with those calculated from substituent increments.

KEY WORDS ^1H NMR ^{13}C NMR COLOC sequence Substituent effects Quaternary ammonium bromides

INTRODUCTION

The title compounds, $[XC_6H_4COCH_2N(CH_3)_2CH_2COCH_3]^+Br^-$, are very useful intermediates in the synthesis of piperidinium[1] and pyridostigmine derivatives,[2] bearing an aryl substituent at the 3-position of the heterocyclic ring. However, the fast hydrogen–deuterium exchange in both methylenic groups for these water-soluble compounds hinders their identification through the corresponding ^1H NMR spectra. The chemical shift assignments for the two methylenic carbons are also not straightforward owing to their similar environment. Therefore, the present work aims at the full characterization of these quaternary ammonium salts by their IR, ^1H and ^{13}C NMR spectra.

RESULTS AND DISCUSSION

Table 1 lists the ^1H NMR chemical shifts and the carbonyl stretching frequencies for the 4-substituted *N*-acetonyl-*N*,*N*-dimethyl-*N*-phenacylammonium bromides **2**–**6**, and the parent compound **1**.

The ^{13}C NMR chemical shifts are shown in Table 2. The signals of the aromatic carbons were assigned by single-frequency off-resonance decoupling (SFORD) and known chemical shift rules.[5] The substituent chemical shifts were taken from Ewing's tabulation[6] and, for the $[COCH_2N(CH_3)_2CH_2COCH_3]^+$ group, estimated from the chemical shifts of the unsubstituted ammonium bromide **1**. The close agreement between the two sets indicates the correctness of the assignments.

In a COLOC sequence experiment,[7] a cross-peak correlates the downfield methylene carbon signal at 68.3 ppm with the terminal methyl proton signal at 2.32 ppm for the *p*-NO_2-substituted derivative **6**. This unambiguously assigns the methylene carbon of the acetonyl residue. The chemical shifts were fully assigned through a classical HETERCOSY experiment, performed for compound **6**, which correlates proton and ^{13}C chemical shifts via $^1J(CH)$ couplings.

EXPERIMENTAL

Materials

The 4-substituted quaternary ammonium salts were prepared by a previously reported procedure[1] from *N*,*N*-dimethylaminoacetone[4] and the corresponding 4-substituted phenacyl bromide.[3] The physical data are shown in Table 3.

Spectra

The ^{13}C NMR spectra of 0.5 M solutions in $CDCl_3$ (or DMSO) with 5% tetramethylsilane as an internal reference, in 12

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