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^{1}H NMR Spectra of Some Amidrazone Derivatives

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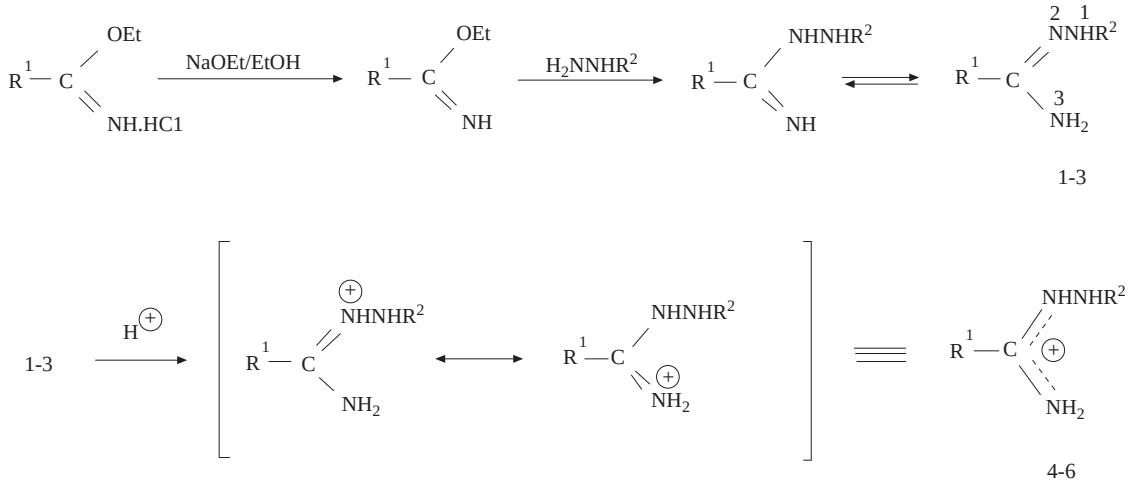
Fifteen amidrazone derivatives (six being new compounds) were synthesized and their proton magnetic resonance spectra were recorded in trifluoroacetic acid (TFA). The protonation shifts, related to alkyl groups and observed on comparison of the spectra run in a neutral solvent and TFA, were attributed to an amidinium-type resonance of the resulting cations in the acidic medium.

Key words: ^{1}H NMR, resonance, amidrazones.

Introduction

In general, amidrazones are weak monoacid bases which form salt with inorganic acids[1]. However, little quantitative work appears in the literature on measurements of the base strengths of amidrazones[1,2]. Amidrazones are able to exhibit tautomerism between N^2 and N^3 atoms[1,3–6]. Some amidrazones exist in an amide hydrazone structure while others are exclusively in hydrazide imide form[7]. Gol'din et al. have recently shown that N^3-unsubstituted amidrazones exist exclusively in the amide hydrazone structure[8]. Indeed, in our earlier papers[9,10], we also established from spectroscopic data that the amidrazone derivatives: amide ethoxycarbonylhydrazones **(1)**, amide tert-butoxycarbonylhydrazones **(2)** and amide carbamylhydrazones **(3)**, exist exclusively in the amide hydrazone form. In the present study, the ^{1}H NMR spectra of some **1, 2** and **3** type compounds measured in a neutral solvent such as hexadeuterodimethyl sulphoxide (DMSO-d_6) and an acidic solvent such as trifluoroacetic acid (TFA) were examined and the observed protonation shifts were interpreted. For this purpose, six new amidrazone derivatives **(1d-f, 3c-e)** were synthesized **(Scheme 1)** and identified by microanalyses and spectral data including ^{1}H NMR spectra in DMSO-d_6, as described below. The other nine compounds, necessary for the study **(Scheme 1)** were obtained using previously reported[9–11] methods. The ^{1}H NMR spectral data of the latter compounds in DMSO-d_6 have been described in previous papers[9–11].



	R^2
1,4	CO_2Et
2,5	$CO_2{}^tBu$
3,6	$CONH_2$

1-6	R^1
a	Me
b	Et
c	CH_2Ph
d	4-$MeC_6H_4CH_2$
e	4-$ClC_6H_4CH_2$
f	4-$O_2NC_6H_4CH_2$

Scheme 1

Experimental

Melting points were determined with a Büchi oil-heated melting-point apparatus and are uncorrected. ^{1}H NMR spectra were recorded at ambient temperature on a Varian A60 spectrometer (60 MHz) for ca. 0.3 M solutions in TFA or acetone-d_6 with TMS as the internal standard. IR spectra were run as potassium bromide discs on a Shimadzu Model 408 spectrophotometer. Combustion analyses were performed on a Carlo Erba Model 1106 elemental analyzer.

The starting compounds, alkyl imidate hydrochlorides, were synthesized by previously reported[12] routes. The required chemicals were obtained from Fluka.

Synthesis of Amide Ethoxycarbonylhydrazones (1d-f). General Procedure. In a stoppered flask equipped with a magnetic stirrer, a solution of the corresponding alkyl imidate hydrochloride (0.01 mole) in an appropriate amount of absolute ethanol was treated with an ethanolic sodium ethoxyde solution prepared by dissolving sodium (0.01 mole) in 15 ml of absolute ethanol. After stirring for 10 minutes, a solution of ethyl carbazate (0.01 mole) in 40 ml of absolute ethanol was added, and the resulting mixture was stirred at room temperature for 14 hours and then filtered. Evaporation of the filtrate at 25-30 °C under reduced pressure and several recrystallizations of the residue from an appropriate solvent afforded pure compound **1**.

4-Methylphenylacetamide ethoxycarbonylhydrazone (1d).- Yield 1.74 g. (74%) of colourless crystals, mp. 170 °C (ethanol-water, 1:4); IR(KBr): 3380, 3150 and 3050(NH_2, NH), 1690(C=O), 1610(C=N) cm^{-1}; ^{1}H NMR(DMSO-d_6): δ 1.25(t,3H,CH_3), 2.38(s,3H,CH_3), 3.40(s,2H,CH_2), 4.20(q,2H,CH_2), 6.05(s,2H,NH_2),

7.20(s,4H,arom. H), 9.15(s,1H,NH).

Anal. Calcd for $C_{12}H_{17}N_3O_2$(235.28) : C, 61.25; H, 7.28; N, 17.86
Found : C, 61.55; H, 7.44; N, 18.14

p-Chlorophenylacetamide ethoxycarbonylhydrazone (1e).- Yield 2.00 g. (78%) of colourless crystals, mp. 175 °C (ethanol-water, 1:4); IR(KBr): 3400, 3200 and 3050(NH_2,NH), 1695(C=O), 1615(C=N) cm^{-1}; ^{1}H NMR(DMSO-d_6): δ 1.22(t,3H,CH_3), 3.46(s,2H,CH_2), 4.22(q,2H,CH_2), 6.10(s,2H,NH_2), 7.30(s,4H,arom. H), 9.10(s,1H,NH).

Anal. Calcd for $C_{11}H_{14}N_3O_2Cl$(255.70) : C, 51.67; H, 5.52; N, 16.43
Found : C, 51.96; H, 5.58; N, 16.68

4-Nitrophenylacetamide ethoxycarbonylhydrazone (1f).- Yield 1.52 g. (57%) of yellowish crystals, mp. 67 °C (ethanol-water, 1:4); IR(KBr): 3430, 3170 and 3060(NH_2,NH), 1720(C=O), 1610(C=N) cm^{-1}; ^{1}H NMR(DMSO-d_6): δ 1.26(t,3H,CH_3), 3.40(s,2H,CH_2), 4.20(q,2H,CH_2), 6.10(s,2H,NH_2), 7.50(d,2H,arom. H), 8.20(d,2H,arom. H), 8.90(s,1H,NH).

Anal. Calcd for $C_{11}H_{14}N_4O_4$(266.25) : C, 49.62; H, 5.30; N, 21.04
Found : C, 49.78; H, 5.44; N, 20.81

Synthesis of Amide Carbamylhydrazones (3c-e). General Procedure. In a stoppered flask equipped with a magnetic stirrer, a solution of the corresponding alkyl imidate hydrochloride (0.005 mole) in an appropriate amount of absolute ethanol was treated with an ethanolic sodium ethoxyde solution prepared by dissolving sodium (0.01 mole) in 15 ml of absolute ethanol. After stirring for 10 minutes, a solution of semicarbazide hydrochloride (0.005 mole) in 5 ml of water was added dropwise. The resulting mixture was stirred at room temperature for 16 hours and then filtered. Evaporation of the filtrate at 25-30 °C under reduced pressure and several recrystallizations of the residue from an appropriate solvent gave pure compound **3**.

Phenylacetamide carbamylhydrazone (3c).- Yield 0.98 g. (51%) of colourless crystals, mp. 150 °C (benzene-petroleum ether, 1:1); IR(KBr): 3470, 3380, 3310 and 3180(NH_2,NH), 1680(C=O), 1590(C=N) cm^{-1}; ^{1}H NMR(DMSO-d_6): δ 3.42(s,2H,CH_2), 5.90(s,4H,2NH_2), 7.16(s,5H,arom. H), 8.80(s,1H,NH).

Anal. Calcd for $C_9H_{12}N_4O$(192.22) : C, 56.23; H, 6,29; N, 29.15
Found : C, 56.52; H, 6.45; N, 29.44

4-Methylphenylacetamide carbamylhydrazone (3d).- Yield 0.95 g. (46%) of colourless crystals, mp. 155 °C (benzene-petroleum ether, 1:1); IR(KBr): 3460, 3350, 3300 and 3180(NH_2,NH), 1690(C=O), 1580(C=N) cm^{-1}; ^{1}H NMR(DMSO-d_6): δ 2.35(s,3H,CH_3), 3.42(s,2H,CH_2), 5.90(s,4H, 2NH_2), 7.17(s,4H,arom.H), 8.75(s,1H,NH).

Anal. Calcd for $C_{10}H_{14}N_4O$(206.24) : C, 58.23; H, 6.84; N, 27.17
Found : C, 57.94; H, 6.81; N, 27.48

4-Chlorophenylacetamide carbamylhydrazone (3e).- Yield 1.20 g. (53%) of colourless crystals, mp. 124 °C (benzene-petroleum ether, 1:1); IR(KBr): 3420, 3360, 3300 and 3140(NH_2,NH), 1680(C=O), 1580(C=N) cm^{-1}; ^{1}H NMR(DMSO-d_6): δ 3.42(s,2H,CH_2), 5.92(s,4H,2NH_2), 7.20(s,4H,arom. H), 8.80(s,1H,NH).

Anal. Calcd for $C_9H_{11}N_4OCI$(226.67) : C, 47.77; H, 4.90; N, 24.75
Found : C, 47.47 H, 5.14; N, 24.98

Results and Discussion

The ^{1}H NMR data for compounds **1, 2** and **3** recorded in TFA are given in **Table 1.** By comparison of these spectral data with the corresponding ^{1}H NMR values obtained in DMSO-d_6, it was seen that the

signals from the group attached to azomethine carbon of compounds **1-3** were shifted downfield in TFA, as shown in **Table 2.**

It is obvious that compounds **1-3** form different cationic species in TFA owing to their nitrogen atoms. The protonation of N^2 leads to the formation of the cationic species **4-6** by an amidinium-type resonance in acidic medium **(Scheme 1).** Indeed, the protonation shifts, observed by comparison of the spectral data measured in TFA and DMSO-d_6, are in agreement with the stabilization of the cations in the acidic medium by an amidinium-type resonance. This situation is in accordance with the reported values for several N-methylimidazoles and N-methyl-1,2,4-triazoles and for a series of 4,5-dihydro-1H-1,2,4-triazol-5-ones[12,13].

Table 1. ^{1}H NMR data for compounds **1, 2** and **3** [60 MHz, δ (ppm) in TFA]

Compd	CH_3	CH_3	$3CH_3$	CH_2	$ArCH_2$	CH_2	Ar-H
1a	1.44 (t)	2.56 (s)	-	-	-	4.46 (q)	-
1b	1.44 (t)	1.58 (t)	-	2.78 (q)	-	4.46 (q)	-
1c	1.44 (t)	-	-	-	4.12 (s)	4.44 (q)	7.33 (s,5H)
1d	1.44 (t)	2.44 (s)	-	-	4.10 (s)	4.46 (q)	7.26 (s,4H)
1e	1.44 (t)	-	-	-	4.14 (s)	4.45 (q)	7.36 (s,4H)
1f	1.44 (t)	-	-	-	4.08 (s)	4.48 (q)	7.58 (d,2H)
							8.34 (d, 2H)
2b	-	1.44 (t)	1.76 (s)	2.68 (q)	-	-	-
2c	-	-	1.77 (s)	-	4.00 (s)	-	7.35 (s,5H)
2d	-	-	1.74 (s)	-	3.97 (s)	-	7.20 (s,4H)
2e	-	-	1.73 (s)	-	3.98 (s)	-	7.38 (s,4H)
3a	-	2.44 (s)	-	-	-	-	-
3b	-	1.45 (t)	-	2.67 (q)	-	-	-
3c	-	-	-	-	4.12 (s)	-	7.25 (s,5H)
3d	-	2.44 (s)	-	-	4.14 (s)	-	7.24 (s,4H)
3e	-	-	-	-	4.12 (s)	-	7.30 (s,4H)

Table 2. Protonation shifts [$\Delta\delta$ (TFA-DMSO-d_6)] for compounds **1, 2** and **3**

Compd	CH_3	CH_2	$ArCH_2$	Compd	CH_3	CH_2	$ArCH_2$
1a	0.76	-	-	**2d**	-	-	0.71
1b	0.38	0.68	-	**2e**	-	-	0.67
1c	-	-	0.67	**3a**	0.74	-	-
1d	-	-	0.70	**3b**	0.40	0.67	-
1e	-	-	0.68	**3c**	-	-	0.70
1f	-	-	0.68	**3d**	-	-	0.72
2b	0.41	0.67	-	**3e**	-	-	0.70
2c	-	-	0.69				

It can be seen that the protonation shift values for the β-hydrogens of ethyl groups are lower than those of the α-hydrogens of the same groups **(Table 2)**. Moreover, protonation shifts were observed for ethoxy and tert-butoxy groups of compounds **1a-f** and **2b-e** to a lesser degree. The observed shifts for the OCH_2CH_3 and $OC(CH_3)_3$ groups can be attributed to the protonation of the oxygen of these groups, leading to the formation of a positive charge. Obviously, the NH and NH_2 groups of compounds **1-3** could not be observed in the spectra recorded in TFA due to protonation.

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