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Synthesis and properties of novel acetamidinium salts

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Acetamidines are starting materials in the synthesis of many chemicals, some of which go on to be used for synthesis of biochemically active compounds and energetic materials. Acetamidinium chloride, which is hygroscopic, is currently one of the only commercially available acetamidinium salts. The aim of this study was to synthesize a range of acetamidinium salts that will allow the inconvenience associated with acetamidinium chloride to be avoided. The acetamidinium salts were characterized with elemental analysis, mass spectrometry, NMR and, in the case of energetic salts, differential thermal analysis. The structures of several previously unknown acetamidinium salts were determined by X-Ray diffraction analysis. Hygroscopicities of eight of the acetamidinium salts were monitored over time at 90% humidity. The different hygroscopicity values obtained were corroborated by the results of crystal structure analysis. We found that two-dimensional (2D) layered structures were not highly hygroscopic. These were the nitrate, formate, oxalate, and dinitromethanide acetamidinium salts. However, compounds with a 3D-type structure containing rather large cavities were highly hygroscopic. These were the chloride, acetate, sulfate, and perchlorate acetamidinium salts.

Introduction

Acetamidines are used as starting reagents in the synthesis of a number of chemicals, such as imidazoles, pyrimidines, and triazines, which are then used for synthesis of biochemically active compounds.[1](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/#B1)-[5](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/#B5) In the field of energetic materials, acetamidine is employed in the synthesis of 2-methoxy-2-methylimidazolidine-4,5-dione[6](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/#B6) and 2-methylpyrimidine-4,6-diol.[7](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/#B7)-[9](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/#B9) Both are further transformed to 2,2-dinitro-1,1-ethenediamine, also known as FOX-7 or DADNE, which is an explosive with low sensitivity to external stimuli.[6](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/#B6),[10](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/#B10)

The free-base form of acetamidine is hygroscopic and decomposes into ammonia and acetonitrile at higher temperatures.[11](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/#B11) Acetamidinium carbonate is formed within 24 h when acetamidine is exposed to air at room temperature.[12](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/#B12) It is therefore unsuitable as a starting material, so use of an acetamidinium salt is necessary for synthetic reactions.

Acetamidinium chloride (**1**) is the most commonly used salt of acetamidine and is commercially available. It is prepared by the Pinner method from acetonitrile and alcohol in the presence of hydrogen chloride. Ammonia is added to the iminoether intermediate to yield **1**.[13](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/#B13) Reaction of acetonitrile with cobalt or nickel nitrates and oximes yields acetamidinium nitrate (**2**).[14](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/#B14),[15](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/#B15) Another acetamidine salt, acetamidinium acetate (**3**), is readily prepared from triethyl orthoacetate, ammonia, and ammonium acetate.[16](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/#B16) This method is convenient for both laboratory and industrial-scale synthesis, and the acetate may be further transformed to yield other salts, such as the formate (**4**)[17](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/#B17), sulfate (**5**)[18](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/#B18), and dinitromethanide salts (**6**).[19](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/#B19) Many synthetic routes for acetamidines have been reviewed [20](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/" \l "B20),[21](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/" \l "B21).

The main disadvantage of acetamidinium chloride is that it is relatively hygroscopic. The formation of the free base in methanol by using sodium methoxide produces sodium chloride, which is partially soluble in the solvent (~1 g/100 mL).[22](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/#B22) The presence of any chloride source is unfavorable in certain syntheses, such as nitrations, and the complete removal of chloride is tedious.[6](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/#B6)

Here we describe the synthesis, crystal structure, hygroscopicity, and thermal stability of several of the acetamidine salts shown in Fig. [​1](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/figure/F1/" \t "figure).

Results and discussion

Synthesis

We previously reported a procedure for the preparation of acetamidinium sulfate (**5**) from **1** via an ion exchange reaction.[22](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/#B22) We used this procedure to synthesize **2**, as well as acetamidinium oxalate (**7**). Thus, it may be considered a universal method for the preparation of acetamidine salts from **1**(Fig. [​2](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/figure/F2/)).

Based on a previously reported method for the preparation of (**5**),[18](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/" \l "B18) starting from acetamidine acetate and based on the reaction of the latter with an acid stronger than acetic acid, we obtained acetamidinium perchlorate (**8**) from **3** and perchloric acid. We also prepared **8** from **5** by an ion exchange reaction with barium perchlorate in water (Fig. [​3](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/figure/F3/" \t "figure)).

Acetamidinium formate (**4**) was prepared from trimethyl orthoacetate and ammonium formate. A similar method has been published by Taylor for preparation of **3.**[16](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/#B16)

Hygroscopicities

Hygroscopicities of acetamidinium salts were determined at 90% humidity and 30 °C[23](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/#B23) and were compared with those of ammonium acetate (**10**), guanidinium nitrate (**11**) and guanidinium chloride (**12**); the hygroscopicities were represented as the percent weight increase compared with the weight of the original sample. The results are shown in Fig. [​4](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/figure/F4/), and the values for certain days are presented in Table [1](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/table/T1/). In the case of compounds with known structures determined by X-Ray diffraction (XRD) analysis, information about the spatial structure is also included. The influence of the structure on hygroscopicity is discussed later in this report.

X-Ray crystallography

Acetamidinium cations may serve as counterions for a wide variety of anions, like simple halides, carboxylates, and complex metal anions. The parent acetamidine is characterized by large cavities and an extensive network of hydrogen bonding within its structure. The distances between the pivot carbon atom and the amino and amido nitrogen atoms are 1.344 Å and 1.298 Å, respectively.[24](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/#B24) The hydrogen bridging observed in acetamidinium chloride (**1**),[26](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/" \l "B26) acetamidinium sulfate (**5**),[18](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/" \l "B18) and an acetamidinium (2-hydroxyethoxy)acetate polymorph[25](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/#B25) results in three-dimensional (3D) structures with large cavities. On the other hand, acetamidinium tetrazolate[27](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/#B27) and acetamidinium dinitromethanide (**6**)[19](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/#B19) are two-dimensional (2D), staircase-like structures. Acetamidinium hexafluorosilicates, germanates, stannates, and titanates[28](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/#B28) are interesting examples of 2D structures. Other examples include Re-Se cluster-acetamidinium adducts,[29](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/#B29) in which multicenter NH...F or NH...Se contacts are found.

In this study, we used XRD analysis to determine the crystal structures of several acetamidinium salts. Acetamidinium oxalate (**7**), shown in [​Fig. 5](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/figure/F5/" \t "figure), had a 2D structure comprising interconnected layers with limited H-bonding. In contrast, acetamidinium perchlorate (**8**, [​Fig. 6](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/figure/F6/" \t "figure)) had a 3D structure with layers that were interconnected by extensive H-bonding.

The perchlorate and oxalate structures were rather unique among the acetamidinium structures examined. In our analysis, the acetamidinium C-NH2group formed an H-bond with a single oxygen atom in perchlorate, and the distance between the pivot carbon atom and the NH2moiety in thisgroup was 1.323(3) Å. The other nitrogen-containing group formed two H-bonds with the perchlorate ion. The distance between the pivot carbon and nitrogen atoms in this group was 1.297(4) Å. In the oxalate structure, the distances between the respective pivot carbon and nitrogen atoms were even greater at 1.339(5) Å and 1.280(5) Å. Our observations were not consistent with delocalization, and they differed from values found in the literature, which fall between 1.302 and 1.312 Å. In these reports, the H-bonds to the oxalate moiety are equidistant.

The structure of acetamidinium oxalate consists of two acetamidinium units and one oxalate ion. Both ions participate in extensive H-bonding. Eight- and fourteen-membered rings are formed by **7**, as shown in Fig. [​7](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/figure/F7/" \t "figure). Acetamidinium perchlorate (**8**) primarily forms rings with 22 members, as shown in Fig. [​8](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/figure/F8/).

In light of the results of the XRD analysis, the hygroscopicity data presented in Table [​1](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/table/T1/" \t "table) clearly indicate that the 2D layered structures containing counterions linked by H-bridges—**2**, **4**, **6**, **7**, and **11**—were not hygroscopic. Fig. [​9](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/figure/F9/" \t "figure) illustrates the [ ] of **7**. On the other hand, the compounds that displayed 3D structures—**1**, **3**, **5**, and **8**—were more hygroscopic. Fig. [​10](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/figure/F10/" \t "figure) shows the [ ] for **8**. This was probably due to easier incorporation of water molecules into the larger cavities of the 3D structures compared to the intercalation of water into the 2D structures.

NMR spectroscopy

The NMR data for acetamidinium salts **2**, **4**, **7,**and **8**obtained with deuterated water (D2O) are summarized in ​Table 2. A close inspection of the proton NMR spectra revealed an equilibrium between deuterated and non-deuterated molecules, which were identified by marked decreases in the signal intensities of acidic protons. The equilibrium shifted almost entirely to the side of the deuterated forms, indicating that approximately 98% of the molecules were deuterated. These observations contradicted findings published by Kopylovich,[14](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/#B14) in which no deuteration was described, and two signals per 2H were observed.

On the other hand, the direction of the equilibrium was reversed in mixtures containing deuterated dimethyl sulfoxide (DMSO-d6), in which approximately 90% of the compounds were in non-deuterated form in all of the samples analyzed. With the exception of acetamidinium formate (**4**) in DMSO-d6, two distinct broad peaks belonging to the 2 × NHaHb arrangement were observed, which were attributable to the delocalization of positive charge throughout the amidinium group. **4**in DMSO-d6 produced a single broad peak, which represented all four protons bound to nitrogen. Our NMR results were in accordance with the observations published by Krechl[17](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/#B17) and similar to the results obtained by Tominey[27](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/#B27) for acetamidinium tetrazolate complexes. These observations may have been due to differences in the interactions between formate anion and amidinium groups in different solvents. The interactions within several acetamidinium complexes were studied by Tominey and Krechl using NMR, XRD analysis, and quantum chemical treatment.[17](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/#B17),[27](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/#B27)

Differential thermal analysis

Acetamidinium nitrate (**2**), acetamidinium dinitromethanide (**6**), and acetamidinium perchlorate (**8**) are energetic materials. The have potential for use in pyrotechnic applications, where they may replace guanidinium nitrate or perchlorate salts. The acetamidinium salts have a higher carbon content than their guanidinium analogs, as an amino group in guanidine is replaced by a methyl group in acetamidine. Nevertheless, acetamidinium salts have a relatively high nitrogen content. Compounds **6**and **8** exhibited acceptable decomposition temperatures as determined by differential thermal analysis (DTA). The DTA thermograms from the compounds are shown in Fig. [​11](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275501/figure/F11/" \t "figure). Both the nitrate (**2**)and the perchlorate (**8**)decomposed upon melting. The decomposition temperatures of **2**and **8**were 183 °C and 248 °C, respectively. The maxima of the decomposition ranges for **2**and **8**were 255 °C and 390 °C, respectively. In comparison, decomposition of guanidinium nitrate on the same thermal stability device started at 270 °C, and guanidinium perchlorate started to decompose at 350 °C.

Conclusions

Acetamidinium salts were synthesized and characterized by elemental analysis, electrospray mass spectrometry, and NMR. The energetic salts were also examined with DTA. The structures of several previously unknown acetamidines were identified by XRD analysis. Hygroscopicities of eight acetamidinium salts were determined at 90% humidity. The results of the hygroscopicity analysis were corroborated by the structural determinations performed by XRD. The acetamidinium salts with 2D layered structures were not hygroscopic, while the acetamidinium salts with 3D layered structures were highly hygroscopic.

Conflicts of interest

In accordance with our policy on [Conflicts of interest](http://www.rsc.org/journals-books-databases/journal-authors-reviewers/author-responsibilities/#code-of-conduct) please ensure that a conflicts of interest statement is included in your manuscript here. Please note that this statement is required for all submitted manuscripts. If no conflicts exist, please state that “There are no conflicts to declare”.

Acknowledgements

The acknowledgements come at the end of an article after the conclusions and before the notes and references.

Notes and references

‡ Footnotes relating to the main text should appear here. These might include comments relevant to but not central to the matter under discussion, limited experimental and spectral data, and crystallographic data.

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