Tetrahedron, 1967, Vol. 23, pp. 1489 to 1497. Pergamon Press Ltd. Printed in Northern Ireland

NMR SPECTRAL STUDIES—IV[1]

SOME ^{15}N—H COUPLING CONSTANTS

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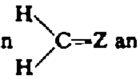
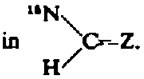
Abstract—PMR spectra of several ^{15}N-labeled compounds have been studied and values of short and long range ^{15}N—H coupling constants have been tabulated. A similarity has been observed between the geminal H—H couplings in  $(H)(H)C{=}Z$ and ^{15}N—H couplings in  $(^{15}N)(H)C{=}Z$.

THE isotope ^{15}N has a nuclear spin = ½ and no nuclear quadrupole moment. The usefulness of NMR spectra of ^{15}N-labeled compounds for valuable information about structure and stereochemistry has been recognized. For example, the keto-enol equilibrium of Schiff bases has been studied with the help of ^{15}N-enriched compounds[2] and tautomeric structures and sites of hydrogen bonding in pyrimidines,[3,4] purines,[5] and 2-picolylketones[6] have been investigated. Until recently ^{15}N—H coupling constants were reported for only a few simple compounds, lately Roberts *et al.*[7] have published ^{15}N—H coupling constants for several types of organic structures.

In the course of our mass spectral investigations[8] we have examined the PMR spectra of several ^{15}N-labeled molecules. Short and long range ^{15}N—H couplings for these compounds are discussed here (Table 1).

A. *Coupling of nitrogen-*15 *with directly bonded proton*

The nuclear spin-spin interaction of nitrogen-15 with directly bonded hydrogen was first observed in ^{15}N-labeled ammonia.[9] In the proton spectrum the ^{15}N—H coupling in $^{15}NH_3$ gives rise to two sharp lines separated by 61 ± 0·9 c/s.[10] The proton coupling to a quaternary nitrogen-15 is larger; in ammonium chloride and methylamine hydrochloride $J_{^{15}N-H}$ has been found to be 73·2 c/s and 75·6 c/s, respectively.[7]

A considerable increase in the $J_{^{15}N-H}$ value is observed in compounds where nitrogen is bonded to trigonally hybridized carbon.[7] Roberts *et al.*[7] have interpreted

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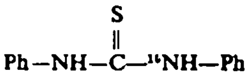
[1] Part III, A. K. Bose and I. Kugajevsky, *J. Am. Chem. Soc.* **88**, 2325 (1966).
[2] G. O. Dudek and E. P. Dudek, *J. Am. Chem. Soc.* **86**, 4283 (1964); *Ibid.* **88**, 2407 (1966).
[3] B. W. Roberts, J. B. Lambert and J. D. Roberts, *J. Am. Chem. Soc.* **87**, 5439 (1965).
[4] E. D. Becker, H. T. Miles and R. B. Bradley, *J. Am. Chem. Soc.* **87**, 5575 (1965).
[5] J. A. Happe and M. Morales, *J. Am. Chem. Soc.* **88**, 2077 (1966).
[6] G. Klose and E. Unlemann, *Tetrahedron* **22**, 1373 (1966).
[7] G. Binsch, J. B. Lambert, B. W. Roberts and J. D. Roberts, *J. Am. Chem. Soc.* **86**, 5564 (1964).
[8] A. K. Bose, I. Kugajevsky, P. T. Funke and K. G. Das, *Tetrahedron Letters* 3065 (1965).
[9] R. A. Ogg, *J. Chem. Phys.* **22**, 560 (1954).
[10] J. D. Baldeschweiler, *J. Chem. Phys.* **36**, 152 (1962).

the $^{15}N{-}H$ coupling constants in terms of the Fermi contact coupling mechanism. Except for some cases where the electron distribution around the nitrogen atom is highly anisotropic, Roberts has found a quantitative correlation between the s-character of $^{15}N{-}H$ bonds and the values of $^{15}N{-}H$ coupling constants. The calculations show that the J-values falling in range between 88 and 94 c/s correspond to s-character of 31–34%.[7]

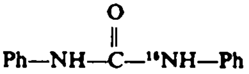
We have examined the proton spectrum of ^{15}N-labeled diphenylthiourea (I) and compared it with the spectrum of the corresponding unlabeled compound.



$Ph{-}NH{-}\overset{\overset{S}{\|}}{C}{-}^{15}NH{-}Ph$ $\quad J_{^{15}NH} = 89{\cdot}8 \pm 0{\cdot}2$ c/s

I

The spectrum (Fig. 1) shows both the ^{14}NH and ^{15}NH resonance. The ^{14}NH signal at τ 0·23 occurs at a position which corresponds to the average of the two ^{15}NH peaks. The distance between the two peaks has been measured from four runs to be 89·8 ± 0·2 c/s. A similar spectrum has been obtained for diphenylurea (II). The substitution of $\overset{\overset{S}{\|}}{{-}C{-}}$ group by a CO does not produce any noticeable change in the



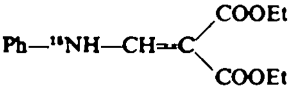
$Ph{-}NH{-}\overset{\overset{O}{\|}}{C}{-}^{15}NH{-}Ph$ $\quad J_{^{15}NH} = 89{\cdot}7 \pm 0{\cdot}1$ c/s

II

^{15}NH coupling constant.

The comparison of $J_{^{15}NH}$ in diphenylurea (II) with that of unsubstituted urea ($J_{^{15}NH} = 89 \pm 1$)[7] indicates that the replacement of one hydrogen in the $-NH_2$ group by a phenyl does not affect the magnitude of the $^{15}N{-}H$ coupling constant.

There is no significant change in the magnitude of the $^{15}N{-}H$ coupling constant when nitrogen-15 is bonded to a carbon-carbon double bond instead of a CO group as in I and II as is evident from the spectrum of diethyl anilinomethylenemalonate (III).

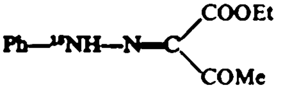


$J_{^{15}NH} = 91{\cdot}4 \pm 0{\cdot}2$ c/s

III

The doublet ($J = 91{\cdot}4 \pm 0{\cdot}2$) centered at τ −1·01, associated with the $^{15}N{-}H$ signal is further split ($J = 13{\cdot}7$ c/s) due to the coupling of the NH proton with the methine proton. The same splitting appears in the absorption of the methine proton.

We have examined the PMR spectra of ^{15}N-labeled hydrazones IV and V. The



IV

$Ph{-}^{15}NH{-}N{=}CHPh$

V

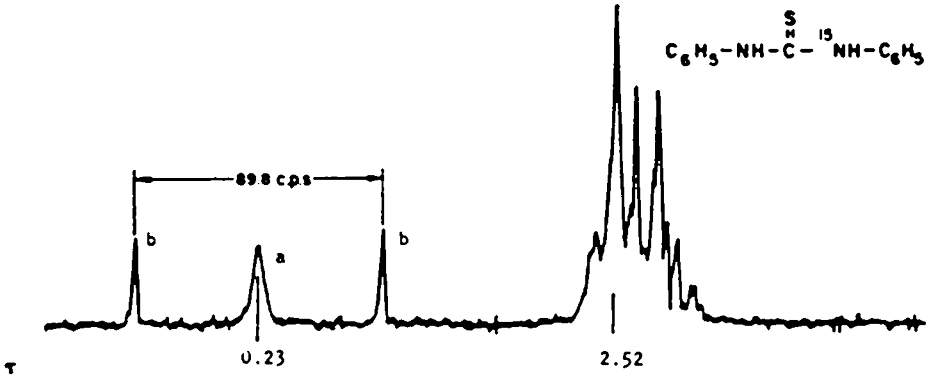
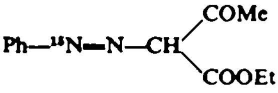


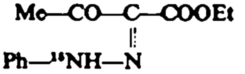
FIG. 1. PMR spectrum (DMSO-d_6) of ^{15}N-labeled diphenylthiourea
(a) ^{14}N—*H* (b) ^{15}N—*H*

^{15}N-phenylhydrazone IV was prepared by the condensation of ^{15}N-benzenediazonium chloride with ethyl acetoacetate. This condensation should result in the formation of the azo compound (VI) which is tautomeric with the hydrazone IV. It



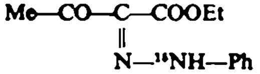
VI

has been suggested that the hydrazone is the stable form whenever condensation occurs at a methylene carbon.[11] IR absorption data[12] corroborates this view. The PMR spectrum of VI is consistent with Tanner's[12] conclusion based on IR spectra.



$$\begin{array}{l} Me-CO-C-COOEt \\ \qquad\qquad\quad \| \\ Ph-{}^{15}NH-N \end{array}$$

IVa



$$\begin{array}{l} Me-CO-C-COOEt \\ \qquad\qquad\quad \| \\ \qquad\qquad\; N-{}^{15}NH-Ph \end{array}$$

IVb

The PMR spectrum of IV contains two doublets, both corresponding to the ^{15}N—*H* signal, which is indicative of the presence of two geometrical isomers IVa and IVb. The coupling constant of the doublet centered at τ −2·61 was found to be 96·1 ± 0·3 c/s and that of the doublet centered at τ −4·83 to be 94·7 ± 0·3 c/s. The assignment of these signals in the PMR spectrum to specific structures IVa or IVb cannot be made with certainty.

^{15}N-Phenylhydrazone of benzaldehyde (V) exists only in one form this is indicated by the PMR spectrum (Fig. 2). The ^{15}N—H coupling constant for V has been measured from four runs to be 92·7 ± 0·2 c/s.

B. *Coupling of nitrogen-15 with protons separated by two or three bonds*

The ^{15}N—C—H coupling through an sp^3-hybridized carbon atom is small-ranging from 0·6 c/s in ^{15}N-benzalmethylamine to 1·4 c/s in ^{15}N-methylphthalimide.[7]

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[11] A Mustafa, W. Asker, A. H. Harhash, N. A. Messiha and M. H. Elhagdi, *Tetrahedron*, **21**, 217 (1965).

[12] E. M. Tanner, *Spectro. Chem. Acta* 20 (1959).

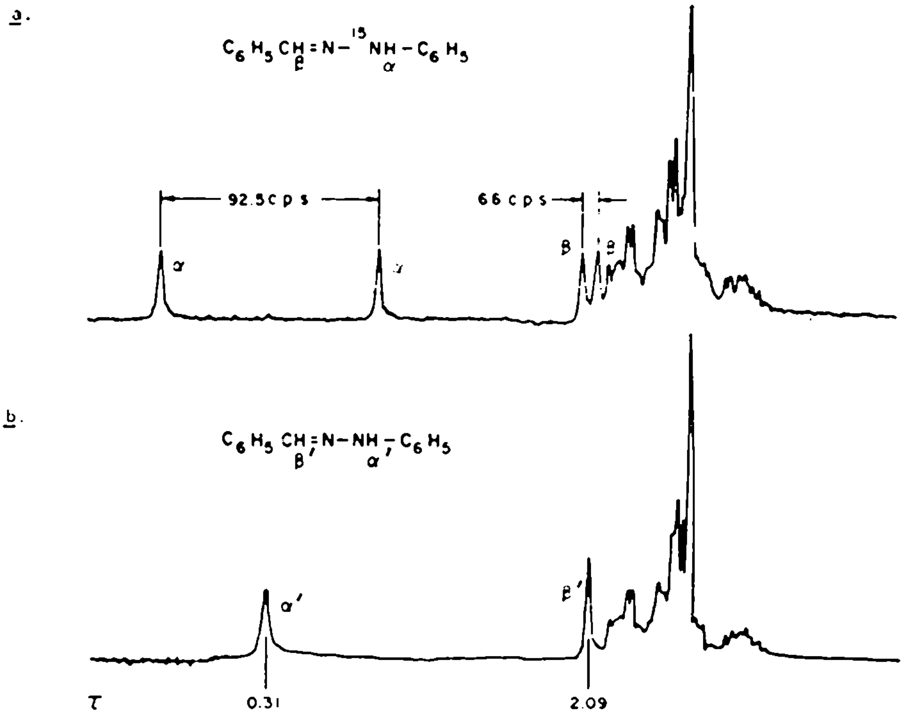
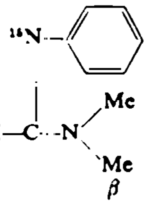


Fig. 2. PMR spectrum (DMSO-d_6) of (a) ^{15}N-labeled (b) unlabeled benzaldehyde phenylhydrazone.

The ^{15}N=C—H coupling is larger as is evident from the spectrum of N,N-dimethyl-^{15}N-phenylformamidine (VII). The singlet at τ 2·69 in the spectrum of



$J_{^{15}N=C-H} = 2·4 \pm 0·1$ c/s

$J_{^{15}N-CH_{\beta}} = 0$ c/s

VII

unlabeled N,N-dimethyl-N′-phenyl-formamidine becomes a doublet (J = 2·4 ± 0·1 c/s) in the spectrum of VII. The $J_{^{15}N=C-H}$ for benzalaniline VIII was found to be 3·8 ± 0·1 c/s. This value for the coupling constant is in agreement with that in

Ph—CH=^{15}N Ph $J_{^{15}N=C-H} = 3·8 \pm 0·1$ c/s

VIII

^{15}N-benzalmethylamine.[7]

Large ^{15}N—C—H coupling constants have been observed between the formyl proton and the nitrogen-15 in ^{15}N-formamide[13] (19·0 c/s), in ^{15}N-dimethylformamide[14]

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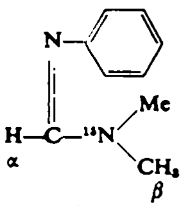
[13] B. Sunners, L. H. Piette and W. G. Schneider, *Canad. J. Chem.* **38**, 681 (1960).

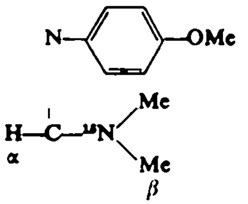
[14] A. J. R. Bourn and E. W. Randall, *J. Mol. Spectroscopy* **13**, 29 (1964).

(15·6 c/s), and in ^{15}N-n-butylformamide (15·0 and 14·3 c/s).[15] We have examined the PMR spectra of the formamidines IX, X and XI.


IX

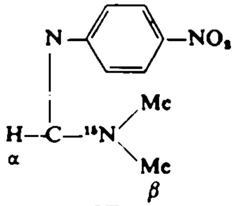
$J_{^{15}NCH_\alpha} = 8{\cdot}4 \pm 0{\cdot}1$ c/s

$J_{^{15}NCH_\beta} = 0$ c/s


X

$J_{^{15}NCH_\alpha} = 8{\cdot}3 \pm 0{\cdot}1$ c/s

$J_{^{15}NCH_\beta} = 0$ c/s


XI

$J_{^{15}NCH_\alpha} = 7{\cdot}5 \pm 0{\cdot}1$ c/s

$J_{^{15}NCH_\beta} = 0$ c/s

The ^{15}N—C—H coupling in N,N-dimethyl-^{15}N-phenyl-formamidine (IX) has been measured to be 8·4 ± 0·1 c/s (average of 6 observations). The *p*-methoxy substitution on the phenyl ring does not affect the magnitude of the ^{15}N—C—H coupling constant, since $J_{^{15}N-C-H}$ in X has been found to be 8·3 ± 0·1 c/s. A decrease of the ^{15}N—C—H coupling constant to 7·5 ±0·1 c/s has been observed in the *p*-nitro-substituted form-amidine XI.

The restricted rotation about the C—N bond in amides results in non-equivalence of the two N-methyls in the PRM spectrum of ^{15}N-dimethylformamide.[14] The N—Me protons in the spectra of formamidines IX, X, XI give rise to only a single resonance signal which is probably due to unrestricted rotation about the central C—N bond in amidines. This is consistent with the observation of Neuman and Young[16] who were not able to resolve the N—Me signal in PMR spectrum of N,N-dimethylacetamidine even on lowering the temperature to −40°.

The comparison of $J_{^{15}N-C-H}$ in formamides (15–19 c/s) with that in formamidines (7·5–8·4 c/s) indicates that the magnitude of ^{15}N spin coupling with proton on sp^2 hybridized α-carbon atom varies directly with the electronegativity of the atom linked to carbon through a double bond. Therefore we would expect $J_{^{15}N-C-H}$ to be smaller

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[15] M. T. Rogers and L. A. LaPlanche, *J. Phys. Chem.* **69**, 3648 (1965).

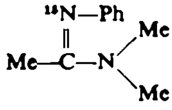
[16] R. C. Neuman, Jr. and L. Brewster Young, *J. Phys. Chem.* **69**, 2570 (1965).

if the carbon is bonded to another carbon atom through a double bond. In the spectrum of III $J_{^{15}NCH}$ was found to be approximately 0·2 c/s.

It is interesting to note that certain similarity exists between the nitrogen-15 coupling with a proton on sp^2 hybridized carbon and *gem* proton-proton coupling. It has been observed[17] that the substitution of an electronegative atom in a position α to the CH_2 group leads to a positive shift in the geminal H—H coupling constant.

In Table 2 we have listed *gem* proton-proton coupling constants and corresponding nitrogen-15-proton couplings. Diethyl anilinomethylenemalonate (III) cannot be directly compared with acrolein since the presence of extra electronegative group in the β-position may alter the magnitude of the coupling constant. However, it can be seen that there exists the same trend in the absolute values of the two sets of coupling constants. The sign of the $^{15}N—C—H$ coupling constant has been determined in the case of formamide.[19] The two types of coupling, therefore, have a large positive value when the electronegative atom is oxygen. The signs of the coupling constants are not known for the other compounds cited in Table 2.

The coupling of nitrogen-15 with the proton separated by three bonds is generally small.[7] Examination of the PMR spectrum of N,N-dimethyl-^{15}N-phenylacetamidine (XII) and comparison of it with the spectrum of the corresponding unlabeled compound indicate that the coupling of ^{15}N to the C-methyl protons is 1·1 ± 0·1 c/s.

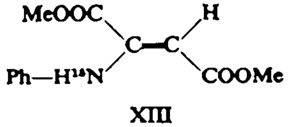


$J_{^{15}NCCH} = 1\cdot1 \pm 0\cdot1$ c/s

XII

A relatively large long range coupling has been found in ^{15}N-phenylhydrozone of benzaldehyde (V) (Fig. 2). The coupling of ^{15}N to the aldehyde proton in V was measured from four runs to be 6·6 ± 0·1 c/s. The $^{15}N—N—C—H$ coupling has not been reported in literature, however, similar coupling $^{13}C—N—C—H$ has been observed in benzalmethyl-^{13}C-amine (J = 13·2 c/s).[7]

In order to study the coupling of nitrogen-15 with the vinyl proton we have carried out the addition of ^{15}N-aniline to dimethyl acetylenedicarboxylate.[20] The *trans* addition of aniline to the triple bond would result in the formation of anilino-fumarate (XIII), the *cis* addition would produce anilinomaleate (XIV)



$J_{^{15}NH} = 91\cdot2 \pm 0\cdot4$ c/s

$J_{^{15}NC-CH} = 3\cdot5$ c/s

XIII

Recently, Dolfini[21] reported that the stereochemistry of addition of aziridine to acetylenic compounds is a function of the solvent. The product of reaction of

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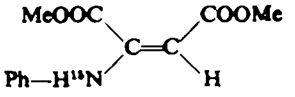
[17] J. A. Pople and A. A. Bothner-By, *J. Chem. Phys.* **42**, 1339 (1965).

[18] A. W. Douglas and J. H. Goldstein, *J. Mol. Spectra.* **16**, 1 (1965).

[19] A. J. R. Bourn, D. G. Gillies and E. W. Randall in *NMR in Chemistry* p. 277. Academic Press, New York (1965).

[20] W. C. Agosta, *J. Org. Chem.* **26**, 1724 (1961).

[21] J. E. Dolfini, *J. Org. Chem.* **30**, 1298 (1965).

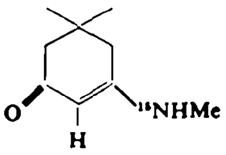

XIV

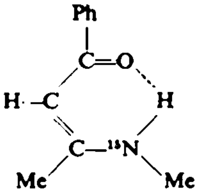
$J_{^{15}NH} = 92\cdot8 \pm 0\cdot3$ c/s

$J_{^{15}NC=CH} = 1\cdot9$ c/s

aziridine with dimethyl acetylenedicarboxylate in methanol consisted of 67% of *trans* ester and 33% *cis* ester. When dimethylsulfoxide or 1:1 cyclohexane-benzene was used as the solvent, the reaction product consisted of 95% *cis* ester.[21]

In the hope of obtaining the *cis* ester XVI, we have carried out the reaction of ^{15}N-aniline with dimethyl acetylenedicarboxylate in hexane–benzene as solvent. The PMR spectrum of the reaction product shows the presence of both isomers XIII and XIV which indicates that both *cis* and *trans* addition of aniline to the triple bond takes place under the reaction conditions used The spectrum shows two doublets due to coupling of nitrogen-15 with directly bonded protons, low field doublet (J = 91·5 ± 0·4 c/s) centered at τ 0·29 and the second doublet (J = 92·8 ± 0·3 c/s) centered at τ 2·92. Since the resonance signal of aromatic protons occurs at τ 2·78–3·50, the chemical shift of the N*H* proton in one of the isomers could not be determined from the spectrum of the unlabeled compound. Further, the spectrum of the reaction product shows two superimposed doublets at τ 4·72 and τ 4·74 which are assigned to the coupling of nitrogen-15 with vinyl protons. The two coupling constants were found to be 1·7 ± 0·1 c/s and 3·5 ± 0·2 c/s. By analogy with H—H coupling, we would expect the *cis* ^{15}N—C=C*H* coupling constant to be smaller than the corresponding *trans* coupling constant. That this is actually the case, is shown by the value of *cis* ^{15}N-vinyl coupling (1·9 c/s) in XV and *trans* ^{15}N-vinyl coupling (3·6 c/s) in XVI reported by Dudek.[8]


XV


XVI

The initially formed *cis* ester XIV on standing isomerises to the more stable *trans* ester XIII; this is evident from the PMR spectrum of the reaction product recorded the next day. The PMR spectrum shows a doublet (J = 91·2 ± 0·4 c/s) at τ 0·29 corresponding to ^{15}N—H coupling; the doublet (3·6 ± 0·2 c/s) at τ 4·74 is assigned to the *trans* ^{15}N-vinyl coupling.

The addition of ^{15}N-aniline to dimethyl acetylenedicarboxylate was repeated by carrying the reaction directly in an NMR tube using deuteriobenzene as solvent. The PMR spectrum of the additon product shows the ^{15}NH doublet (91·5 ± 0·4 c/s) centered at τ —0·16 which is assigned to the ^{15}N—H resonance of fumarate XIII. The resonance signal of the vinyl proton of XIII occurs at τ 4·36 as the doublet (J = 3·6 c/s). The doublet (J = 1·8 c/s) corresponding to the vinyl proton of maleate XIV is centered at τ 4·49. The signal at τ 4·58 is probably one of the peaks of the ^{15}N*H* doublet of the unstable *cis* isomer XIV. The PMR spectrum of the same sample recorded after several hours, shows only the presence of resonance signals attributed to the fumarate XIII. Further work on this type of addition reaction is in progress.

TABLE 1. THE NITROGEN-15-PROTON COUPLING CONSTANTS (c/s)

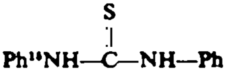
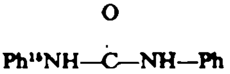
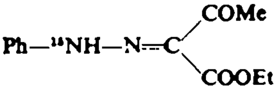
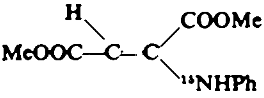
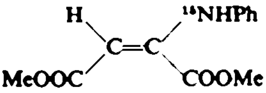
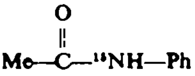
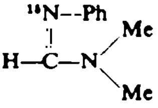
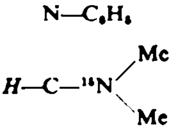
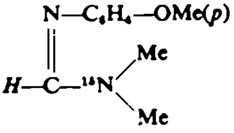
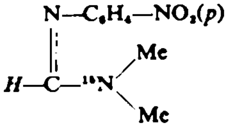
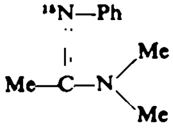
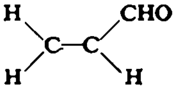
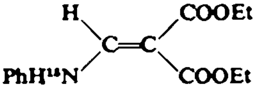
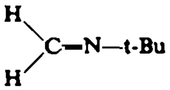
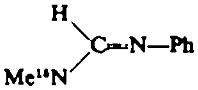
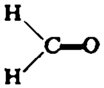
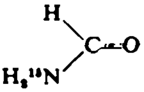
Compound	Solvent	$J_{^{15}NH}$	$J_{^{15}NCH}$	$J_{^{15}NCCH}$	$J_{^{15}NNCH}$
 $Ph^{15}NH{-}C(=S){-}NH{-}Ph$	DMSO-d_6	89·8 ± 0·2			
 $Ph^{15}NH{-}C(=O){-}NH{-}Ph$	DMSO-d_6	89·7 ± 0·1			
$Ph{-}^{15}NH{-}CH{=}C(CO_2Et)_2$	CDCl$_3$	91·4 ± 0·2			
$Ph{-}CH{=}N{-}^{15}NH{-}Ph$	DMSO-d_6	92·7 ± 0·2			6·6 ± 0·1
	CCl$_4$	94·7 ± 0·3 96·1 ± 0·3			
	CCl$_4$	91·2 ± 0·4		3·5 ± 0·2	
	CCl$_4$	92·8 ± 0·3		1·7 ± 0·1	
 $Me{-}C(=O){-}^{15}NH{-}Ph$	CDCl$_3$	89·9			
$Ph{-}CH{=}^{15}N{-}Ph$	CDCl$_3$		3·8 ± 0·1		
	CCl$_4$		2·4 ± 0·1		
	CCl$_4$		8·4 ± 0·1		
	CCl$_4$		8·3 ± 0·1		
	CCl$_4$		7·5 ± 0·1		
	CCl$_4$			1·1 ± 0·1	

TABLE 2

Gem-Proton–proton coupling constants		*Gem*-Nitrogen-15-proton coupling constants	
Compound	J_{HCH}	Compound	$J_{^{15}NCH}$
	1·0 c/s[16]		≃0·2 c/s
	16·5 c/s[17]		8·4 c/s
	+40·2 – 42·4 c/s[17]		+19·0 c/s[18]

EXPERIMENTAL

The PMR spectra were obtained with a Varian DP-60 high resolution spectrometer operating at 56·4 Mc or with a Varian A-60A spectrometer operating at 60 Mc. TMS was used as the internal standard.

The ^{15}N-labeled compounds were prepared by the procedures described in literature. The physical properties were compared with those of unlabeled compounds. ^{15}N-Aniline (97% isotopic purity) and ^{15}N-dimethylformamide (97% isotopic purity) were purchased from Merck, Sharp and Dohme of Canada.

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