Synthesis and Characterization of Some New 1,3,4-Thiadiazol Derivatives

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Abstract

Fifteen compounds of 2-amino-5-mercapto-1,3,4-thiadiazole derivatives were synthesized and classified into three groups A, B and C. Group A compounds were prepared by condensation reaction of 2-amino-5-mercapto-1,3,4-thiadiazole with some para substituted benzaldehyde and then reacted with ethyl iodide to give the same group C compounds. Group B compounds were synthesized by the reaction of 2-amino-5-methylthio-1,3,4-thiadiazole with the same aldehyde. While, group C compounds were prepared in reverse method to group A compounds by condensation reaction of 2-amino-5ethylthio-1,3,4-thiadiazole with the same para substituted benzaldehyde. All compounds were characterized by elemental analysis, IR and ^{1}HNMR spectral data. These data were confirmed the structural formula of all synthesized compounds.

الخلاصة

تم تحضير خمسة عشرمركبا من مشتقات 2-أمينو-5-ميركابتو-1,3,4-ثايادايازول وتم تصنيفها الى ثلأثة مجاميع A و B و C . حيث حضرت مركبات المجموعة A من تكثيف 2-أمينو-5-ميركابتو-4,3,1-ثايادايازول مع البنزلدهايد المعوض في الموقع 4 ثم فوعلت مع يوديد الأثيل فأعطت نفس مركبات مجموعة C .وحضرت مركبات المجموعة B من تكثيف 2-أمينو-5-مثيل ثايو-4,3,1-ثايادايازول مع نفس الالادهايدات بينما حضرت مركبات المجموعة C بطريقة معاكسة الى مركبات المجموعة A وذلك من تفاعل 2-أمينو-5-اثيل ثايو-4,3,1-ثايادايازول مع نفس الالادهايدات . تم تشخيص جميع المركبات المحضرة باستخدام التحليل الدقيق للعناصر و مطيافية الاشعة تحت الحمراء والرنين النووي المغناطيسي التي اثبتت صحة تراكيب المركبات المحضرة

Introduction

The growing patent literature from the sixties demonstrate that the 1,3,4-thiadiazole and its derivatives have received much attention. This is primarily due to large number of uses of 1,3,4-thiadiazoles in the most diverse areas, for examples, dyestuffs industry, photography and corrosion inhibitors[1-3]. Numerous 1,3,4-thiadizoles have been synthesized and reported as bactericides[4], fungicides[5], insecticides[6], herbicides[7,8], flower control agent [9], herbicides anti-inflammatory[10], tranquilizing agent[11] and hypoglycemic activity[12]. Recently thiadiazolyl-2-propanol amine derivatives have been prepared and showed some activity toward blood pressure and hart

rate[13,14]. On the other hand, Schiff bases are well known to possess promising biological activities[15,16]. In view of the above observations it was considered worthwhile to synthesize some 1,3,4-thiadiazoile Schiff-base derivatives starting from 2-amino-5-mercapto-1,3,4-thiadizole compound, in view of the fact that a number of these compounds possessing biological activity.

Experimental

All chemicals used in this study were purchase from Aldrich Chemicals and were used with out further purification.

All melting points are uncorrected were determined using Gallenkamp thermal point apparatus. IR spectra were recorded with Pye-Unicam SP300S spectrophotometer. The ^{1}HNMR spectra were determined with Brucker WM 250 spectrometer. Elemental analysis was obtained using Carlo Erba element analyzer.

Synthesis of 2-amino-5-mercapto-1,3,4-thiadiazole

A solution of thiosemicarbazide (4.5 g, 0.05 mole) in 20 mL of absolute ethanol was placed in round bottom flask fitted with an efficient condenser. To this solution anhydrous sodium carbonate (2.7 g, 0.025 mole) and carbon disulfide (3.7 g, 0.05 mole) was added and the mixture was heated in a steam bath for six hours. The ethanol was evaporated using rotary evaporator. The residue was diluted by addition of 25 mL of H_2O and the solution was acidified by concentrated HCl and filtered. On filtration and washing with H_2O several times, a yellow crystalline 2-amino-5-mercapto-1,3,4-thiadiazole was obtained. M. p. 227 ^{o}C (Lit.[17] 226.4 ^{o}C).

Synthesis of 2-amino-5-methyl- or ethylthio-1,3,4-thiadiazole

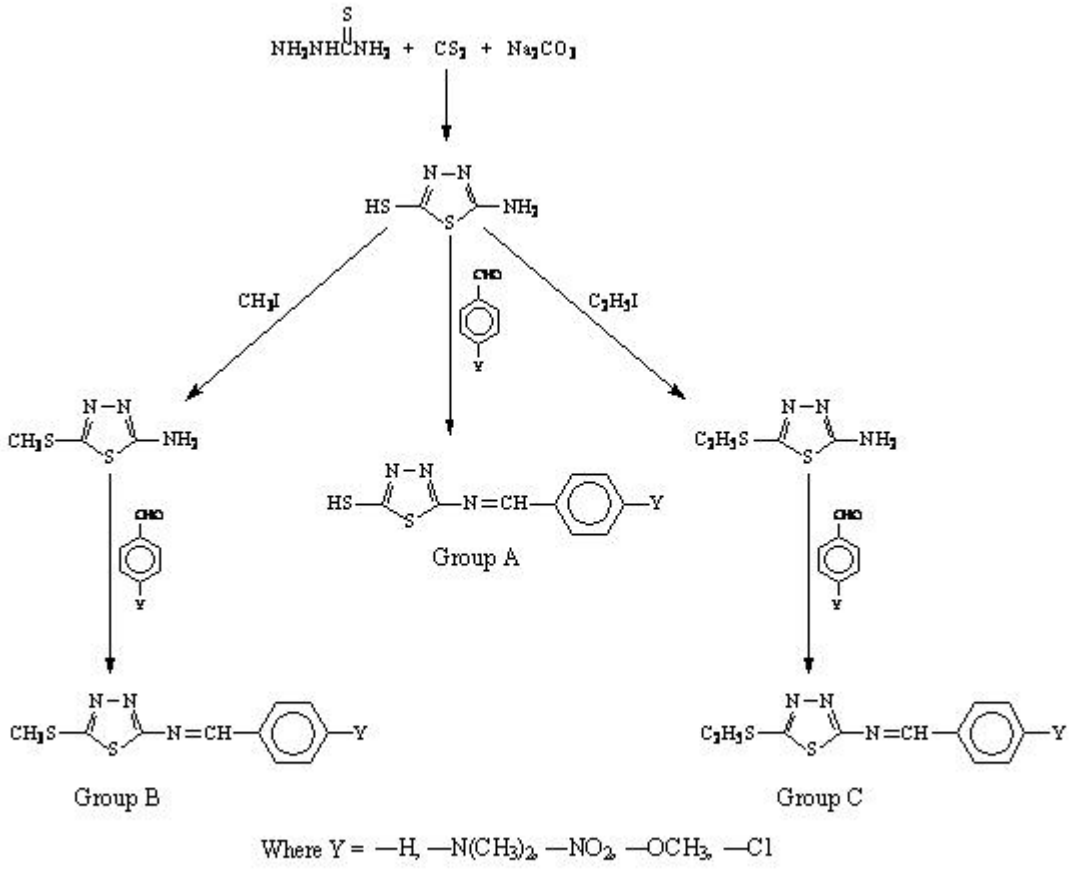
Potassium hydroxide (0.68 g, 0.12 mole) dissolved in minimum volume of H_2O, was added drop wise to a stirred solution of 2-amino-5-mercapto-1,3,4-thiadiazole (1.33 g, 0.01 mole) in 10 mL of dioxane at 25 ^{o}C. After heating the mixture for 15 minutes and cooling, methyl or ethyl iodide (0.01 mole) was added drop wise. The solution was refluxed for 2 hours, afterwards the solvent was evaporated on rotary evaporator. Ice-water (100 mL) was added, the resulting precipitate was collected, and recrystallized from ethanol. The melting points of 2-amino-5-methylthio-1,3,4-thiadiazole and 2-amino-5-ethythio-1,3,4-thiadiazole are 168 ^{o}C and 130 ^{o}C respectively.

General Procedure for Synthesis of 2-Benzylidneamino-5-mercapto-1,3,4-thiadiazole Derivatives

A mixture of 2-amino-5-mercaptto-1,3,4-thiadiazole (0.1 mole), 50 mL of absolute ethanol and appropriate aldehyde (0.1 mole) was refluxed for five hours with continuous stirring. Ethanol was evaporated using rotary evaporator and the yellow precipitate was recrystallized three times from ethanol to obtain the desired Schiff-base products.

Results and Discussion

The starting compound 2-amino-5-mercapto-1,3,4-thiadiazole was prepared by the reaction of ethanolic solution of semicarbazide with carbon disulfide in the presence of sodium bicarbonate. From this compound three groups of compounds, A, B and C were synthesized according to Scheme 1.



Scheme 1

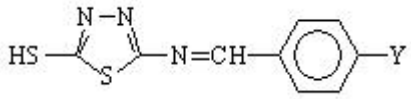
All synthesized compounds were characterized by elemental analysis, IR and 1HNMR spectral data, Tables 1, 2 and 3. Elemental analysis data, Table 1 of some of these compounds were consistent with the expected composition of the structural formula of these compounds.

IR spectra of the synthesized compounds, show characteristics absorption bands, Table 2 at 1580-1680 cm-1 which are assignable to $\nu_{C=N}$ stretching for all compounds of the three groups. A weak absorption bands at 1290-1325 cm^{-1} which are attributed to $\nu_{C=S}$ for group A compounds. This confirm that thiol group SH is in the thione form. For group B compounds a medium bending absorption band occurs at 1415-1440 cm^{-1} due to δ_{CH3S} bending. While, the characteristic medium peak of group C compounds appear at 1420-1440 cm^{-1} could be attributed to ν_{CH2S}. Figures 1-3 illustrated IR spectra of compounds A2, B1 and C1 respectively as a representative examples of the synthesized compounds.

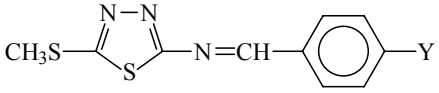
The chemical shifts in 1HNMR spectra of some of these compounds are listed in Table3 and illustrated in Figures 4, 5 and 6 for compounds A3, B1 and C2 respectively.. These chemical shifts indicate the presence of aromatic protons around δ=7.21-8.39 as multiplets. The singlet at δ = 9.06-10.14 are attributable to the proton of azomethine group. The characteristics peaks for other protons inside of chemical structural formula of these compounds are also presented in Table 3.

The biological activity of these compounds will be the object of the next publication which is in progress.

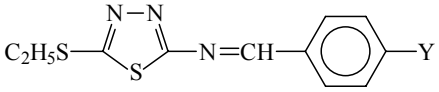
Table 1. Characteristic IR absorption Bands of the synthesised compounds



Compound	Y	$\nu_{C-H(arom)}$	$\nu_{C-H(aliph)}$	$\nu_{C=S}$	$\nu_{C=N}$
A1	-H	3100-3000	3000-3170	1310	1675
A2	-N(CH_3)$_2$	3060-3120	3000-3080	1310	1540
A3	-NO_2	3015-3120	3000-3070	1325	1690
A4	-OCH_3	3000-3080	3000-3170	1290	1645
A5	-Cl	3020-3100	3000-3280	1325	168



Compound	Y	$\nu_{C-H(arom)}$	$\nu_{C-H(aliph)}$	ν_{CH_3-S-}	$\nu_{C=N}$
B1	-H	3060-3120	2916-2960	1415	1630
B2	-N(CH_3)$_2$	3020-3140	2810-2910	1440	1670
B3	-NO_2	3020-3100	2900-2960	1430	1660
B4	-OCH_3	3020-3100	2920-3000	1415	1630
B5	-Cl	3040-3100	2920-2980	1415	1675



Compound	Y	$\nu_{C-H(arom)}$	$\nu_{C-H(aliph)}$	ν_{-CH_2-S-}	$\nu_{C=N}$
C1	-H	3040-3100	2910-3000	1420	1630
C2	-N(CH_3)$_2$	3060-3140	2900-2960	1440	1660
C3	-NO_2	3060-3100	2910-2980	1440	1670
C4	-OCH_3	3020-3130	2900-2980	1430	1630
C5	-Cl	3020-3100	2900-3000	1420	1680

Table 2. Elemental analysis data for the synthesized compounds

Compounds	Theoretical			Experimental		
	C%	H%	N%	C%	H%	N%
A1	48.86	3.16	19.00	48.69	3.30	18.85
A2	50.00	4.54	21.21	49.73	4.59	21.51
A4	47.80	3.58	16.73	47.42	3.61	17.02
A5	42.25	2.34	16.43	24.41	2.48	16.25
B1	51.10	3.28	17.87	51.34	3.51	17.91
B2	51.79	5.03	20.14	51.73	5.16	20.55
B3	42.85	2.85	20.00	43.03	2.92	19.76
C2	53.42	5.48	19.17	53.17	5.55	19.42
C3	44.89	3.40	19.04	45.07	3.51	19.42
C5	46.54	3.52	14.81	46.68	3.48	14.53

Table 3. Nuclear magnetic resonance data for some of the synthesised compounds

Compounds	Coupling Constant	Chemical Shift/ppm
A3		δ = 7.07 (-SH, 1H, s) δ = 13.55 (-NH, 1H, s) δ = 10.14 (N=CH, 1H, s) δ =8.31 (arom., 4H, m)
B1		δ =2.57 (-CH_3, 3H, s) δ = 8.7 (N=CH, 1H, s) δ = 7.21 (arom., 5H, s)
B3		δ = 2.78 (-CH_3, 3H, s) δ = 9.06 (N=CH, 1H, s) δ = 8.31 (arom., 4H, q)
C2	J= 7.32 J=7.32 J=8.85	δ = 1.35 (C-CH_3, 3H, t) δ = 3.15 (-S-CH_2, 2H, q) δ = 8.57 (N=CH, 1H, s) δ = 3.01 (N-$(CH_3)_2$, 6H, s) δ = 7.73 (arom., H, 4H, dd)
C3	J=6.5 J=6.5 J=7.0	δ = 2.45 (C-CH_3, 3H, t) δ = 4.14 (S-CH_2-, 2H, q) δ = 10.15 (N=CH, 1H, s) δ = 8.39 (arom., H, 4H, dd)

s(singlet), d(doublet), m(multiplet), q(quartate)

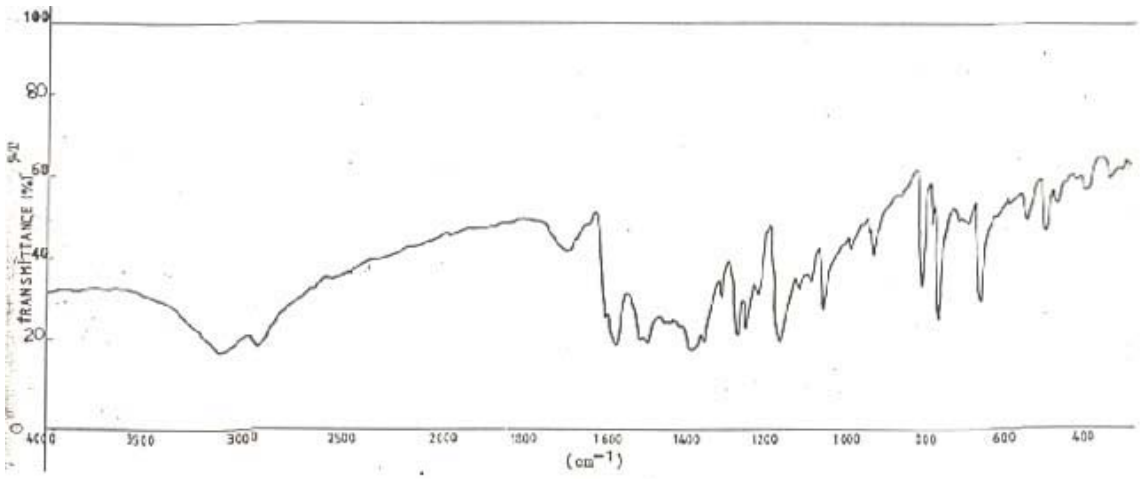


Figure 1. IR spectrum of compound A2

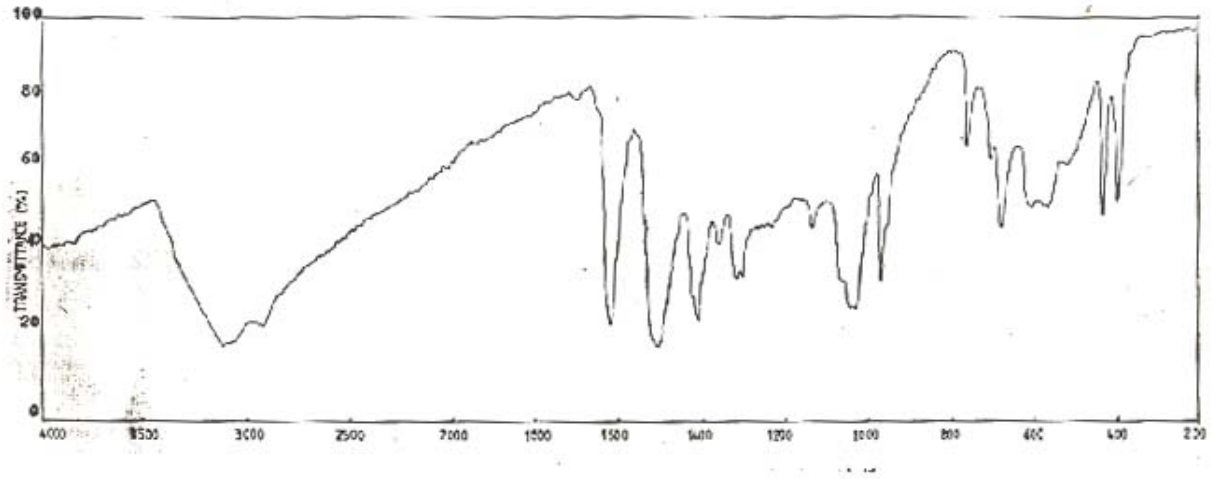


Figure 2. IR spectrum of compound B1

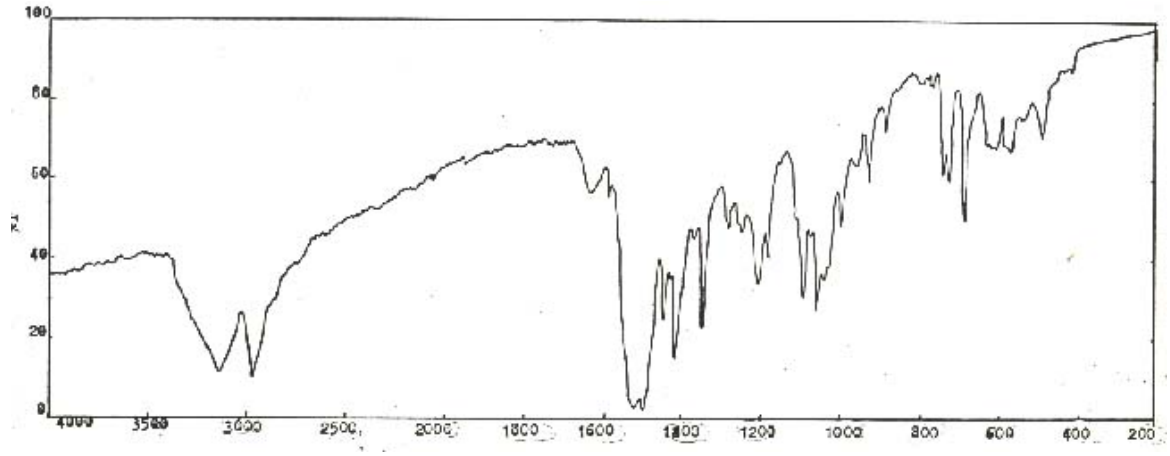


Figure 3. IR spectrum of compound C1

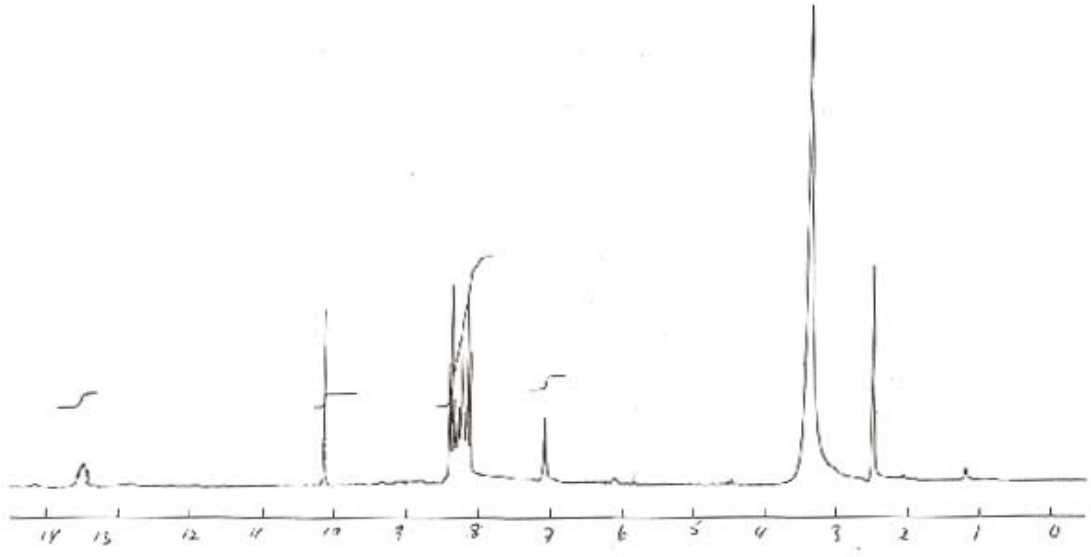


Figure 4. ^{1}HNMR spectrum of compound A3

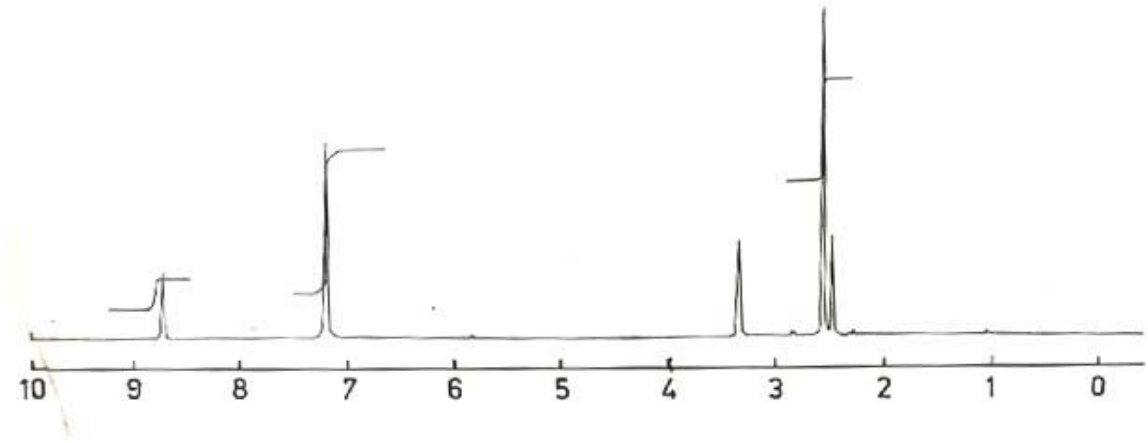


Figure 5. ^{1}HNMR spectrum of compound B1

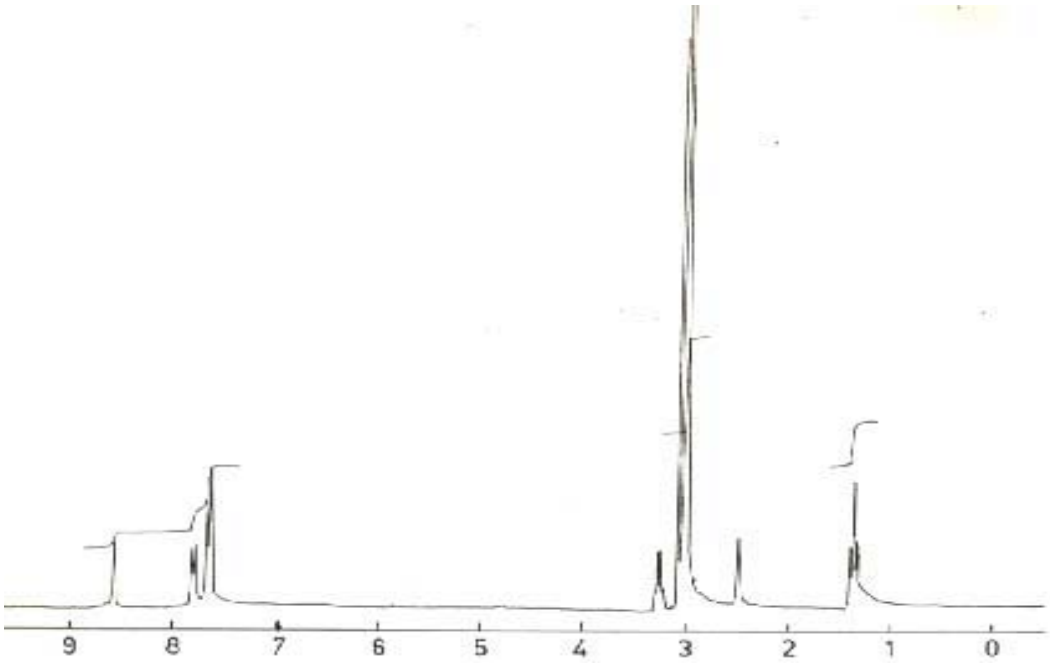


Figure 6. ^{1}HNMR spectrum of compound C1

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