

Solvent and Substituent Effects on Proton and Carbon-13 NMR Parameters of some Mono-and N,N'-Di-substituted Thioureas and Ureas

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ABSTRACT. The proton and carbon-13 NMR spectra for a number of mono-and N,N'-Di-substituted thioureas; RNHC(S)NHR' , $\text{R} \neq \text{R}'$ or $\text{R} = \text{R}' = \text{H}$, ethyl, cyclohexyl, phenyl and 1-naphthyl and some analogous ureas; RNHC(O)NHR' (for comparison), have been recorded. Substituent effects (R and R') on the ^1H chemical shifts for the H-NR (or R') group of the N,N'-disubstituted thiourea were elucidated. Determination of ^1H data for EtNHC(S)NHPh in a range of solvents reveals that the δ value of H-NEt and H-NPh is almost always shifted downfield as the donor number (DN) of the solvent increases.

The ^{13}C chemical shifts of carbon atoms for 1-naphthyl group (those other than C-1, C-9 and C-10 were deduced by comparison with known 1-substituted naphthalenes. Solvent effects on ^{13}C chemical shifts for some thiourea compounds were also checked by changing from donor solvent (DMSO-d_6) to inert solvent (CDCl_3).

Urea, thiourea, mono-substituted and N,N'-di-substituted compounds have given rise to much discussion. Most interest in this field has centered on the possibilities of making exact structural assignments using infrared spectroscopy (Gosavi *et al.* 1967, Jose 1969, Aitkin *et al.* 1971 and Mido 1972). Most of these compounds have found much use as a bidentate ligands in the field of coordination chemistry (Mandal 1974, Kasayap *et al.* 1975, Prasad and Banerji 1976 and Saha *et al.* 1982).

Collected data on these compounds indicate variations in ^1H NMR with the change of environment, and to our knowledge there is a little information available about ^1H and ^{13}C NMR spectra for thiourea derivatives (Gonzales *et al.* 1982 and Levy *et al.* 1980). Because of this, and in order to obtain additional information about substituent effects and the nature of solute-solvent interactions for some of these compounds not previously studied, we have examined the ^1H and ^{13}C NMR spectra for mono-and N,N'-di-substituted thiourea RNHC(S)NHR' in both inert

and donor solvents, as well as for some urea derivatives RNHC(O)NHR' for comparison.

Experimental

General

Natural abundance, proton-decoupled FT ^{13}C NMR spectra were recorded at 25°C on a Bruker-WH90 DS spectrometer, operating at 22.63 MHz, equipped with an Aspect 2000, 32k computer. The pulse width of 6 μs and 3s delay time were used, and between *ca.* 300 to 2000 scans (depending on the nature of the compound) were accumulated into 16k data points with a spectral width of 4807 Hz.

^1H NMR spectra were recorded on the same spectrometer (above), using the deuterium signal of the solvent as field lock signal.

Table 1. Proton chemical shifts (δ ppm)^x for the compounds RNHC(S)NHR' measured in CDCl_3

R	$\delta\text{H-NR}$	δ Others(R) ^y	R'	$\delta\text{H-NR'}$	δ Others(R') ^y
Et	6.40	$\text{CH}_3=1.26\text{t}$, $J=7.2$ Hz, $\text{CH}_2=3.32$ (b)	H	5.90	
Et	6.00	$\text{CH}_3=1.2$ t, $J=7.2$ Hz, $\text{CH}_2=3.48$ dq(a), $J=6.4$ Hz	Cy	3.94	$\text{C}_6\text{H}_{11}=1.46-2.2$ m(b)
Et	6.08	$\text{CH}_3=1.08\text{t}$, $J=7.2$ Hz, $\text{CH}_2=3.66$ dq(a), $J=6.3$ Hz	Ph	8.38	$\text{C}_6\text{H}_5=7.2-7.53$ m
Et	5.70	$\text{CH}_3=1.06\text{t}$, $J=7.2$ Hz, $\text{CH}_2=3.6$ dq(a), $J=6.3$ Hz	1-Np	8.15	$\text{C}_{10}\text{H}_7=7.46-8.1$ m
Al	6.50 ^z	$\text{C}_3\text{H}_5=4.0$ (b); 5.18–5.38 m; 5.68–6.1 m	H	6.50 ^z	
Al	6.14	$\text{C}_3\text{H}_5=4.07\text{t}$, $J=5.4$ Hz; 5.14–5.4 m; 5.7–6.12 m	Cy	3.92	$\text{C}_6\text{H}_{11}=1.24-2.08$ m(b)
Al	6.16	$\text{C}_3\text{H}_5=4.3$ t, $J=5.4$ Hz; 5.07–5.3 m; 5.7–6.14 m	Ph	8.30	$\text{C}_6\text{H}_5=7.2-7.6$ m
Al	obscured	$\text{C}_3\text{H}_5=4.2$ t, $J=5.5$ Hz; 4.88–5.08 m; 5.56–6.0 m	1-Np	8.30	$\text{C}_{10}\text{H}_7=7.46-8.1$ m
Ph	8.28	$\text{C}_6\text{H}_5=7.2-7.5$ m	H	6.20	
Ph	8.54	$\text{C}_6\text{H}_5=7.2-7.5$ m	Cy	4.26	$\text{C}_6\text{H}_{11}=1.2-2.18$ m(b)
Ph	8.24	$\text{C}_6\text{H}_5=7.24-7.42$ m	Ph	8.24	
Ph	8.10 ^z	aromatic =7.35,7.6 and 7.8–8.0 m	1-Np	8.10 ^z	

^x Downfield from internal TMS.

^y Abbreviations: s, t, p, m, dq (b) means, singlet, triplet, pentet, multiplet, doublet of quartet, and (broad) signals, respectively.

^z Overlapping between the two signals.

(a) Collapses to quartet on addition of D_2O .

Preparation of Compounds

The mono-substituted compounds, EtNHC(O)NH_2 and RNHC(S)NH_2 , R=Et, Al, Ph (BDH and Fluka) were used after recrystallization from ethanol. The di-substituted ureas, RNHC(O)NHR' , R=R'=Ph and R=Ph, R'=Cy , and the di-substituted thioureas, RNHC(S)NHR' , R=R'=Ph ; $\text{R=Et, R'=Ph, Cy, 1-Np}$; R=Ph, R'=Cy, 1-Np , were prepared by using the following standard method (Moore and Crossley 1962):

Equimolar quantities of the amino compounds (RNH_2) and the corresponding isocyanate (RNCO) or isothiocyanate (RNCS) were taken in ethanol. The mixture was heated under reflux for 10 to 90 min. The solution thus formed was kept in ice-cold water for *ca.* 30 min, and by which time a white solid started to deposit. The resulting solid was recrystallized from ethanol and dried *in vacuo* for several hours. In the case of isocyanate, the solid was obtained immediately on mixing with the amino compounds. The compounds obtained were characterized on the basis of their elemental analyses and IR spectra (Al-Allaf *et al.* 1987).

Results and Discussion

The ^1H chemical shifts for the compounds RNHC(S)NHR' , $\text{R=ethy (Et), allyl (Al), phenyl (Ph)}$; $\text{R'=H, cyclohexyl (Cy), Ph, 1-naphthyl (1-Np)}$ are listed in Table 1. The ^1H chemical shifts for both NH groups of the compound EtNHC(S)NHPh in various solvents are listed in Table 2. The ^{13}C chemical shifts for the thiourea compounds (above) and some urea compounds RNHC(O)NHR' (R=Et, R'=H ; $\text{R=Cy and Ph, R'=Ph}$) are listed in Table 3.

Table 2. Proton chemical shifts (δ ppm)^a for H-NEt(Ph) groups of the compound EtNHC(S)NHPh in various solvents

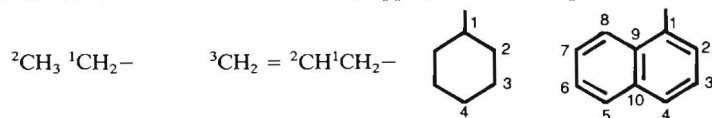
Solvent	DN ^b	$\delta\text{H-NEt}^c$	$\delta\text{H-NPh}^c$
Benzene-d ₆	0.1	5.75	9.18
CDCl_3	d	6.08	8.38
$\text{CH}_3\text{CN-d}_3$	14.1	6.61	8.18
$\text{CH}_3\text{NO}_2\text{-d}_3$	2.3	6.66	8.30
Dioxane-d ₈	14.8	6.71	8.66
Acetone-d ₆	17.0	7.18	8.77
DMSO-d ₆	29.8	7.67	9.37
Pyridine-d ₅	33.1	8.27	10.77

a- Downfield from internal TMS.

b- Donor numbers taken from (Jensen 1980).

c- Solvent effects on chemical shifts of Et and Ph protons are too small.

d- Not available.

Table 3. Carbon-13 chemical shifts (δ ppm)^a for the compounds RNHC(S)NHR'

R	Solvent ^b	C-1	C-2	C-3	C-4	CS (CO) ^c	R' = 1-Np									
							C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10
Et	DMSO	39.0	14.4			181.6	134.6	128.2	123.0	128.2	126.7 ^d	125.2 ^e	126.2 ^d	125.8 ^e	134.1	130.0
	CDCl ₃	40.3	14.5			181.5	132.1	128.9 ^d	123.0	128.6 ^d	127.5 ^e	125.4	127.2 ^e	125.9	134.7	130.0
Al	DMSO	46.3	135.0	115.3		182.0	134.5	128.1	122.8	128.1	126.7 ^d	125.3 ^e	126.1 ^d	125.7 ^e	134.0	130.0
	DMSO	139.6	124.0	128.3	124.5	181.3	135.0	128.1	123.0	128.1	126.7 ^d	125.3 ^e	126.1 ^d	125.6 ^e	133.9	129.9
R' = Ph																
H	DMSO					180.9	138.8	123.0	128.6	124.5						
Et	DMSO	38.6	14.1			180.1	139.2	123.1	128.5	123.9						
Al	DMSO	46.0	134.7	115.7		180.6	139.2	123.2	128.5	124.1						
	CDCl ₃	47.5	133.3	116.9		180.5	136.5	125.1	130.0	127.0						
Cy	DMSO	52.0	31.9	24.5	25.2	179.3	139.7	122.7	128.4	123.6						
	DMSO	(47.6)	(33.0)	(24.4)	(25.4)	(154.5)	(140.7)	(117.6)	(128.6)	(120.8)						
Ph	DMSO	139.3	123.6	128.4	124.3	179.6	139.3	123.6	128.4	124.3						
	CDCl ₃	137.3	125.3	129.6	127.1	179.9	137.3	125.3	129.6	127.1						
	DMSO	(139.9)	(118.3)	(128.8)	(121.9)	(152.6)	(139.9)	(118.3)	(128.8)	(121.9)						
R' = Al																
H	DMSO					183.2	46.1	134.9	115.4							
Cy	DMSO	51.8	32.3	24.6	25.2	181.3	45.8	135.3	115.3							
	CDCl ₃	53.2	32.9	24.8	25.5	180.7	46.8	133.7	117.3							
R' = Et																
H	DMSO					182.7	38.4	14.2								
Cy	DMSO					(159.6)	(34.3)	(15.6)								
	DMSO	51.7	32.4	24.6	25.3	180.9	38.2	14.5								

^a Downfield from internal TMS.^b DMSO used as DMSO-d₆.^c Numbers in parentheses are for RNHC(O)NHR' compounds.^{d,e} Assignment could be reversed.

¹H NMR Measurements

A recent article (Gonzalez *et al.* 1982) has discussed solvent effects on δ HN for the compounds MeNHC(S)NH_2 and $\text{Ph}_2\text{NC(S)NH}_2$. However, we found that it might be of interest to examine the ¹H NMR spectra of the compounds RNHC(S)NHR' at a standard concentration and to focus our study on the effects of both R and R' on the chemical shifts of the protons attached to nitrogen (δ H-NR or R'); (Table 1), as well as the solvent effects on δ H-NEt or Ph for the compound EtNHC(S)NHPH (Table 2).

With the compounds RNHC(S)NH_2 , the signals of the NH_2 group (*ca.* 6 ppm) appeared very close to that of H-NR, R=Et, Al, but could be distinguished by integration. On the other hand, the signals of H-NR, R=Ph or 1-NP, appeared well downfield from TMS (*ca.* 8 ppm), whereas it appeared at *ca.* 4 ppm in the case of R=Cy. This can be explained on the basis of electronegativity considerations. Therefore, it can be concluded that δ values of H-N group vary clearly with the nature of R group attached to N, and move downfield in the following sequence: alicyclic < aliphatic < aromatic.

In order to examine the solute-solvent interactions, the ¹H NMR spectrum of the compound EtNHC(S)NHPH was examined in various solvents (Table 2). It appeared that the chemical shifts are varied considerably with the donor number (DN) of the solvent used and to some extent correlate linearly with DN. Although Table 2 showed that δ H-NEt (5.75 ppm in benzene) is in agreement with DN for benzene (0.1) (Jensen 1980), δ H-NPh (9.10 ppm in benzene) is further downfield than the expected value (*ca.* 8 ppm). This suggests that benzene can form a charge-transfer complex with the compound EtNHC(S)NHPH through the phenyl group (Emsley *et al.* 1967), and this inductively affects the chemical shift of the proton attached to nitrogen (H.NPh).

The values of both δ H-NEt (6.66 ppm) and δ H-NPh (8.30 ppm) measured in $\text{CH}_3\text{NO}_2\text{-d}_3$ (DN, 2.3) are higher than those (6.61 and 8.18 ppm) measured in $\text{CH}_3\text{CN-d}_3$ (DN, 14). This could be attributed to the nature of $\text{CH}_3\text{-NO}_2$ structure; nitrogen in the nitro group is rather electronegative and hence stronger hydrogen bonding could be formed compared to that of CH_3CN .

¹³C NMR Measurements

The ¹³C NMR spectra of the compounds RNHC(S)NHR' were recorded together with some analogous urea compounds in order to examine: first, the effects of the solvent on carbon atoms of both aliphatic, aromatic and alicyclic groups attached to NH, especially the carbon atom of attachment (C-1), second; the effects of replacing CS by CO for the compounds RNHC(S)NHR' on the carbon atoms of the organic groups (above).

Carbon atoms of the simple aromatic and aliphatic nuclei were assigned easily by comparison with known compounds. With the naphthalene nucleus, the quaternary carbons, *i.e.* C-1, C-9 and C-10 were assigned by off-resonance noise decoupling, as non-proton bearing carbons, and they appeared on the spectrum as less intense than the remaining carbons (protonated) (Hansen 1979). C-1 appeared at lowest field (β -effect), and could be assigned as a result of broadening due to nitrogen quadrupole effect (dipole-dipole effect). The remaining carbons of 1-Np were assigned by comparison with other related 1-substituted naphthalenes as model compounds *e.g.* methyl (Wilson and Stothers 1974), amino, nitro and formyl (Seita *et al.* 1978), hydroxy and methoxy (Ernst 1975) naphthalenes.

However, inspection of Table 3, shows a clear change in the chemical shifts of C-1 on going from CDCl_3 to DMSO-d_6 . For example, with the compound PhNHC(S)NHAl , C-1, of C_6H_5 moves downfield by 3 ppm, C-2 and C-4 move upfield by 2 and 3 ppm respectively and to a lesser extent C-3 by 1.5 ppm, *i.e.* DMSO-d_6 affects C-1 in the opposite direction of its effect on C-2 and C-4 which may be as a result of induced polarization effect. Similar observations have been reported previously (Nelson *et al.* 1972), where it was concluded that strong solvent interactions could be taking place to the aniline on going from CCl_4 to DMSO . They, however, attributed this to hydrogen bonding and protonation, which appeared to be regular and predictable on the basis of electronic considerations.

On the other hand, the effects of solvent on the C-1 of the aliphatic (ethyl) and alicyclic (cyclohexyl) can be applied almost inversely to its effects on the aromatic species (phenyl or 1-naphthyl); *viz.* C-1 moves upfield by *ca.* 1.5 ppm on going from CDCl_3 to DMSO-d_6 and this is due to an inductive effect.

With the allyl group, C-1 and C-3 move upfield and C-2 moves downfield by *ca.* 1.5 ppm on going from CDCl_3 to DMSO-d_6 which is a result of an allylic induced polarization effect.

Table 3 also showed significant differences in the carbon chemical shifts for both ethyl, cyclohexyl and phenyl groups on going from urea compounds RNHC(O)NHR' to the analogue thiourea compounds RNHC(S)NHR' .

With aliphatic and alicyclic species, the chemical shift of C-1 usually moves downfield by *ca.* 4 ppm while C-2 moves upfield by *ca.* 1 ppm when going from urea compound to the analogues thiourea compound which could be attributed to β -effect and γ -gauche effect. The matter is different with the aromatic species, C-1 and C-3 move upfield by *ca.* 0.5 ppm (which is smaller than expected), while C-2 and C-4 move downfield by *ca.* 5 and 2.5 ppm respectively and this could be attributed to the β - and γ -resonance effect. On the other hand, the chemical shift of C(X) moves downfield by *ca.* 27 ppm on going from C(O) to C(S) . This would

result from replacing a carbonyl group by thiocarbonyl, which leads to less shielding of the nucleus (Levy *et al.* 1980). However, similar studies have been reported, dealing with ketones and thioketones (Pedersen *et al.* 1978), and a relation ($\delta \text{CS} = 1.57 \times \delta \text{CO} - 71.45$) between the values of δCS and δCO has been derived. Our findings are almost in agreement with this relationship.

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تأثير المذيب والمجموعة المعوضة على أطيف الرنين النووي المغناطيسي للبروتون والكربون - ١٣ لعدد من مركبات اليوريا والثيووريا أحادية وثنائية التعويض

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سجلت مواقع خطوط الطيف للبروتون وللكربون - ١٣ لعدد من مركبات الثيووريا أحادية وثنائية التعويض (N, \bar{N}) عندما تكون المجموعة المعوضة تمثل هيدروجين، اثيل، اليل، سيكلوهكسيل، فيل و ١ - نفتيل، إضافة إلى بعض مركبات اليوريا المناظرة (لغرض المقارنة). وقد تركزت الدراسة على تأثير المجموعة المعوضة على قيم الإزاحات الكيماوية للبروتون وللكربون - ١٣ لهذه المركبات وكذلك على تأثير المذيب على هذه القيم عند الإنحدار من الكلوروفورم إلى ثنائي مثيل سلفوكسيد كمذيب.

سجلت مواقع خطوط الطيف للبروتون لمركب واحد من الثيووريا ثنائي التعويض (حاوي على مجموعتي اثيل وفيل) في مذيبات مختلفة تتراوح ما بين مذيبات خاملة إلى مذيبات مانحة للإلكترونات حيث وجد أن قيمة الإزاحة الكيماوية لبروتون $H-NEt$ (or Ph) في الغالب تزاح إلى مجال أوطا (أكثر بعداً عن المصدر TMS) كلما ازدادت قيمة عدد المنح (DN) للمذيب.