Stable Quinonoid Nitronates. A Structure Investigation of Ethyl 2-Nitrophenylpyruvate Anions based on Nuclear Magnetic Resonance Spectroscopy and MO-SCF-HAM/3 Calculations

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Ethyl 2-nitrophenylpyruvate anions have o-quinonoid nitronate structures while their corresponding acids are aromatic α-enol and/or α-keto esters. A semiempirical quantum chemical study of the different tautomers of these systems using HAM/3 has suggested a non-planar ring conformation of the nitronic acids and the nitronates. The presence of a hydrogen bond between 6-H and its neighbouring carbonyl oxygen in the title compound is inferred by an unusually low field proton resonance.

The existence of aromatic *aci*-nitro compounds, *i.e.* o-quinonoid nitronic acids and nitronates such as (1) and (2), has been recognized for a long time. Indirect evidence for their occurrence is presented throughout the literature, although, with one exception,[1] no characterizations of stable species have been reported. However, the closely related Meisenheimer complexes as well as the aliphatic nitronic acids and nitronates have been thoroughly investigated in terms of physical data and chemical reactivity.[2,3]

Recently, we suggested nitronates as transients in a new indole synthesis,[4] which is believed to be related mechanistically to other recent synthetic methods.[5-7] Out of these crucial transients, which are derivatives of (2) and (3), the potassium salt of the latter was described by Wislicenus and Thoma in 1924.[8] These authors considered the nitronate form as a

possible alternative to the enolate structure (4). From this salt, two tautomeric forms of the corresponding acid were isolated. They were assigned the enol (5) and the keto (6) structure respectively while the nitronic acid structure (7) was considered to be impossible.

In order to elucidate the alternatives (3) *versus* (4) and (5) *versus* (7) [the keto ester (6) was easily distinguished from (5) and (7)] we have now made an n.m.r. study of these compounds and some derivatives thereof. Unfortunately, we had to refrain from using X-ray diffraction in the structure elucidation due to instability of compound (5)—(7) and difficulties in obtaining suitable crystals of the salt (3)—(4). This was to a certain extent compensated for by a series of semiempirical MO-SCF-HAM/3 calculations where the geometries were optimized from the electronic spectra.


(1)   (2)   (3)   (3a)

(4)   (5)   (6)   (7)

δ 8·08   (8)   (9)   (10)   (11)

(12)   (13)   (14)
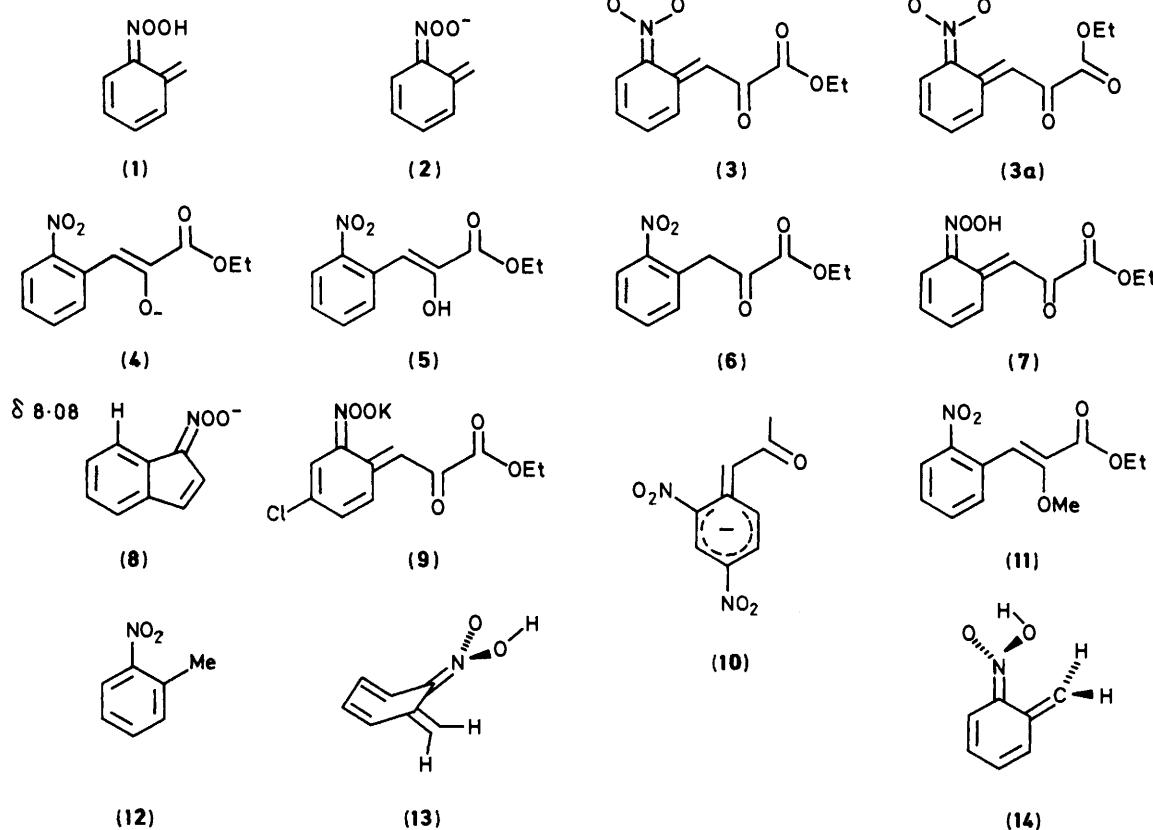
Table 1. ^{13}C N.m.r. data of compounds (3), (3a),* (5), (6), and (11). Chemical shifts in p.p.m. *versus* Me_4Si

Compound	CH_3-C	CH_2-O	Vinyl/CH_2	C-1	C-2	C-3	C-4	C-5	C-6	Keto/enol	Ester
(3)	14.9	59.5	79.3	138.4	141.0	124.4	118.8	131.8	127.4	169.1	164.1
(3a)	14.4	59.8	87.9	138.3	141.5	124.5	118.8	131.9	127.6	169.4	163.8
(5)	14.1	63.2	103.7	141.7	148.4	124.4	128.1	132.6	131.7	128.4	165.6
(6)	3.9	62.9	44.4	†	148.2	125.4	129.0	134.0	133.8	189.5	160.5
(11)	14.3	59.7	117.1	147.6	148.4	124.5	128.9	132.8	131.7	128.2	163.4

* Unknown tautomer of (3). † Resonance not observed.

Table 2. ^1H N.m.r. data of compounds (3), (3a), (5), (6), (9), and (11). Chemical shifts relating to Me_4Si, coupling constants J in Hz

| Compound	CH_3C	CH_2O	Vinyl/CH_2	3-H	4-H	5-H	6-H	OH	$J_{3,4}$	$J_{3,5}$	$J_{4,5}$	$J_{4,6}$	$J_{5,6}$	J_{Et}
(3)	1.25	4.11	6.52	7.72	6.70	7.25	9.40		8.3	1.3	7.0	1.3	8.5	7.1
(3a)	1.23	4.08	8.32	7.68	6.65	7.03	9.38		8.4	1.3	7.0	1.3	8.4	7.1
(5)	1.40	4.39	6.91	8.24	7.38	7.60	7.91	6.7	7.9	1.4	6.6	1.4	8.1	7.1
(6)	1.37	4.33	4.50	8.12	7.15—7.65				7.0	2.8				
(9)	1.22	4.00	6.54	7.76	7.22		9.45			3.0			9.0	7.0
(11)	1.42	4.33	7.25	7.9	7.35—7.75									

Results and Discussion

The ^{13}C n.m.r. spectrum of (3)—(4) is quite conclusive as it displays two distinct resonances at δ 169.1 and 164.1 p.p.m. The other signals are also fully compatible with structure (3) (Table 1). Upon standing in [$^2H_6$]dimethyl sulphoxide for one week, compound (3) isomerizes into what is probably a rotamer of (3), (3a). The electronic spectrum, i.r., ^1H and ^{13}C n.m.r. spectra of (3a) are almost identical with those of (3) with the exception that the vinylic resonances (C and H) are shifted towards lower fields by 8.6 and 1.8 p.p.m., respectively. A probable structural change that would retain all spectral properties except for the above mentioned down-field shifts is a rotation of the ethoxycarbonyl group which would alter the carbonyl anisotropy effect on the vinylic position.

The ^1H n.m.r. spectrum of (3) exhibits a ring proton resonance at δ 9.40. At first, this was assumed to be due to an *ortho*-effect from the nitronate group by analogy with that reported for compound (8).[9] However, the spectrum of the corresponding 4-chloro-derivative (9) revealed the resonance to be attributable to the proton adjacent to the pyruvate group (Table 2). In a study of the Zimmerman reaction,[10] Kimura *et al.* isolated compound (10) for which a similar chemical shift was observed (δ 9.34 p.p.m.).[1] Of the three possible phenomena responsible for this shift, namely electron withdrawal through the π-system, anisotropy, or hydrogen bonding, the first can be ruled out by the following arguments. Electron-withdrawing groups on an aromatic nucleus are unlikely to produce down-field shifts beyond that of 2,4,6-trinitrobenzaldehyde (δ 9.18 p.p.m.).[11] Furthermore, the removal of a proton (*i.e.* formation of the anion) generally causes a shift towards higher field due to the increase in electron density throughout the entire molecule.

It was also noted that 6-H of (3) resonates at a lower field than that of (10) even though the latter has an additional nitro group present. Concerning the anisotropy effect it was noted that the other ring protons of (3) are not shifted in the same fashion as 6-H. Therefore, if an anisotropy effect were to operate, it would most certainly originate from the pyruvate moiety and thus also affect C-6. However, such an effect is not observed in the ^{13}C n.m.r. spectrum of (3) and we therefore conclude that the down-field shift is caused by a moderately strong C-H-O hydrogen bond between 6-H and its neighbouring carbonyl oxygen [see (15)].

Interestingly, this phenomenon seems to be quite common, *e.g.* when ethyl 2-nitrophenylacetate is treated with potassium ethoxide in dimethyl sulphoxide this compound displays a ^1H
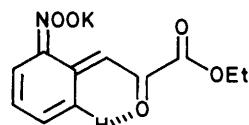
(15)
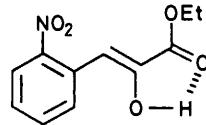
(16)

n.m.r. spectrum similar to that of (3) with the 6-H resonance as a double doublet at δ 8.57.

The n.m.r. spectra of compound (5)—(7) [obtained upon protonation of (3) at −78 °C with HCl–ether] differed from those of (3) in two major respects. In the ^1H n.m.r. spectrum, 6-H (δ 9.40) was shifted to higher field (δ 7.91) which is interpreted as a loss of hydrogen bonding and in the ^{13}C n.m.r. spectra, a higher field shift of the keto carbonyl was observed (δ 169.1—128.4 p.p.m.). This latter result clearly indicates the protonation of the keto function to form the enol, *i.e.* formation of (5).

In dimethyl sulphoxide, (5) equilibrates into *ca.* 44% of (6) and addition of potassium acetate to the solution of the two tautomers gives quantitatively (3) (as measured by ^1H n.m.r.). This indicates that (5) has a pK_a considerably below that of acetic acid (4.76). Such an acidity is characteristic of quinonoid nitronic acids[12] but unreasonably low for the proposed enol structure (5). In order to resolve this apparent contradiction, (3) was methylated with dimethyl sulphate in dimethyl sulphoxide giving compound (11) in good yield. Methylation of (5) with diazomethane in ether gave the same product in a less clean reaction. The n.m.r. spectra of (11) were practically identical with those of (5) and conclusive evidence for the structure of (11) was obtained from its mass spectrum which was compared with known fragmentation and rearrangement patterns of similar compounds[13] such as derivatives of 2-nitrocinnamic acid. Carbonyl i.r. bands of (5) and (11) differed by 25 cm^{-1} which is believed to be due to the loss of hydrogen bonding to the ester carbonyl in (11).

In spite of the very high acidity of (5) we feel that these results strongly suggest (5), rather than the nitronic acid (7), as the true structure of the isolated unstable acidic tautomer.

MO-SCF Calculations.—The program used, HAM/3,[14] is a semiempirical MO-SCF method relying on Slater shielding efficiencies determined from photoelectron spectroscopy. It is

Table 3.

Compound	λ^{max}_{exp}/nm	Optimal bond lengths (Å)						λ^{max}_{calc}/nm	f_{calc}^{rel}	ΔE/eV	ΔH_{calc}^{f}/kcal mol^{-1}
		C=C	C–C	C–H	C–N	N–O	O–H				
(8)	259(EtOH)	1.38	1.51	1.08	1.48	1.24		256	0.21	0.06	14.7
		1.40		1.09				235	0.32		
								188	1.06		
								168	1.32		
(1)	380(H$_2$O)	1.34	1.46	1.08	1.31	1.36	0.96	396	0.72	0.13	62.0
			1.54			1.22		252	0.70		
								225	0.12		
								184	0.33		
								181	0.28		
(2)	415(H$_2$O)	1.34	1.46	1.08	1.35	1.27		424	0.57	0.06	29.5
			1.54					266	0.10		
								252	0.16		
								245	0.70		
								243	0.48		

Table 4.

Compound	λ^{max}_{exp}/nm	$f^{rel} = \int d\lambda/\lambda$	λ^{max}_{calc}/nm	f_{calc}^{rel}	ΔE/eV
(3)	565	0.47	550	0.66	−0.06
			383	0.28	
	360	0.84			−0.1—0.2
			350	0.23	
	265	1.0	263	0.51	−0.04
(4)	565	0.47	620	0.53	0.19
	360	0.84	418	0.29	0.48
	265	1.0	271	0.45	0.11
(7)	a	a	517	0.70	a
			387	0.19	
	329	0.12			0.45—0.56
	270	0.35	276	0.11	−0.11
(5)	a	a	407	0.47	a
	329	0.12	321	0.34	−0.09
	270	0.35			0.02—0.16
			261	0.44	
	b	b	234	0.39	b

^{a} The $\pi \rightarrow \pi^*$ transition was not observed, possibly due to aggregation. ^{b} No maximum was observed, the calculated absorption is hidden in the absorption 'slope'.

known to be particularly useful in predicting electronic spectra, i.e. photoelectron and u.v.–visible absorption spectra,[15] frequently even superior to the far more complicated and expensive ab initio calculations.[16] Our comparative calculations were focussed on the easily obtainable absorption spectra. The basic geometry of the nitronate ring conformation was optimized using o-nitrotoluene (12). For this, its nitronic acid tautomer and corresponding nitronate, i.e. (12), (1), and (2), spectral data were available for aqueous solutions.[17] Standard bond lengths and angles adopted from Pople and Beveridge[18] were used as starting geometries and the parameters altered included C–N, C–Me, and C=CH$_2$ rotations and all bond lengths except C–H values and ring conformation [(1) and (2) only]. Surprisingly, the preferred conformation of (1) and (2) seems to be the non-planar (13), rather than (14) with twisted nitronate and methylene groups. Since this is neither supported nor contradicted by any experiments we can merely make it plausible by estimating the torsional strains involved in the twistings or rotations.[19] In the case of (14), the C=N and C=CH$_2$ bonds each have to be rotated ca. 50° in order to obtain reasonable interatomic distances. The torsional strain for this is estimated to be of the order of 50 kcal mol^{-1}. This is considerably more than what is expected from a partial loss of the conjugation over the four single bonds in the ring upon a

twist less than 20° (say 15 kcal mol^{-1}). The results of the geometry optimization are shown in Table 3.[20]

Table 4 contains the results of the calculations for compounds (3)—(5) and (7). The calculated spectrum of compound (3) is in excellent agreement with experimental data. Even the normally less accurate oscillator strengths are in good agreement with the spectrum obtained in dimethyl sulphoxide. The observed absorption maximum at 360 nm apparently consists of two absorptions which are essentially two $n(NO_2^-)$ $\rightarrow \pi^*$ (keto ester) transitions at 383 and 350 nm, respectively. The energy difference between the calculated and experimental absorptions are all of the order of 0.1 eV which is far better than that of (4), i.e. the calculation confirms the structure assignment.

In the case of compounds (5) and (7) the situation is complicated by a calculated HOMO(enol-π)$\rightarrow$LUMO(nitro-π^*) transition which was not observed. The calculated transitions may be computational artifacts but on the other hand, being a hydrogen-bonding moiety, the enol-HOMO is most certainly affected by solvation i.e. the HOMO energy is lowered compared with that of the gas phase (= calculated state). It is noted that the calculated HOMO is not involved in any of the other major transitions and thus we hold a selective extinction of the $\pi \rightarrow \pi^*$ transition as plausible. Nevertheless, it can be easily seen that the structure corresponds better to the

experimental spectrum than does (7) and hence, also supports the assignment based on the n.m.r. spectra. In spite of the good agreements between calculations and experiments presented here we would like to emphasize the need for X-ray diffraction data for this class of compounds.

Experimental

The n.m.r., i.r., mass, and u.v.–visible absorption spectra were obtained using 200 MHz Bruker WP 200, Pye–Unicam SP1000, LKB 3000, and PE Hitachi 200 instruments, respectively. The computer used for the calculations was an IBM Amdahl 470/V7A.

Ethyl 2-Nitrophenyl Pyruvate Potassium Salt (3).—The procedure is essentially that of W. E. Noland and F. J. Baude, *Org. Synth.*, 1973, Coll. Vol. 5, 567. To potassium metal (3.9 g, 0.10 g-atom) in diethyl ether (200 ml) absolute ethanol (23 g, 0.5 mol) was added dropwise under nitrogen. After all the metal was consumed the solution was cooled to *ca.* 10 °C and diethyl oxalate (17.5 g, 0.12 mol) in diethyl ether (100 ml) was added and the solution was stirred for 5 min. Addition of 2-nitrotoluene (18 g, 0.13 mol) and stirring for an additional 20 min produced a deep red solution from which the product precipitated upon standing overnight. Filtration under nitrogen and washing with diethyl ether–10% ethanol (5 × 20 ml) and diethyl ether (5 × 25 ml) gave (3) as dark red crystals (14.2 g, 52%). This product was stable when stored under vacuum, $v_{max.}$ 2 980, 1 687, 1 596, 1 547, 1 500, and 1 200 cm^{-1}; $\lambda_{max.}$ 565, 360, and 265 nm.

Ethyl 2-Nitrophenylpyruvate Enol Tautomer (5).—The potassium salt (3) (5 g) was slurried in diethyl ether (100 ml), cooled to −78 °C, and HCl-saturated ether (5 ml) was added to the slurry. The mixture was stirred for 5 min by leading a gentle stream of nitrogen through it. Filtration followed by evaporation of the diethyl ether and excess of HCl at room temperature under vacuum gave (5) (4.2 g, 98%) as yellow crystals, m.p. 70—71 °C. The product was stable for weeks stored under vacuum at −5 °C, $v_{max.}$ 3 420(br), 2 980, 1 695, 1 525, 1 400, 1 340, 1 250, 1 010, and 860 cm^{-1}; $\lambda_{max.}$ 329 and 270 nm.

Ethyl 2-Nitrophenylpyruvate Keto Tautomer (6).—Crystals of (5) (*ca.* 2 g) were stored at room temperature in an open flask for 48 h which resulted in bleaching of the crystals and a lowering of the m.p. to 44—45 °C (lit.,[8] 46—47 °C). The conversion was also achieved by acid or base catalysis in chloroform, $v_{max.}$ 2 980, 1 733, 1 520, 1 345, 1 258, 1 055, and 860 cm^{-1}.

Ethyl 4-Chloro-2-nitrophenylpyruvate Potassium Salt (9).— The same procedure as for the synthesis of (3) was used giving

the highly air- and moisture-sensitive (9) as a brownish red solid (6 g, 20%).

Ethyl 2-Nitro-α-methoxycinnamate (11).—*A* To a solution of the potassium salt (3) (2.75 g, 0.01 mol) in dimethyl sulphoxide (65 ml) dimethyl sulphate (2.52 g, 0.02 mol) was added. The purple colour faded after 5 min of swirling and sodium hydrogen carbonate was added until the additions produced no further colour. The solution was poured into water (*ca.* 100 ml) and extracted with ether (75 ml). Evaporation of the solvent gave a yellow oil which was crystallized from light petroleum (b.p. 40—60 °C) to give a yellowish solid (2.0 g, 80%), m.p. 47 °C (lit.,[8] 46—47 °C).

B To an ethereal solution of diazomethane[21] (20 ml, *ca.* 10 mmol) the enol (5) (0.25 g, 1 mmol) was added and the solution was stirred for 24 h at room temperature. Partitioning of the reaction mixture between aqueous potassium carbonate (20 ml) and ether (50 ml) and evaporation of the ether gave an oil containing *ca.* 50% of the product described above, $v_{max.}$ 2 980, 1 720, 1 525, 1 440, 1 345, 1 250, 1 200, 1 100, 1 030, and 850 cm^{-1}; *m/e* 251 (*M*$^+$), 221, 206, 189, 178, 162, 146, 130, 120, 105, and 89 (B$^+$).

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