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SHORT COMMUNICATION

POTENTIOMETRIC AND SPECTROSCOPIC INVESTIGATIONS OF THE AQUEOUS PHASE ACID–BASE CHEMISTRY OF URAZOLES AND SUBSTITUTED URAZOLES

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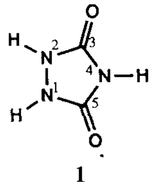
Aqueous-phase equilibrium acidity constants have been determined for urazole (1,2,4-triazolidine-3,5-dione), several substituted urazoles and other selected imides. Aqueous phase $\mathrm{p}K_a$ values for urazole (5·8), 1-methylurazole (5·3), 4-methylurazole (5·7) and 1,4-dimethylurazole (5·3) indicate that (in water) the methyl group acidifies the urazole moiety when bonded to N-1 but has little effect on acidity when bonded to N-4. Aqueous phase $\mathrm{p}K_a$ values for hydantoin (9·0) and 1-methylhydantoin (9·1) suggest that a 1-methyl substituent has little effect on the acidity of the imide proton present in hydantoin. These data, combined with aqueous phase $\mathrm{p}K_a$ values for 1,2-dimethylurazole (7·5), a substituted urazole lacking amide protons, indicate that an amide proton in urazole (i.e. the proton bound to either N-1 or N-2 in urazole) is *ca* 1·5 $\mathrm{p}K_a$ units more acidic than the imide proton (i.e. the proton bound to N-4). Changes in ^{13}C NMR chemical shifts for the carbonyl carbon atoms present in variously substituted D_2O phase urazoles, hydantoins, succinimide and their conjugate bases also confirm that amide N—H bonds found in urazole and 1-methylurazole are weaker, in a heterolytic acid–base sense, than imide N—H bonds.

razole (1,2,4-triazolidine-3,5-dione) (**1**) and 1- bstituted urazoles contain two varieties of protons: e proton(s) bonded to the N-1 and/or N-2 [i.e. the mide proton(s)] and the proton bonded to N-4 (i.e. the nide proton). Without reference to which proton is ost sensitive to base, Gordon and Audrieth[1] deter- ined that the aqueous phase $\mathrm{p}K_a$ of urazole was 5·8. he acidic nature of urazoles has been exploited in fforts aimed at rendering polybutadienes water sol- ble. For example, when suitably substituted triazoline- iones are allowed to react with various olybutadienes, the urazole-substituted polyenes that result are soluble in alkaline (aqueous) solution,[2] partly because models for the pendant urazolyl moieties in these polymers have been shown to have $\mathrm{p}K_a$ values similar to that of acetic acid.[3] Other aqueous phase $\mathrm{p}K_a$ values for substituted urazoles given in the literature include 1-phenylurazole (4·85), 1-phenyl-4-methylurazole (4·73) and 1-methyl-2-phenylurazole (6·97).[4] Based on these data, Gordon and Katritzky[4] suggested that the ratio of the two possible anions formed when 1-phenylurazole is deprotonated is about 100:1 in favor of the anion that results when the amide proton in 1-phenylurazole is removed.



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In this paper we report studies in which we have (a) duplicated the previous aqueous phase value for the $\mathrm{p}K_a$ of urazole, (b) measured aqueous phase $\mathrm{p}K_a$ values for four methylated urazoles and (c) collected ^{13}C NMR data for the urazoles and their respective conjugate bases. These data, combined with acidity and spectroscopic data for hydantoin (**2**), 1-methylhydantoin and succinimide (**3**), provide conclusive evidence that the most acidic proton in urazole (**1**), when dissolved in water, is the amide and not the imide proton.

Aqueous phase $\mathrm{p}K_a$ values for urazole, four methylated urazoles, hydantoin, 1-methylhydantoin

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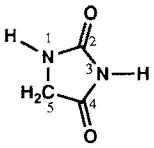

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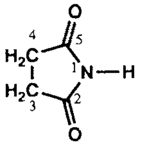

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and succinimide are listed in Table 1. Inspection of the data reveals that our value for the aqueous phase pK_a of urazole (5·8) is identical with that previously reported.[1] Urazole and 1-methylurazole (pK_a = 5·3) are similar in that protons attached to both amide and imide nitrogens are found in these species. On the other hand, 4-methylurazole and 1,4-dimethylurazole (pK_a = 5·7 and 5·3, respectively) possess only amide NH protons. Comparison of the pK_a data for 4-methylurazole and 1,4-dimethylurazole indicates that substitution of a methyl group for hydrogen on N-1 in 4-methylurazole acidifies the urazolyl moiety (via a weakening, in a heterolytic sense, of the adjacent amide N—H bond) by 0·4 pK_a units. Conversely, 4-methyl substituents appear to have little or no effect on urazole acidities.

Also given in Table 1 are pK_a values for three species that possess only imide NH protons (1,2-dimethylurazole, 1-methylhydantoin and succinimide), together with the value for hydantoin itself. The pK_a values for succinimide (9·5) (literature value[6] 9·7), hydantoin (9·0) (literature value[6] 9·5) and 1,2-dimethylurazole (7·5) indicate that successive replacement of methylene groups with nitrogen atoms acidifies (in aqueous solution) the resulting imide by about 0·5–1·5 pK_a units. A solvent effect due to water is operative here since the dimethyl sulfoxide (DMSO) phase pK_a values for succinimide (14·75[7]) and hydantoin [15·0[8] (comparison of the DMSO and aqueous phase data suggest that the relative aqueous phase acidities of the amide and imide urazole protons is the result of an aqueous solvent effect)] are in an opposite order.

It is instructive to compare the aqueous phase pK_a values for 1,2-dimethylurazole (7·5) and 1,4-dimethylurazole (5·3). Evidently, the anion that results when 1,4-dimethylurazole is deprotonated is more stable than the anion derived from 1,2-dimethylurazole, an order similar to that observed for the anions derived from 1-phenyl-4-methylurazole and 1-methyl-2-phenylurazole.[4] Since 1-methylhydantoin (pK_a = 9·1) is 0·1 pK_a units less acidic than hydantoin, we estimate that the pK_a of the imide proton in urazole is 7·3 [7·3 = 7·5 − (2 × 0·1)], where 7·5 and 0·1 refer to the pK_a of 1,2-dimethylurazole and to the estimated effect of each of the two methyl groups on the imide NH acidity of 1,2-dimethylurazole. These data indicate that

Table 1. N—H equilibrium acidity constants (pK_a, in aqueous solution[a]) for urazole, substituted urazoles and other imides and aqueous phase ^{13}C chemical shifts for the carbonyl carbon atoms[b] present in urazoles, substituted urazoles and other imides and the conjugate bases derived from these species[c]

		Aqueous phase carbonyl ^{13}C chemical shifts (ppm)					
		C(O) in HA		C(O) in A$^-$		Δ[HA − A$^-$]	
Acid (HA)	pK_a	A	B	A	B	A	B
Urazole (**1**)	5·8	158·9	158·9	161·2	161·2	−2·3	−2·3
1-Methylurazole	5·3	157·2	156·7	159·9	156·3	−2·7	+0·4
4-Methylurazole	5·7	158·8	158·8	159·5	159·5	−0·7	−0·7
1,4-Dimethylurazole	5·3	157·4	156·9	159·8	155·9	−2·4	+1·0
1,2-Dimethylurazole	7·5	156·6	156·6	169·9	169·9	−13·3	−13·3
Hydantoin (**2**)	9·0	179·5	162·9	192·8	176·6	−13·3	−13·7
1-Methylhydantoin	9·1	177·7	161·3	191·6	175·2	−13·9	−13·9
Succinimide (**3**)	9·5	185·9	185·9	202·3	202·3	−16·4	−16·4

[a] Aqueous phase pK_a determinations at 25 ± 1 °C: (a) A Fisher Model 930 pH meter was standardized using a two-point (pH 7 and 10) buffer system; (b) nitrogen acids were titrated against aqueous KOH (0·1 M); (c) pK_a values obtained via the method described by Albert and Sergeant.[5] At least two trials were performed for each acid, and the initial nitrogen acid concentrations were 0·1 M. The standard deviations for the collected pK_a values within a given run were generally $\leqslant$0·06. We therefore estimate that the listed pK_a values are accurate to ±0·1 pK_a unit. The Debye–Hückel correction to zero ionic strength has not been applied to these data.

[b] The designations A and B for each carbonyl carbon atom refer to C-3 and C-5 for the urazoles, C-4 and C-2 for the hydantoins and C-2 and C-5 for succinimide.

[c] A Varian VXR-300 MHz spectrometer was used to collect the NMR data. The D_2O phase neutral species were present at concentrations of 0·3 M; DSS [3-(trimethylsilyl)-1-propanesulphonic acid, sodium salt], an NMR reference, was present at a concentration of 0·05 M. The total NMR tube solution volumes were about 0·7 ml. The conjugate bases of the various nitrogen acids were generated by allowing, in the NMR tube, the respective acids to react with aqueous KOH (1 equivalent, 2.5 M). All spectra were collected at 25 ± 1 °C.

the aqueous phase ΔpK_a for amide and imide protons in urazole is about 1·5 pK_a units. These data also suggest that the most acidic proton in 1-methylurazole is the proton bound to N-2. Therefore, it appears that the same variety of proton (i.e. an amide proton) is lost when urazole, 1-methylurazole, 4-methylurazole and 1,4-dimethylurazole are allowed to react, in aqueous solution, with KOH (1 equivalent).

Table 1 gives the ^{13}C NMR chemical shifts for the carbonyl carbons present in D_2O phase substituted urazoles, hydantoins and succinimide and the conjugate bases derived from these species. The shift for the neutral succinimide, hydantoin and urazole species indicate that the carbonyl carbons are shielded by successive replacement of succinimide methylene groups with nitrogen. Also of interest are the relative values of the chemical shifts for each carbonyl carbon found in 1,4-dimethylurazole [C-3(O) = 157·4 ppm; C-5(O) = 156·9 ppm; $\Delta = 0{\cdot}5$ ppm]; the similarity of these values is suggestive of little or no tautomerization in 1,4-dimethylurazole (and also 1-methylurazole, where an identical 0·5 ppm difference is observed for the chemical shifts of the two carbonyl carbons).

Further inspection of the chemical shift data in Table 1 reveals that the carbonyl carbons present in 1,2-dimethylurazole, 1-methylhydantoin and succinimide are, on deprotonation, deshielded by amounts ranging from 13·3 to 16·4 ppm. Common to these species is an acidic imide proton. On the other hand, chemical shift data for the carbonyl carbon atoms found in 4-methylurazole indicate, on deprotonation, a deshielding effect of only 0·7 ppm, whereas similar data for 1,4-dimenthylurazole indicate that C-3 is deshielded by 2.4 ppm, whereas C-5 is shielded by 1·0 ppm. Common to 4-methylurazole and 1,4-dimethylurazole is the presence of an acidic amide proton. Arguments based on the aqueous phase acidity data in Table 1 suggested that amide protons found in urazole and 1-methylurazole are more acidic than imide protons present in the same species. The chemical shift data in Table 1 for urazole and 1-methylhydantoin and succinimide, are supportive of this claim: deprotonation of urazole results in a 2·3 ppm deshielding of the carbonyl carbons, whereas deprotonation of 1-methylurazole results in a 2·7 ppm deshielding of C-3 and a 0·4 ppm shielding of C-5. The NMR data for urazole, 1-methylurazole and their conjugate bases are thus very similar to those obtained for 4-methylurazole and 1,4-dimethylurazole. Therefore, both the pK_a and the NMR data support the supposition that, in aqueous solution, amide N—H bonds in urazole and substituted urazoles are more sensitive than imide N—H bonds to hydroxide.

We are currently investigating DMSO phase NH acidities and homolytic bond dissociation energies of substituted urazoles. Preliminary results indicate that, in DMSO, amide and imide protons in urazole are of nearly equal thermodynamic acidity ($pK_a \approx 13$),[8] but that the amide N—H bond in urazole is about 15 kcal mol^{-1} weaker (in a homolytic sense) than the imide N—H bond in urazole.[9] Further examination of solvent effects on the acid–base chemistry of substituted urazoles and investigations of polymers that contain urazoles are in progress. In collaboration with Prof. Taft (University of California–Irvine), studies of the intrinsic (gas-phase) acidities of substituted urazoles are also in progress.

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