

¹³C N.M.R. Examination of Ethyl Cyano(arylhydrazono)acetates

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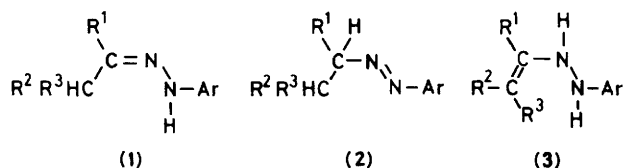
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The products of the condensation of aryldiazonium salts with ethyl cyanoacetate are the (*Z*)- and (*E*)-isomers of the hydrazono forms. These have been examined separately by ¹³C n.m.r. spectroscopy which allows their specific identification. The effects of the geometric configurations and of substituents within the aromatic rings on the cyanoacetic acid carbon resonances have been examined.

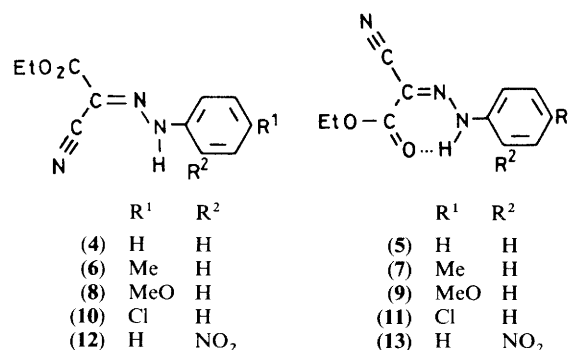
The condensations of arylhydrazines with carbonyl compounds¹ and of aryldiazonium salts with compounds with active methylene groups² give products which may exist in the hydrazono- (1), azo- (2), or ene-hydrazine- (3) tautomeric forms,



each of which, in the case of unsymmetrical examples, exhibits geometric isomerism. In the case of arylhydrazones of simple aldehydes and unsymmetrical ketones, the compounds exist in form (1)³ and (*Z*)- and (*E*)-isomers are well recognised.⁴ Likewise the products, which have been known for more than a century,⁵ derived from aryldiazonium salts, have also been shown to exist in this form by u.v.^{6,7} and i.r.⁷ spectra as well as more recent theoretical⁸ and *X*-ray diffraction⁹ procedures. ¹H N.m.r. spectroscopy has proved particularly valuable for the determination of the geometric configurations of the hydrazones since the nitrogen-bonded protons resonate at positions which are strongly dependent upon the presence of a *syn*-related carbonyl group (1; R², R³ = O). In such cases the NH resonance is observed near δ 13 whereas, in the geometric isomers which preclude N-H...O=C hydrogen bonding, this value is near δ 9.^{10,11} Finally, ¹⁵N n.m.r. spectroscopy has confirmed the hydrazono structure (1) for the product of the condensation of benzenediazonium chloride with ethyl acetoacetate.¹²

Despite this evidence, reports have continued to appear in which products derived from active methylene compounds are described in forms other than the hydrazone (1).¹³ In order to evaluate ¹³C n.m.r. spectroscopy as a structural tool for the study of hydrazones of this class, and to reinvestigate the structures of some members, a set of products derived from ethyl cyanoacetate have been examined—in particular because the isomeric forms are readily separated from each other.¹⁴ The parent compounds (4) and (5) have already been characterised individually by i.r. and ¹H n.m.r. spectroscopy, the former showing a non-hydrogen-bonded C=O i.r. stretching absorption and only weakly bonded C≡N and N-H stretching, whereas the latter showed an i.r. absorption for a strongly bonded carbonyl group. In particular, the N-H ¹H n.m.r. resonances for these isomers occurred at δ 9.93 and 12.95, respectively.¹⁴

In a preliminary examination of the products derived from symmetrical active methylene compounds, compound (14) gave a ¹H n.m.r. spectrum showing, as expected,¹⁰ a low-field NH resonance (δ 12.5) and indistinguishable ethyl signals. In the ¹³C n.m.r. spectrum, however, both the methyl resonances and the

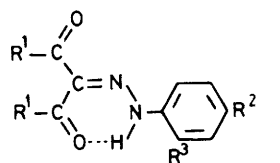


methylene signals were distinguishable, although only one carbonyl resonance was observed (δ 162.5) (Table 1). Of particular significance was the presence of a quaternary resonance [singlet after single frequency off resonance decoupling (SFORD)] at δ 124.4 p.p.m. (C=N), confirming the hydrazone structure (1) for the compound. In the case of the *o*-substituted isomer (15) the differences in the ¹H n.m.r. spectrum between the ester groups were more apparent, and different methylene- and methyl-proton resonances were observed as well as a more deshielded nitrogen-bonded proton, as expected.¹⁰ In the ¹³C n.m.r. spectrum the methyl resonances were not resolved, but the methylene signals were again distinguishable and there were two carbonyl signals. The imino carbon atom resonance was at δ 126.4 p.p.m. indicating that its chemical shift is significantly sensitive to changes within the aromatic ring. In the diketone (16) the methyl resonances were well separated in both the ¹H (δ 2.54, 2.64) and ¹³C (δ 26.7, 31.7 p.p.m.) spectra, but in the latter, the carbonyl resonances were resolved by only 0.12 p.p.m.

The parent compounds (4) and (5) of our main study gave ¹³C resonances as expected for the aromatic and ester groups and, in addition, signals for quaternary carbon atoms (SFORD) near δ 112 and 105 p.p.m. which again confirm their hydrazone structures (Table 1). The former signal is affected by 4.5 p.p.m. by alteration of the configuration about the double bond, but the latter is affected by only 0.8 p.p.m., and on this basis they are assigned to the nitrile and the imine carbon atoms, respectively. Since carbonyl carbon atoms are shielded when *cis*-related to oxygen atoms across vinylic bonds¹⁵ the isomer with the higher field resonance for its nitrile carbon is assigned structure (4). The carbonyl carbon atom of the other isomer (5) shows a relatively low-field resonance for its carbonyl carbon atom (Δδ 1.8 p.p.m.) consistent with the expected influence of intramolecular hydrogen bonding.¹⁶ The slight shielding of the imine carbon atom in isomer (5) is consistent with the increased polarisation of the carbonyl group in this compound. These assignments of configuration to compounds (4) and (5) are

Table 1. ^{13}C and ^1H N.m.r. chemical shifts (δ values) for compounds (4)–(16) in deuteriochloroform

Compound	CO	C-1	C \equiv N	C=N	CH ₂	NH (^1H)
(4)	160.7	140.9	110.6	105.6	62.2	9.9
(5)	162.5	141.0	115.1	104.8	62.3	13.0
(6)	160.9	138.7	110.8	104.9	62.1	9.9
(7)	162.6	138.7	115.3	103.9	62.2	12.7
(8)	161.1	134.7	111.1	104.0	62.0	10.2
(9)	162.8	134.6	115.6	103.3	62.1	13.1
(10)	160.1	139.3	110.2	106.7	62.4	9.5
(11)	162.4	139.6	114.8	105.5	62.5	13.1
(12)	159.3	134.5	111.5	109.5	62.8	12.1
(13)	160.4	135.0	114.4	109.9	63.1	14.7
(14)	162.5			124.4	61.7	12.5
					62.1	
(15)	161.1			126.4	61.7	14.0
	162.7				62.1	
(16)	197.1				26.7	15.5
	197.2				(Me)	
					31.7	
					(Me)	



	R ¹	R ²	R ³
(14)	EtO	NO ₂	H
(15)	EtO	H	NO ₂
(16)	Me	H	NO ₂

consistent with those based on ^1H n.m.r. and i.r. studies, and they gave C=O stretching bands at 1740 and 1685 cm^{-1} in agreement with the previous report.¹⁴

For the *p*-substituted derivatives (6)–(11) the same isomer effects were observable on the carbonyl, nitrile, and imine resonances, and various other characteristics were also caused by the substituents. Electron-releasing groups increase the polarisation of the carbonyl and nitrile groups, thereby causing a slight deshielding of the carbon atoms (Me: 0.2, 0.1 p.p.m. for C=O; 0.2, 0.2 p.p.m. for C \equiv N; MeO: 0.4 and 0.3 p.p.m. for C=O; 0.5 and 0.5 p.p.m. for C \equiv N), and the electron-withdrawing chlorine has the opposite effect (0.6 and 0.1 p.p.m. for C=O; 0.4 and 0.3 p.p.m. for C \equiv N). Conversely, these effects are reversed for the imine carbon atom: Me shields by 0.7 and 0.9 p.p.m., OMe shields by 1.6 and 1.5 p.p.m., and Cl deshields by 1.1 and 0.7 p.p.m. These general characteristics confirm the assignments of the nitrile and imine resonances.

In the cases of the *o*-nitro compounds (12) and (13), whose nitro groups would also hydrogen-bond with the amino group,^{9,10} most of the above effects were again noted, indicating that the electronic withdrawing influences of the substituents override any *ortho*-effects in determining the ^{13}C n.m.r. spectral features.

For the pairs of *p*-substituted ethyl cyanoacetate derivatives (4)–(11), the non-hydrogen bonded (*E*)-isomers [(4) *etc.*] were precipitated earlier from alkaline solution with strong acid, ran more slowly on silica gel, and had higher m.p.s than the (*Z*)-compounds. The latter, however, are thermodynamically preferred, being present to the extent of about 80% when the (*E*)-derivatives were isomerised for 30 h in refluxing acetone.

Table 2. M.p.s of compounds (4)–(16)

Compound	M.p. ($^{\circ}\text{C}$)	Lit. m.p. ($^{\circ}\text{C}$)	Ref.
(4)	131–132	124–125	<i>a</i>
(5)	84–85	85	<i>b</i>
(6)	110–111	116–118	<i>c</i>
(7)	84–85	75	<i>c</i>
(8)	123–124	120	<i>a</i>
(9)	86–87	83	<i>d</i>
(10)	161–162	157–158	<i>a</i>
(11)	127–128	124–125	<i>a</i>
(12)	133–134	116	<i>e</i>
(13)	161–162	160	<i>e</i>
(14)	80–82	79–82	<i>a</i>
(15)	75–77	77–78	<i>a</i>
(16)	183–184	184	<i>f</i>

^a H. J. Barber, K. Washbourn, W. R. Wragg, and E. Lunt, *J. Chem. Soc.*, 1961, 2828. ^b A. Hantzsch and K. J. Thompson, *Ber.*, 1905, **38**, 2266. ^c F. Krückeberg, *J. Prakt. Chem.*, 1894, **49**, 321. ^d W. Lax, *J. Prakt. Chem.*, 1901, **63**, 1. ^e P. W. Uhlmann, *J. Prakt. Chem.*, 1895, **51**, 217. ^f F. D. Chattaway and D. R. Ashworth, *J. Chem. Soc.*, 1934, 930.

Experimental

N.m.r. spectra were measured in deuteriochloroform using a Varian FT-80A instrument.

The hydrazones were prepared by dissolving the arylamines (0.05 mol) in hydrochloric acid (12.5 ml; conc.), cooling to 0 $^{\circ}\text{C}$, adding sodium nitrite (3.5 g) in water (8.4 ml), filtering, and adding the filtrate slowly to a stirred solution of the active methylene compounds (0.05 mol) in acetone (100 ml) and water (50 ml) containing sodium acetate (9.4 g). Stirring was continued for 6 h and the precipitated solids were removed by filtration, washed with water, and dried in air. Yields were > 90% and the crude products were mainly the (*E*)-isomers [(4) *etc.*].

The isomers were isolated by dissolving the crude products in aqueous alcoholic sodium hydroxide (2M) and neutralising with dilute hydrochloric acid to give the (*E*)-isomers, or with carbon dioxide to give the (*Z*)-compounds. Fractional crystallisation from formic acid, or silica gel column chromatography could also be used. Heating of the crude products at their m.p.s for 10 min gave the (*Z*)-isomers.¹⁴ The products were purified by crystallisation from ethanol. M.p.s are compared with those of previously reported compounds in Table 2.

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Received 19th September 1983; Paper 3/1634