C-13 Nuclear Magnetic Resonance Spectra of Amines

胺類之碳十三核磁共振譜

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Since the first successful determinations of nuclear magnetic ouance spectra of C-13 nuclei in natural abundance, [1] a number organic compounds have been studied covering a wide range of functionalities. Thus, alkanes, [2,3] olefins, allenes and acetylenes, [4] aromatic heterocyclics, [5] benzene derivatives, [6-8] esters, [9,10] carbonyl compounds, [1,11] and norbornyl derivatives, [12] etc. have been reported. Amines, however, have been little investigated except aniline derivatives, [13,14] imines, [14] and some simple aliphatic amines. [15-17]

A previous report from this Institute has shown that di-s-butyl ether exhibited a C-13 NMR spectrum in which the signals for the four carbon atoms are each split in two lines. This splitting was interpreted as due to nonequivalence of the two s-butyl groups caused by the restricted rotation of the C-O bonds. [18] The present study was undertaken to collect more information on the C-13 shieldings for some more aliphatic amines with a special attention on di-s-butylamine.

Experimental

A JEOL JNM-C-60HL High Resolution NMR Instrument was used with its standard C-13 attachments at the frequency of 15.086 MHz. Measurements were carried out at room temperature. The samples were all liquid and used neat. Cyclohexane was used as the internal standard. The spectra were shown in Figs. 1-8. The C-13

shieldings were collected in Table 1. The data were converted to the TMS scale by adding 27.7 ppm[19] and shown in Table 2. Large positive values correspond to downfield.

Preparation of n-Butyl Bromide

n-Butyl bromide was prepared from n-butyl alcohol (138 g), 6 g of red phosphorus, 4 g of yellow phosphorus, and 94 g of bromine according to the literature method.[20] The temperature was 175° and the product distilled at 99-100° 145 g 90% yield.

Preparation of n-Propyl Bromide[20]

n-Propyl bromide was prepared from n-propyl alcohol (180 g, 224 ml, 3.0 moles), 6 g of red phosphorus, 4g of yellow phosphorus, and bromine(135 g, 43.2 ml, 0.84 mole) at an oil bath temperature of 125-140°. The product was obtained in 82% yield(170 g), bp 70-73°.

Preparation of s-Butyl Bromide[20]

A mixture of s-butyl alcohol (138 g, 170 ml, 1.86 moles), 6 g of red phosphorus, and 4 g of yellow phosphorus was heated in an oil bath to 140-150°. Bromine (94 g, 30.1ml, 0.58 mole) was added slowly through a dropping funnel in the period of two hours while the reaction mixture was stirred. After the addition of bromine, the reaction mixture was further heated for 30 minutes and distilled. The distillate was washed with water (3 x 100 ml), dried, and distilled; bp 91-92°, 135 g, 84% yield. The literature[20] gives bp 86-87° which is incorrect; a handbook[21] gives bp 91.2°.

Preparation of Isopropyl Bromide[20]

Isopropyl bromide was prepared from isopropyl alcohol according to the literature method in 81% yield; bp 59-63°.

Preparation of Acetoxime[22]

Hydroxylamine hydrochloride (69 g, 1.0 mole) was dissolved in 140 ml of water and 140 ml of 20% sodium hydroxide solution was added. Acetone (140 ml) was added and the mixture was vigorously stirred for 10 minutes. The reaction mixture was allowed to stand for one day and the crystals were collected by suction. After being dried in a desiccator, the product weighed 45 g or 62% yield; mp 46-47°; lit. 21, mp 46°

Preparation of 2-Butanone Oxime

This oxime was prepared from 2-butanone as described for acetoxime. The reaction mixture was poured into water and extracted with ether. The ether was distilled off to obtain the oily oxime which was dried in a desiccator; 52% yield.

Preparation of n-Butylamine[22a]

A mixture of butyl bromide (138 g, 1 mole), conc ammonium hydroxide (67 ml, 1 mole), and 95% ethanol (800 ml) was heated in an oil bath at 120° for 10 hours. The reaction mixture was acidified with conc hydrochloric acid (89 ml, 1.1 moles) and distilled to remove ethanol. The water solution left behind was neutralized with a solution of sodium hydroxide(44 g, 1.1 moles) in 200 ml of water. The resulting mixture was extracted with ether (500 ml x 4). The combined ether solution was dried ($MgSO_4$) and distilled. The residue was fractionated to obtain n-butyl amine (bp 75-77°, 39.4 g, 54% yield), di-n-butylamine (bp 159-160°, 9.5 g, 13% yield), and tri-n-butylamine (bp 214-216°, 2.9 g, 4% yield). The literature boiling points of these amines are 76-77°, 160°, and 216° respectively.[22a]

Preparation of n-Propylamine[23]

The reaction of propyl bromide and ammonia was carried out in the same way as for n-butyl bromide. The product obtained were n-propylamine (bp 48-50°, 24.8 g, 42% yield) and di-n-propylamine (bp 108-110°, 6.5 g, 11% yield). The literature boiling points are 49-50° and 109-110°, respectively.[23]

s-Butylamine[24]

A solution of 2-butanone oxime (22 g, 0.25 mole) in 200 ml of absolute ether was refluxed, to which was added dropwise under stirring an etheral solution of lithium aluminum hydride(15 g, 0.375 mole). The resulting mixture was further refluxed under stirring for 2 hours, and water (50 ml) was gradually added to decompose the excess of the reducing agent. The mixture was acidified by the addition of 150 ml of conc hydrochloric acid in 500 ml of water and the ether was distilled off. The water solution left behind was made alkaline by the addition of sodium hydroxide (75 g in 250 ml water). The mixture was extracted with ether (500 ml x 4) and the combined ether solution was distilled off through a fractionating column. The residue was distilled to obtain s-butylamine(5.4 g, 30% yield)which had bp 65-68° (lit. 24, bp 66-68°).

Preparation of Isopropylamine[25]

Acetoxime was reduced with lithium aluminum hydride in ether as described above. Isopropylamine was obtained in 25% yield, bp 32-34° (lit. 25, bp 33-34°).

Preparation of Di-s-butylamine[26]

A mixture of s-butylamine (14.6 g, 0.2 mole), s-butyl bromide (27.4 g, 0.2 mole), and ethanol (25 ml) was refluxed for 15 hours. Water (100 ml) containing 9.8 g (0.1 mole) of conc sulfuric acid was added and the mixture was distilled to remove the ethanol and the unchanged s-butyl bromide. The residue was then treated with

2 N sodium hydroxide (100 ml) to liberate the amines, which was extracted with ether (3 x 100 ml). The ether solution was dried ($MgSO_4$) and distilled off.. The residue was distilled to obtain di-s-butylamine, bp 132-133°, 13.4 g (52% yield).

Preparation of Diisopropylamine

This amine was prepared from isopropylamine and isopropyl bromide as described above. The yield was 43% and the amine had bp 83-84°

Preparation of t-Butylamine[27]

(1) t-Butylurea To conc sulfuric acid (105 ml, 193 g, 1.98 moles) cooled by an ice bath was added slowly finely powdered urea (60 g, 1 mole) maintaining the temperature at 20-25°. Then t-butyl alcohol (188 ml, 148 g, 2 moles) was added dropwise at 20-25°. The mixture was further stirred for 30 minutes, allowed to stand at room temperature overnight, and then poured under stirring on 1.5 kg of crushed ice and water. The mixture was made alkaline by slowly adding with stirring a solution of sodium hydroxide (160 g in 750 ml of water). The mixture was cooled (25°maximum) during this period and further cooled down to 15° at which point the precipitate was collected, washed with cold water (2 x 100 ml), and pressed and sucked as dry as possible. The cake was transfered to a beaker containing 500 ml of water. The mixture was heated to boiling and filtered hot. The filtrate was cooled to 0-5° with stirring, and the white precipitate of t-butylurea was collected with suction; 32 g (28% yield), mp 180-183°.

(2) Hydrolysis of t-Butylurea A mixture of sodium hydroxide (60 g, 1.5 moles), 75 ml of water, and 70 g (0.6 mole) of t-butylurea in 225 ml of ethylene glycol was refluxed for 4 hours.

The mixture was distilled and the fraction boiling at 40-60° was collected, which was dried with 7 g of sodium hydroxide pellets

overnight. The dried amine was distilled to collect t-butylamine, bp 44-46°, 28 g (64% yield).

Results and Discussion

Tables 1 and 2 list the C-13 shieldings of eight aliphatic amines studied in this work with seven amines reported elsewhere. The most significant finding of this study is the splitting of the C-13 signals of di-s-butylamine. As in the case of di-s-butyl ether, the splitting may be attributed to the nonequivalence of the two s-butyl groups caused by the restricted rotation of the C-N bonds. The splittings are in the range 0.4-0.8 ppm which are larger than the corresponding figures in di-s-butyl ether (0.15-0.58 ppm), suggesting that the steric restriction of the C-N bonds is more serious than that of the C-O bonds. n-Propyl, isopropyl, and n-butyl groups do not restrict the free rotation of the C-N bonds as indicated by the absence of such splitting in C-13 NMR signals. Interestingly, the alpha-carbon signal in di-s-butylamine is single, in contrast to the case of di-s-butyl ether where a splitting of 0.437 pp, was observed. This splitting in C-13 NMR due to restricted rotation even at room temperature is found for the first time for the s-butyl group. t-Butyl rotation in 2-t-butyl-1,3-diheteroatomic rings has recently been discussed on the basis of proton dynamic nuclear magnetic resonance spectra.[28]

Table 1. C-13 Shieldings of Some Aliphatic Amines Relative To Cyclohexane

Amine	alpha-C	beta-C	gamma-C	delta-C	beta' (Me)	Ref.
Methyl	0.6					16
Trimethyl	19.8					17
Ethyl	9.2	-8.7				16
Triethyl	30.5	-13.9				17
n-Propyl	17.0	-0.4	-16.5			16
Di-n-propyl	24.7	-3.5	-15.5			this work
Tri-n-propyl	29.4	-6.0	-15.2			17
Isopropyl	15.5	-1.0				this work
Diisopropyl	18.0	-3.5				this work
n-Butyl	14.6	9.0	-7.3	-13.7		16
Di-n-butyl	22.6	5.8	-6.5	-13.3		this work
Tri-n-butyl	26.9	3.0	-6.5	-13.2		this work
t-Butyl	14.2	-5.7				this work
s-Butyl	21.3	6.1	-16.8	-3.5		this work
Di-s-butyl	24.0	3.0	-16.8		-6.1	this work
		3.8	-17.2		-6.6	

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Table 2. C-13 Shieldings of Some Aliphatic Amines Relative To TMS

Amine	Alpha-C	beta-C	gamma-C	delta-C	beta' (Me)	Ref.
Methyl	28.3					16
Teimethyl	47.5					17
Ethyl	36.9	19.0				16
Triethyl	58.2	13.8				17
n-Propyl	44.5	27.3	11.2			16
Di-n-propyl	52.4	24.2	12.2			this work
Tri-n-propyl	57.1	21.7	12.5			17
Isopropyl	43.2	26.7				this work
Diisopropyl	45.7	24.2				this work
n-Butyl	42.3	36.7	20.4	14.0		16
Di-n-butyl	50.3	33.5	21.2	14.4		this work
Tri-n-butyl	54.6	30.7	21.2	14.5		this work
t-Butyl	41.9	22.0				this work
s-Butyl	49.0	33.8	10.9		24.2	this work
Di-s-butyl	51.7	30.7	10.9		21.6	this work
		31.5	10.5		21.1	

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In going from primary amines(RNH_2) to secondary amines (R_2NH), where R is n-propyl, isopropyl, or n-butyl, the C-13 shielding difference for alpha, beta, and gamma carbons are plus, minus, and plus, respectively, as shown in Table 3. The same

trend is so observed in going from primary amines (RNH_2) to tertiary amines (R_3N), as shown in Table 4.

Table 3. C-13 Shielding Differences Attending The Change RNH_2 To R_2NH

	n-Px	i-Px	n-Bu
alpha-C	7.9	2.5	8.0
beta-C	-3.1	-2.5	-3.2
gamma-c	1.0		0.8

Table 4. C-13 Shielding Differences Attending The Change RNH_2 To R_3N

	Me	Et	n-Pr	n-Bu
alphah-C	19.2	21.3	12.6	12.3
beta-C		-5.2	-5.6	-6.0
gamma-C			1.3	0.8
delta				0.5

Acknowledgment

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中文摘要

本研究最重要之發見乃是二零丁胺之碳十三核磁共振譜，其四碳中之三碳之信號皆分爲二條。前此，在二零丁醚所發見之此類分支，曾經以二個零丁基間之立體障礙加以解釋。現在於胺所見之現象亦可同樣加以解釋。

於胺之分支較於醚之分支爲大，此似表示立體障礙於胺較於醚爲大。

正丙基，異丙基，正丁基皆不發生立體障礙，蓋此等胺類，其各碳之信號均爲單條。

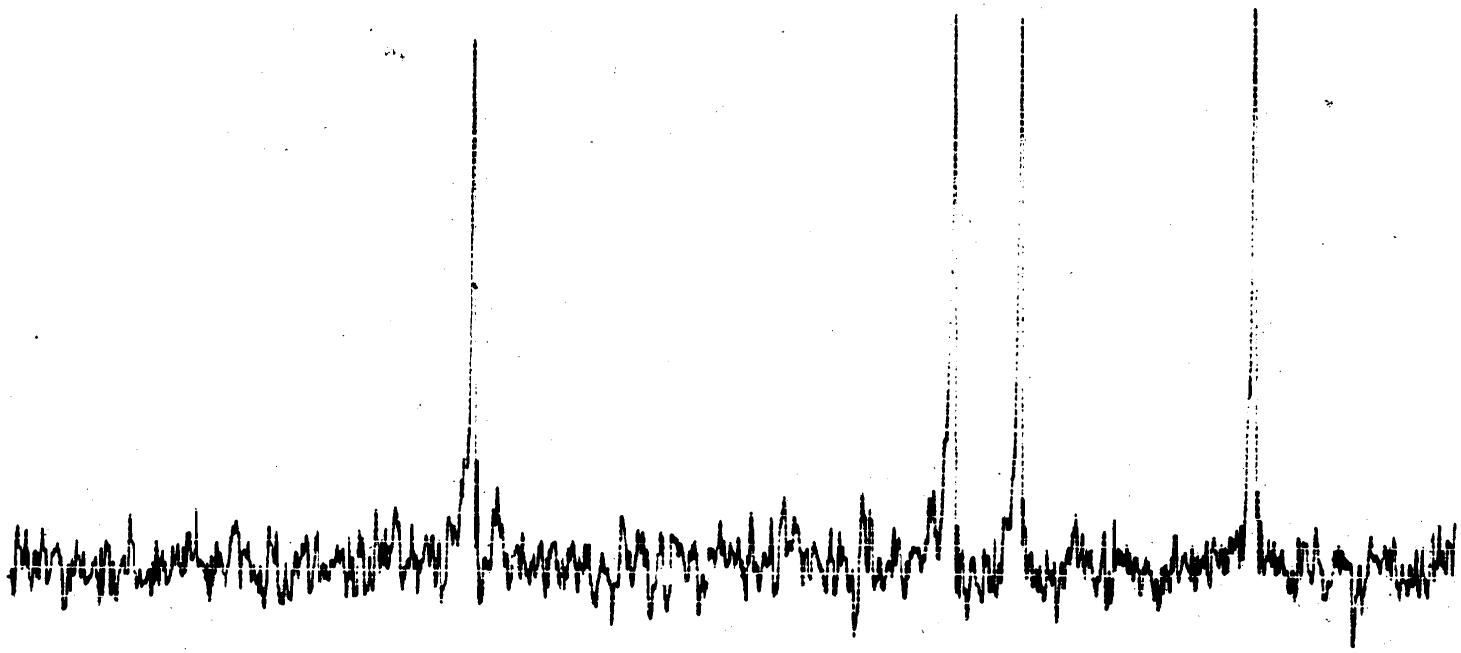
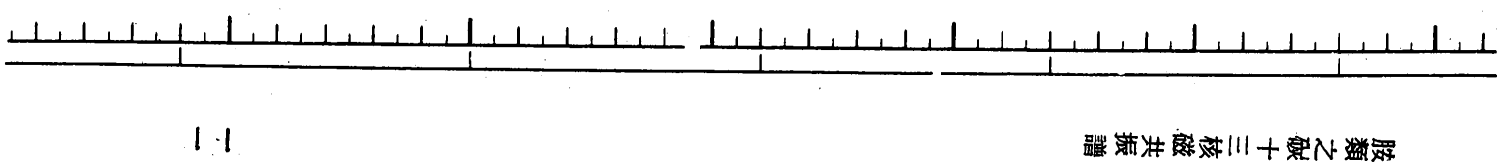


Fig. 1 C-13 NMR Spectrum of Di-n-propylamine



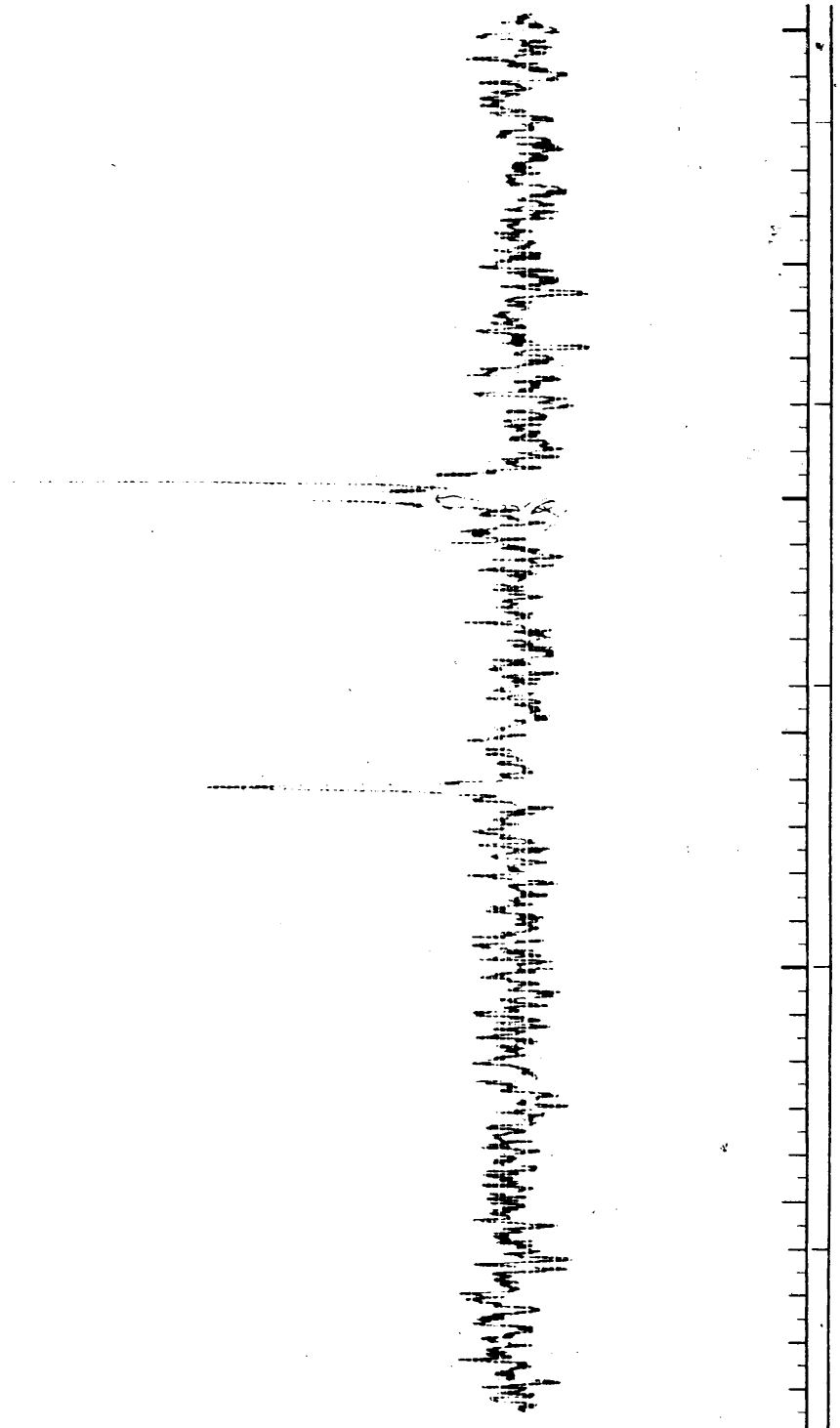


Fig. 2 C-13 NMR Spectrum of Isopropylamine

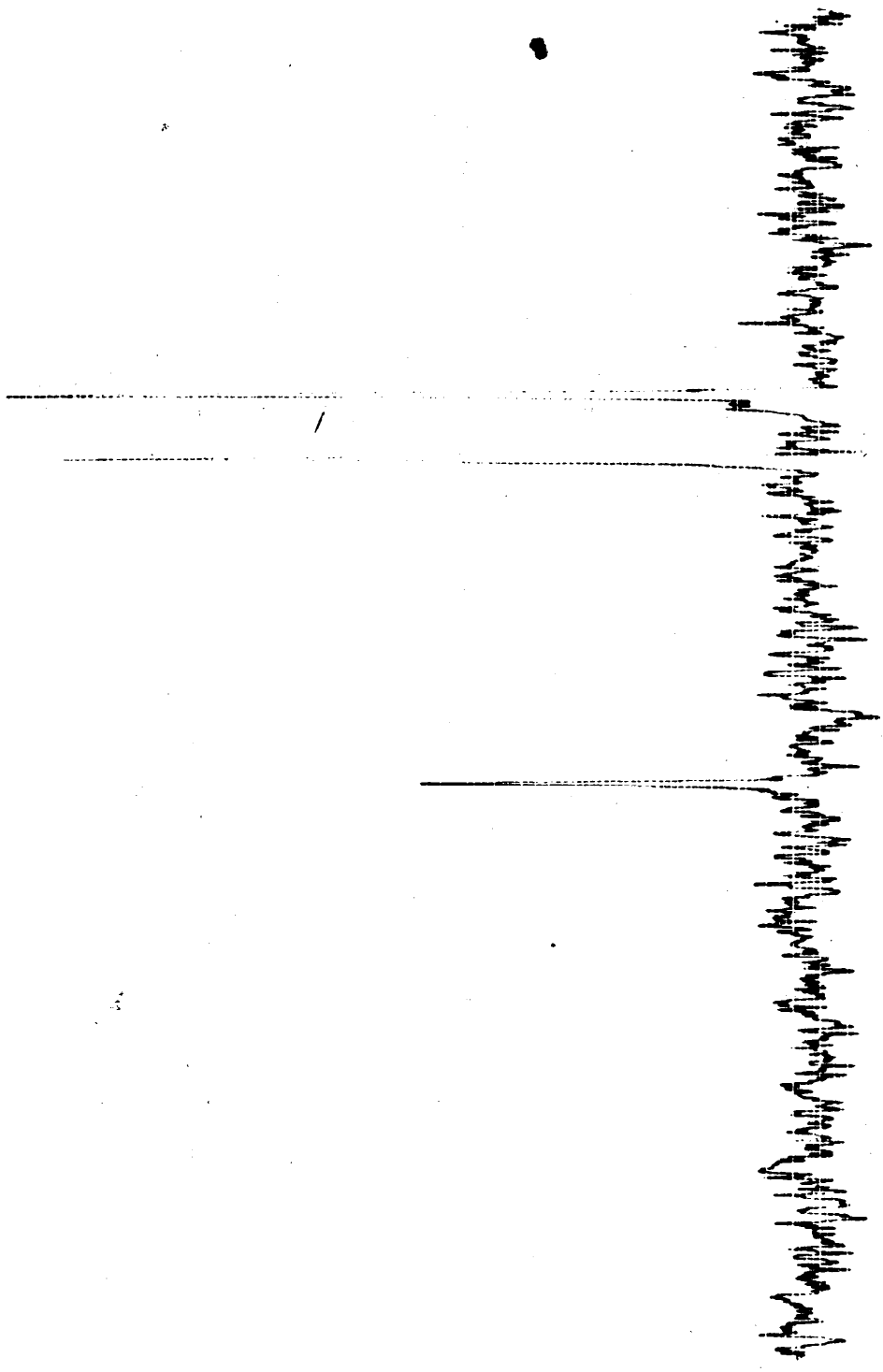


Fig. 3. C-13 NMR Spectrum of Diisopropylamine

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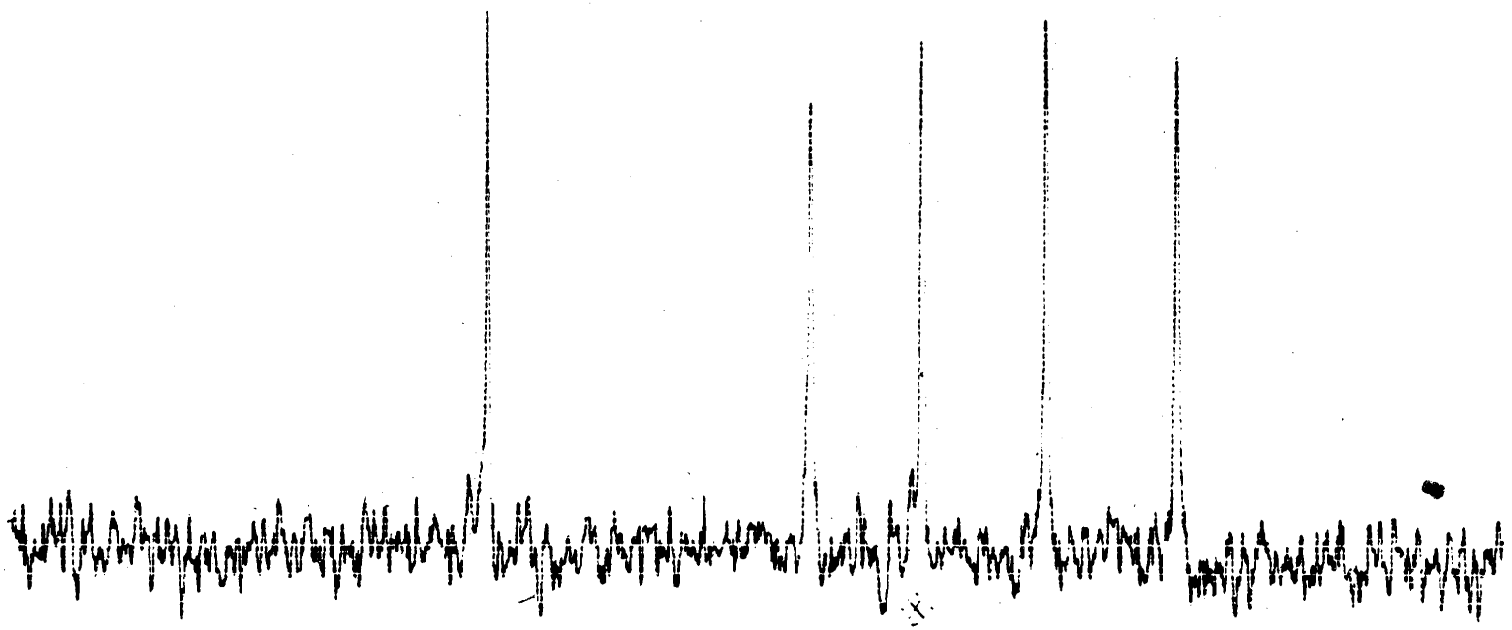
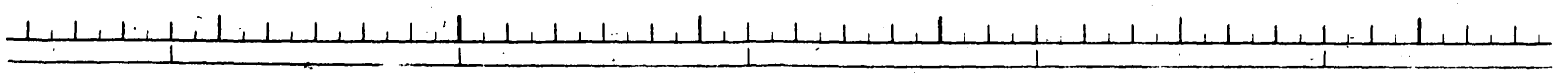


Fig. 4　C-13 NMR Spectrum of Di-n-butylamine



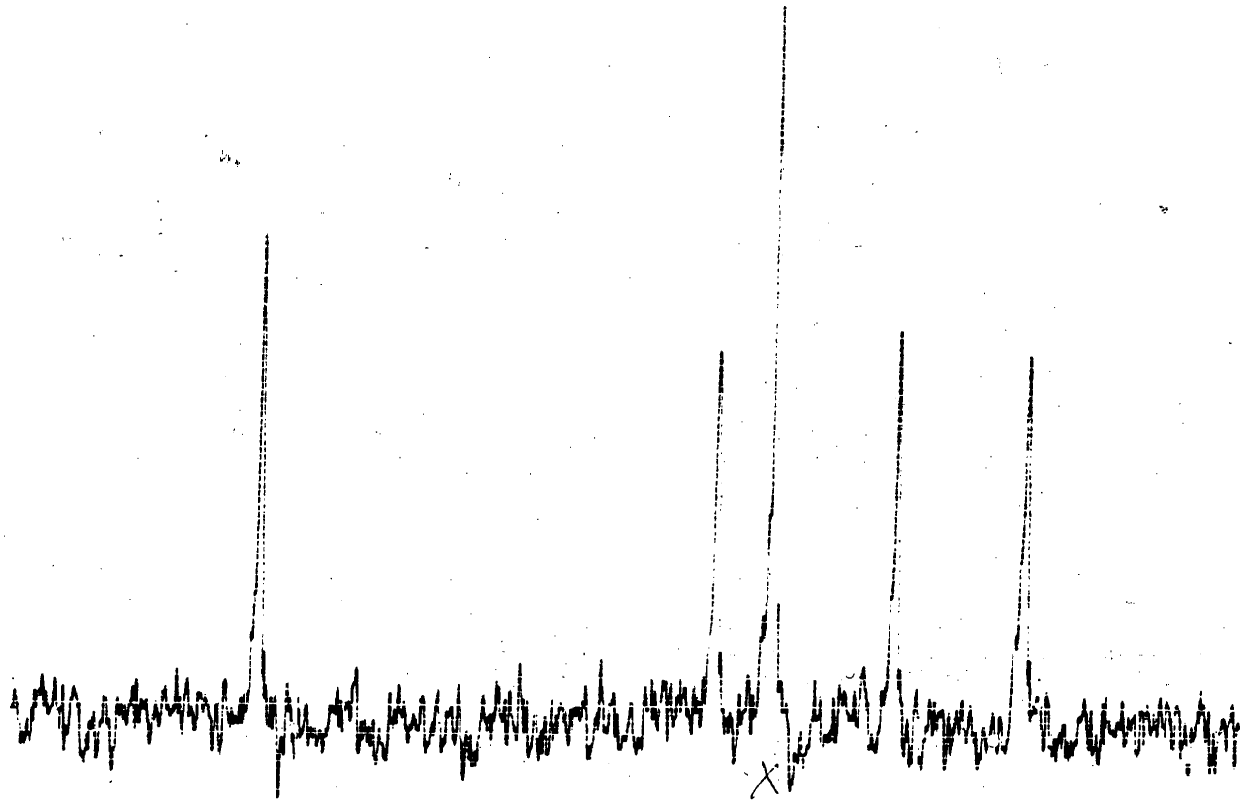
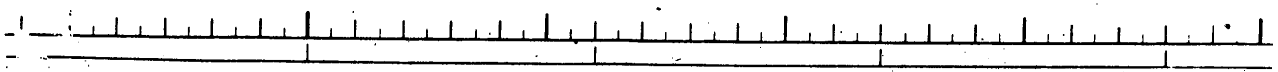


Fig. 5 C-13 NMR Spectrum of Tri-n-butylamine



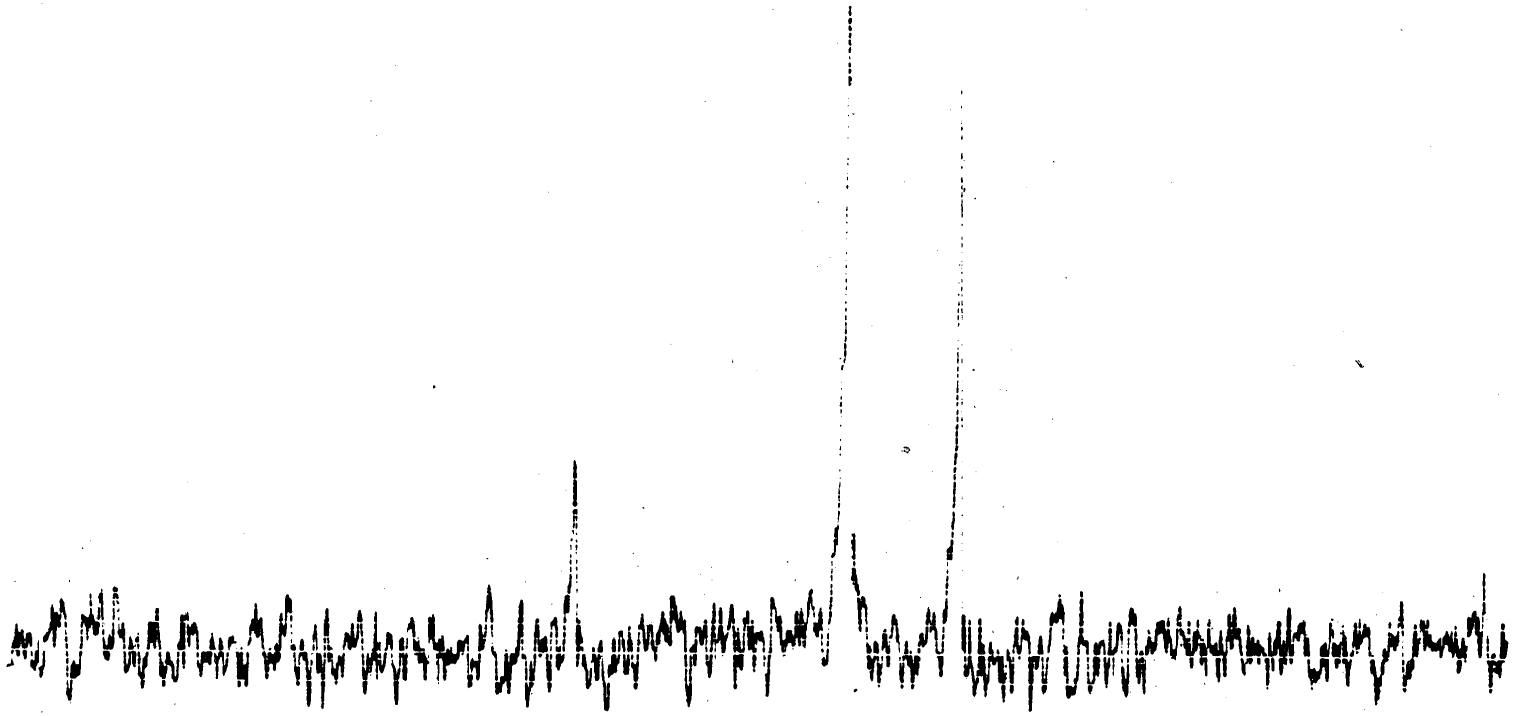
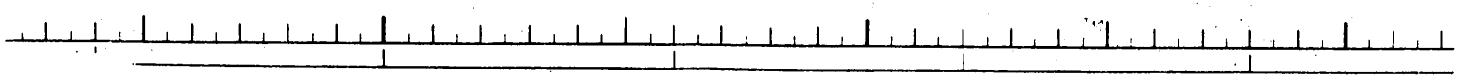


Fig. 6　C-13 NMR Spectrum of t-Butylamine



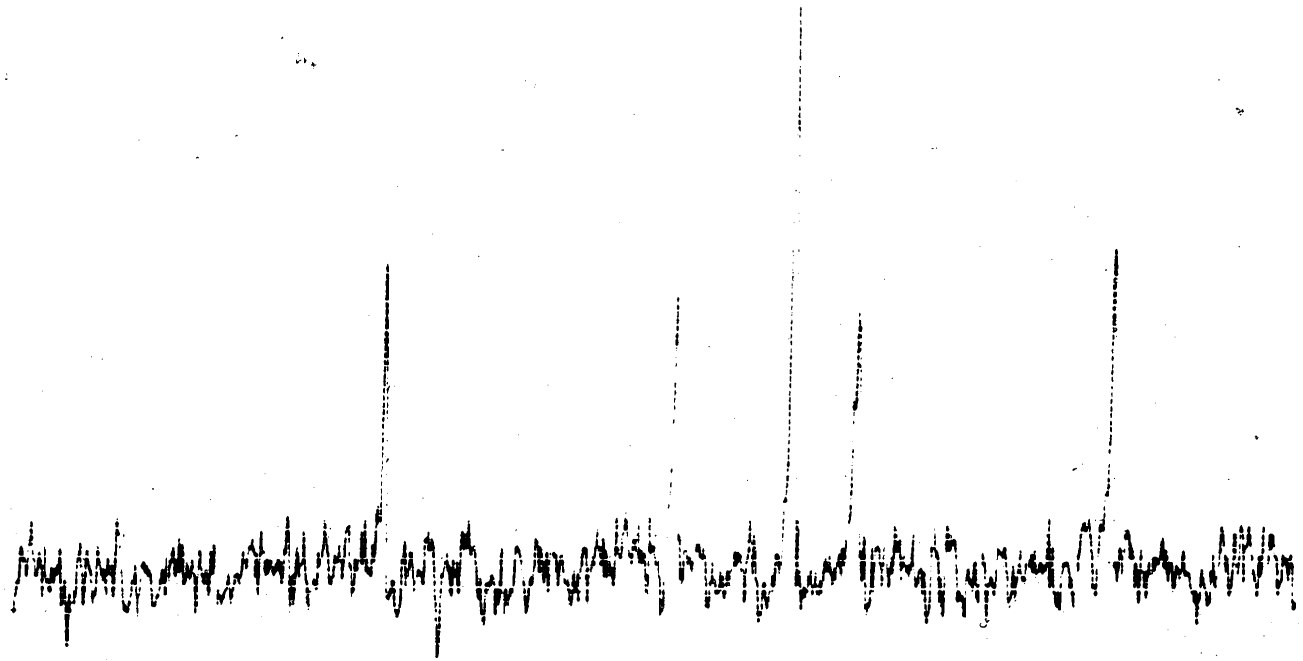
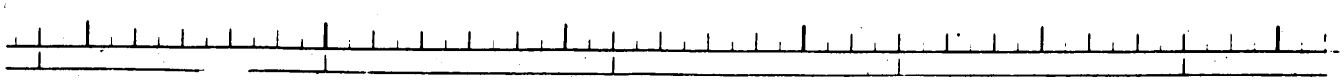


Fig. 7 C-13 NMR Spectrum of s-Butylamine



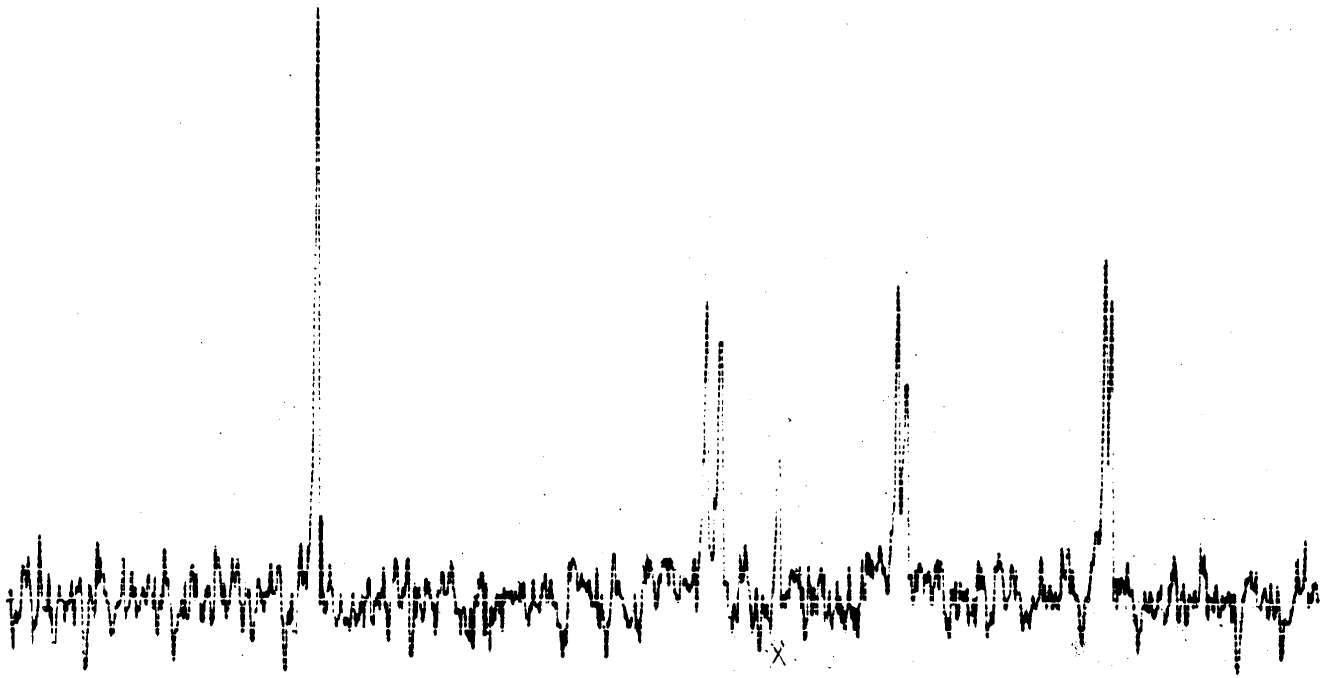


Fig. 8 C-13 NMR Spectrum of Di-s-butylamine