

The NMR Spectral Characteristics of some *meso*-Ionic *s*-Triazoles

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The hetero-ring proton of *anhydro*-1,4-diphenyl-3-mercapto-*s*-triazolium hydroxide (I) is more highly deshielded than its 3-hydroxy analog (II). The chemical shifts of the hetero-ring proton for compounds I and II were found to be solvent dependent due to hydrogen bond formation. Two series of *anhydro*-1,4-diaryl-3-hydroxy-*s*-triazolium hydroxides have been synthesized and their NMR spectra determined. The chemical shift of the hetero-ring proton of these compounds was found to correlate with the Hammett sigma constants of the *meta*- and *para*- substituents in the aryl groups.

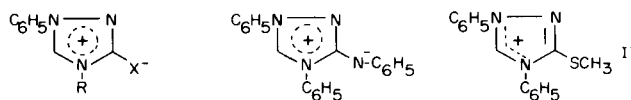
Potts, Roy and Jones (2) have recently reported that the hetero-ring protons of *anhydro*-1,4-diphenyl-3-mercapto-*s*-triazolium hydroxide (I), *anhydro*-1,4-diphenyl-3-hydroxy-*s*-triazolium hydroxide (II) and nitron (IV) are strongly deshielded. These observations provide further evidence in support of the high degree of resonance stabilization which was previously assigned (3) to these *meso*-ionic compounds on the basis of their chemical properties and Hückel LCAO calculations.

Our examination of the NMR spectra of I and II revealed that the reported chemical shift for I is apparently in error and that, contrary to the earlier report, the exocyclic sulfur atom is more effective than oxygen in deshielding the 5-proton. As seen from Table I, the difference in chemical shift ($\delta_{\text{sulfur}} - \delta_{\text{oxygen}}$) ranged from 0.30 to 0.38 ppm. in four different solvents. The greater deshielding by sulfur may be accounted for on the basis of its well-documented (4) diminished electron releasing mesomeric effect relative to oxygen. In I and II, the exocyclic sulfur and oxygen atoms are positioned for a direct mesomeric interaction with the 5-proton. Our observations are also in agreement with those of Freiberg and Kröger (5) who have established that a Hammett-type relationship correlated the chemical shift of the 5-proton with σ_p of 3-substituents in a series of 3-substituted *s*-triazoles. Their data included the 3-methoxy and 3-methylthio substituents and showed the latter to be more effective in deshielding the 5-proton.

As seen from Table I, the 5-proton in *anhydro*-1-phenyl-4-methyl-3-hydroxy-*s*-triazolium hydroxide (III) is more shielded than in the diphenyl analog (II). Methylation of the exocyclic sulfur atom of I to give 1,4-diphenyl-3-methylmercapto-*s*-triazolium iodide (V) result-

ed in enhanced deshielding of the 5-proton. These results are in accord with the predicted effects that these structural modifications would have on the electron density at the 5-position, *i.e.*, substitution of methyl for phenyl should increase electron density at the 5-position. The development of more localized positive charge would have the reverse effect.

From the data given in Table I, it is apparent that the 5-proton resonance of I and II is dependent on the structure of the solvent while the position of the phenyl resonances are essentially solvent independent. It was also observed that an increase of temperature resulted in an upfield shift of the 5-proton. In DMSO, a 19Hz upfield shift was observed for compound II on increasing the temperature from 34° to 145°. The temperature and



I, X = S; R = C₆H₅
II, X = O; R = C₆H₅
III, X = O; R = CH₃

IV

V

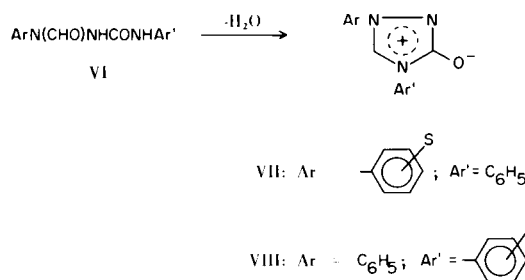


TABLE I

NMR Chemical Shifts (δ) of the 5-H in Various *s*-Triazolium
Compounds (a)

Solvent	Compound			
	I	II	III	V
nitromethane	9.51	9.13		
acetonitrile	9.56			
methanol	10.01	9.65		10.93
acetone	10.04			
<i>N,N</i> -dimethylformamide	10.40	10.10		11.38
dimethyl sulfoxide	10.41 (b)	10.08 (c)	9.38	

(a) Determined at room temperature utilizing hexamethyldisiloxane as an internal standard. (b) Reported (2) δ 8.98. (c) Reported (2) δ 10.1.

TABLE II

Solvent Effects on the Chemical Shift
for Chloroform at Infinite Dilution

Solvent	($\delta_o - \delta_m$) (a)
Nitromethane	22.6
Acetonitrile	29.2
<i>p</i> -Dioxane	35.8
Ethyl Formate	37.2
Methyl Formate	37.2
Ethyl Acetate	43.2
Tetrahydrofuran	45.2
Methanol	47.2
Acetone	53.2
Dimethylformamide	73.2
Dimethylsulfoxide	74.0
Pyridine	77.2

(a) See text.

TABLE III

($\delta_o - \delta_m$), $\Delta\nu_s$, and $-\Delta H$ as
A Measure of Hydrogen Bonding Base Strengths

	($\delta_o - \delta_m$) Hz (a)	$\Delta\nu_s$ cm ⁻¹ (b)	$-\Delta H$ Kcal (c)
	CHCl ₃	CH ₃ OD	phenol
Acetonitrile	29.2	87	4.2
<i>p</i> -Dioxane	35.8	111	4.5
Ethyl Acetate	43.2		4.8
Acetone	53.2	121	
DMF	73.2		6.4
Pyridine	77.2	213	

(a) From Table II. (b) See ref. 7. (c) See ref. 8.

solvent effects suggested that the 5-proton was hydrogen bonded to the solvent. In order to test the hydrogen bonding theory it was decided to compare the behavior of the 5-proton to that of the chloroform proton [a known hydrogen bonding acid (6)] in a series of solvents. The resonance of the chloroform proton was determined at various concentrations in a number of solvents. The shift at infinite dilution was found by extrapolation. Table II records ($\delta_o - \delta_m$) values where δ_o is the chloroform shift at infinite dilution in the solvent and δ_m is the chloroform shift at infinite dilution in cyclohexane (the shift of the non-hydrogen bonded chloroform monomer). The shifts of the 5-proton of compound I in six solvents add of compound II in four solvents were found to correlate very well with ($\delta_o - \delta_m$) values. Using an IBM 1130 computer the data were fitted to the equations:

$$\delta(\text{5-proton of I in Hz}) = 1.08(\delta_o - \delta_m) + 545 \quad (r = 0.993)$$

$$\delta(\text{5-proton of II in Hz}) = 1.11(\delta_o - \delta_m) + 524 \quad (r = 0.998)$$

r = correlation coefficient

The intercept value of 524Hz and 545Hz give the respective 5-proton shifts for the unhydrogen bonded species. The excellent correlation indicates that the 5-proton is hydrogen bonded to the solvents and suggests that ($\delta_o - \delta_m$) values may be used as a measure of the relative hydrogen bonding base strength. Table III indicates that ($\delta_o - \delta_m$) changes as a function of solvent as do other quantities used as a measure of hydrogen bonding base strengths (7).

In order to further study effects of substituents on the chemical shifts of the 5-proton, two series of compounds (VII and VIII) were synthesized in which *meta*- and *para*- substituents were separately introduced into each of the phenyl groups in *anhydro*-1,4-diphenyl-3-hydroxy-*s*-triazolium hydroxide (II). The syntheses of compounds VII and VIII were readily accomplished by thermal cyclization of the appropriately substituted 1,4-diaryl-1-formylsemicarbazides (VI). The latter procedure was first employed by Busch and co-workers (8) for the preparation of a wide variety of *meso*-ionic triazoles which, at that time, were incorrectly assigned bridged-ring *endo*-triazoline structures (9). The NMR spectra of VII and VIII were determined in dimethylsulfoxide and the chemical shifts (Table IV) of the 5-proton correlated satisfactorily with "ordinary" σ_p and σ_m constants giving the following relationships:

$$\text{for VII: } \delta(\text{Hz}) = 23.1\sigma + 587.3 \quad (n = 6, r = 0.984)$$

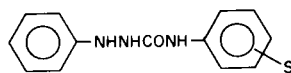
$$\text{for VIII: } \delta = 14.5\sigma + 587.1 \quad (n = 13, r = 0.962)$$

n = number of compounds

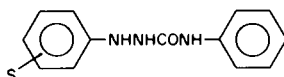
Since our study involves transmission of electronic effects through nitrogen [SC₆H₄-N-C-H], it is of interest to compare our results with those of Rae and Dyal (10) who have reported that the chemical shift of *N*-methyl protons in a series of *N,N*-dimethylanilines correlates with

TABLE IV

1,4-Diarylsenicarbazides



S	Yield %	Recrystallization Solvent	M.P. °C	Formula	Calcd.			Found		
					C	H	Other	C	H	Other
4-Br	97	acetone	204-205	C ₁₃ H ₁₂ BrN ₃ O	51.0	4.0	26.1(Br)	50.9	4.0	26.0(Br)
3-NO ₂	100	acetone-H ₂ O	208-209	C ₁₃ H ₁₂ N ₄ O ₃	57.4	4.4	20.6(N)	57.2	4.3	20.6(N)
4-NO ₂	69	EtOH	226-227	C ₁₃ H ₁₂ N ₄ O ₃	57.4	4.4	20.6(N)	57.3	4.5	20.7(N)
4-OMe	89	benzene	169-170	C ₁₄ H ₁₅ N ₃ O ₂	65.4	5.9	16.3(N)	65.2	6.0	16.1(N)
3-OMe	85	acetone-ligroin	165-166	C ₁₄ H ₁₅ N ₃ O ₂	65.4	5.9	16.3(N)	65.3	5.9	16.4(N)
4-Cl	95	EtOH	184-185	C ₁₃ H ₁₂ ClN ₃ O	59.7	4.6	13.6(Cl)	59.7	4.7	13.9(Cl)
3-Cl	84	EtOH	159-160	C ₁₃ H ₁₂ ClN ₃ O	59.7	4.6	13.6(Cl)	60.0	4.6	13.2(Cl)
4-Me	83	EtOH	207-209	C ₁₄ H ₁₅ N ₃ O	69.7	6.3	17.4(N)	69.9	6.4	17.2(N)
4-(CH ₃) ₂ N	79 (a)	EtOH	192-193	C ₁₅ H ₁₈ N ₄ O	66.6	6.7	20.7(N)	66.5	6.8	20.6(N)
4-EtO	85	EtOH	174-175	C ₁₅ H ₁₇ N ₃ O ₂	66.4	6.3	15.5(N)	66.6	6.4	15.5(N)
4-F	41	acetone-ligroin	147-148	C ₁₃ H ₁₂ FN ₃ O	63.7	4.9	7.7(F)	63.6	4.9	7.7(F)



4-Cl	76	benzene	198-199	C ₁₃ H ₁₂ ClN ₃ O	59.7	4.6	16.1(N) 13.6(Cl)	59.7	5.0	15.9(N) 13.6(Cl)
4-Br	51	acetone-H ₂ O	195-196	C ₁₃ H ₁₂ BrN ₃ O	51.0	4.0	26.1(Br)	51.0	3.7	26.0(Br)

(a) Yield based on 4-dimethylaminobenzoyl azide, see Experimental.

Hammett σ or σ^- constants by $\delta(\text{Hz}) = 10.1\sigma$ (or σ^-) + 174.7. The σ^- constants were used when the substituent was capable of a -M interaction with the dimethylamino group. In our study, larger ρ values were obtained and a good correlation was observed by the use of "ordinary" σ values.

EXPERIMENTAL (11)

NMR Measurements.

All NMR samples other than the chloroform solutions were made by saturating the desired solvent with the sample and the spectra obtained at 60 megacycles with a Hitachi-Perkin-Elmer R-20 spectrometer. The concentrations of the saturated solutions ranged from 3 to 5 mole percent. In the dilute solutions employed, the chemical shift of the 5-proton was not observed to change significantly in the concentration range 5 to 0.5 mole percent. The spectra obtained to verify the hydrogen bonding theory were

run at normal probe temperature, about 34°. The spectra run to determine the effect of ring substituents were obtained at 130° in order to increase the low solubility of the substituted compounds. All peak positions were determined with use of a frequency counter. The counter had a readability of 0.1Hz.

Preparation of 1,4-Diarylsenicarbazides (Table IV).

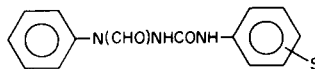
The semicarbazides were prepared by the addition of 0.02 mole of the arylhydrazine to 0.02 mole of the aryl isocyanate in 25 ml. of dry benzene. The crude products were filtered, washed with cold benzene and recrystallized. The known 1-(*p*-tolyl)-4-phenylsemicarbazide (12), 1-(3-nitrophenyl)-4-phenylsemicarbazide (13) and 1-(4-nitrophenyl)-4-phenylsemicarbazide (13) were also prepared by the above procedure.

1-Phenyl-4-(4-dimethylaminophenyl) semicarbazide.

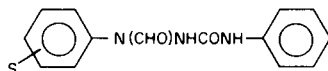
This compound was prepared by the addition of 1.5 ml. of phenyl hydrazine to a solution of 4-dimethylaminophenyl isocyanate prepared *in situ* by heating 1.5 g. of 4-dimethylaminobenzoyl azide (14) in 10 ml. of toluene for 3 hours. The crude product separated immediately and was washed with cold benzene.

TABLE V

1-Formyl-1,4-diaryl semicarbazides



S	Reaction Time (Hrs.)	Recrystallization Solvent	M.P. °C	Yield %	Formula	Calcd.			Found		
						C	H	Other	C	H	Other
4-Br	5.0	isopropanol	195-196	77	C ₁₄ H ₁₂ BrN ₃ O ₂	50.3	3.6	23.9(Br)	50.3	3.9	23.8(Br)
3-NO ₂	5.0	acetone	197-199	63	C ₁₄ H ₁₂ N ₄ O ₄	56.0	4.0	18.6(N)	56.3	4.3	18.8(N)
4-NO ₂	7.5	EtOH	226-227	59	C ₁₄ H ₁₂ N ₄ O ₄	56.0	4.0	18.6(N)	56.0	4.1	18.6(N)
4-OMe	4.5	MeOH	147-149	39	C ₁₅ H ₁₅ N ₃ O ₃	63.2	5.3	14.7(N)	63.4	5.4	14.5(N)
3-OMe	4.5	EtOH	122-123	43	C ₁₅ H ₁₅ N ₃ O ₃	63.2	5.3	14.7(N)	63.4	5.3	14.8(N)
4-Cl	4.5	EtOH	192-193	69	C ₁₄ H ₁₂ ClN ₃ O ₂	58.0	4.2	12.2(Cl)	58.2	4.3	12.5(Cl)
3-Cl	4.5	EtOH	184-185	82	C ₁₄ H ₁₂ ClN ₃ O ₂	58.0	4.2	12.2(Cl)	58.0	4.1	12.4(Cl)
4-Me	4.5	EtOH	178-180	64	C ₁₅ H ₁₅ N ₃ O ₂	66.9	5.6	15.6(N)	66.8	5.9	15.5(N)
3-Me	4.5	EtOH	144-145	59	C ₁₅ H ₁₅ N ₃ O ₂	66.9	5.6	15.6(N)	67.0	5.4	15.9(N)
4-(CH ₃) ₂ N	3.5	EtOH	160	72	C ₁₆ H ₁₈ N ₄ O ₂	64.4	6.1	18.8(N)	64.5	5.8	18.5(N)
4-EtO	4.5	EtOH	140-141	69	C ₁₆ H ₁₇ N ₃ O ₂	64.2	5.7	14.0(N)	64.1	6.0	14.0(N)
4-F	4.5	EtOH	185-187	61	C ₁₄ H ₁₂ FN ₃ O ₂	61.5	4.4	17.0(F)	61.6	4.6	7.0(F)



4-CH ₃	4.5	EtOH	190-191	78	C ₁₅ H ₁₅ N ₃ O ₂	66.9	5.6	15.6(N)	66.9	5.3	15.8(N)
3-NO ₂	5.0	Xylene	165-166	77	C ₁₄ H ₁₂ N ₄ O ₄	56.0	4.0	18.6(N)	55.8	4.2	18.3(N)

The following compounds were prepared by published procedures and had melting points in agreement with literature values: *anhydro*-1,4-diphenyl-3-hydroxy-*s*-triazolium hydroxide (8), *anhydro*-1,4-diphenyl-2-mercapto-*s*-triazolium hydroxide (8), *anhydro*-1-phenyl-4-methyl-3-hydroxy-*s*-triazolium hydroxide (3) and 1,4-diphenyl-3-methylthio-*s*-triazolium iodide (8).

Preparation of 1-Formyl-1,4-diarylssemicarbazides (Table V).

The semicarbazides were refluxed and stirred in 97+% formic acid (10 ml./g.) for the times indicated in Table V. The products were isolated by pouring the reaction mixtures into water. The filtered products were washed with water prior to recrystallization. 1-Phenyl-4-(4-dimethylaminophenyl)semicarbazide was precipitated from the diluted reaction mixture after basification with sodium carbonate. When the 1-(4-nitrophenyl)-4-phenylsemicarbazide, 1-(4-chlorophenyl)-4-phenylsemicarbazide and 1-(4-bromophenyl)-4-phenylsemicarbazide were refluxed in formic acid overnight, the melting points of the crude products indicated that cyclization had occurred. Recrystallization of these crude products from DMF afforded the *meso*-ionic triazoles in the yields reported in Table VI.

Anhydro-3-hydroxy-1,4-diaryl-*s*-triazolium Hydroxides (Table VI)

With the exception of the three cases cited above, the formylated semicarbazides were cyclized by heating at the temperatures

indicated in Table VI for approximately 15 minutes.

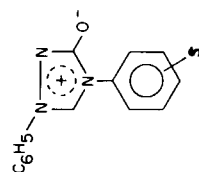
Acknowledgement.

Acknowledgement is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society and to the Research Foundation of the State University of New York for support of this project. The authors are indebted to Mr. Kenneth Fleisher of the Sterling Winthrop Research Institute for microanalyses.

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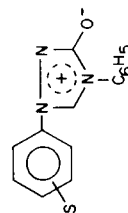
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TABLE VI

meso-Ionic *s*-Triazoles

S	Reaction Temp. °C	Yield (a)	Recrystallization Solvent	M.P. °C	Formula	Calcd.			Found			CHEMICAL SHIFT δ (cps) (b)
						C	H	Other	C	H	Other	
4-Br	220	60	DMF (c)	361-363	$C_{14}H_{10}BrN_3O$	53.2	3.2	25.3(Br)	53.0	3.3	25.2(Br)	593.3
3-NO ₂	(d)	22 (e)	DMF	291-294	$C_{14}H_{10}N_4O_3$	59.6	3.6	19.8(N)	59.9	3.8	19.9(N)	598.6
4-NO ₂	260	90	DMF	353-355	$C_{14}H_{10}N_4O_3$	59.6	3.6	19.8(N)	59.5	3.5	19.5(N)	598.6
4-OMe	210	77	MeOH	288-289	$C_{15}H_{13}N_3O_2$	67.4	4.9	15.7(N)	67.4	5.0	15.6(N)	582.7
3-OMe	240	64	DMF-ether	193-194	$C_{15}H_{13}N_3O_2$	67.4	4.9	15.7(N)	67.6	4.8	16.0(N)	587.3
4-Cl	230	63	DMF	353-354	$C_{14}H_{10}ClN_3O$	61.9	3.7	13.1(Cl)	61.9	4.1	13.3(Cl)	589.4
3-Cl	250	51	DMF	251-252	$C_{14}H_{10}ClN_3O$	61.9	3.7	13.1(Cl)	62.1	3.7	13.2(Cl)	592.4
4-Me	250	48	DMF	300-301	$C_{15}H_{13}N_3O$	71.7	5.2	16.7(N)	71.7	5.3	16.7(N)	583.2
3-Me	250	86	DMF-ether	264-266	$C_{15}H_{13}N_3O$	71.7	5.2	16.7(N)	71.4	5.5	(f)	583.8
4-(CH ₃) ₂ N	220	66	DMF	297-298	$C_{16}H_{16}N_4O$	68.6	5.8	20.0(N)	68.2	6.0	19.7(N)	578.2
4-EtO	280	54	DMF-ether	259-260	$C_{16}H_{15}N_3O_2$	68.3	5.4	14.9(N)	68.5	5.2	14.9(N)	581.6
4-F	225	59	DMF	310-314	$C_{14}H_{10}FN_3O$	65.9	4.0	7.4(N)	66.0	3.7	7.6(F)	588.6
4-Me	230	78	DMF	309-310	$C_{15}H_{13}N_3O$	71.7	5.2	16.7(N)	71.6	5.1	16.6(N)	584.3
4-NO ₂	(d)	7 (e)	DMF	382-383	$C_{14}H_{10}N_4O_3$	59.6	3.6	19.8(N)	59.5	4.0	19.9(N)	605.2
4-Cl	(d)	73 (e)	DMF	362-363	$C_{14}H_{10}ClN_3O$	61.9	3.7	13.1(Cl)	61.8	3.8	12.9(Cl)	591.2
3-NO ₂	200	94	DMF	343-344	$C_{14}H_{10}N_4O_3$	59.6	3.6	19.8(N)	59.7	3.4	19.9(N)	605.3
4-Br	(d)	83 (e)	DMF	353-354	$C_{14}H_{10}BrN_3O$	53.2	3.2	25.1(Br)	53.3	3.2	25.1(Br)	599.4

(a) Recrystallized yields. (b) Determined in DMSO utilizing hexamethyldisiloxane as the internal standard (see Experimental). The unsubstituted compound (S = H) had 588.7. (c) Dimethylformamide. (d) Obtained directly on formylation (see Experimental). (e) Yield based on the semicarbazide. (f) Satisfactory nitrogen analyses could not be obtained on this compound. Found: 14.87, 14.83, 14.64, 15.03.



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and are uncorrected. Analyses are by Mr. K. Fleischer of the Sterling-Winthrop Research Institute.

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Received January 1, 1970

Geneseo, N. Y. 14454