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# Substituted phenylarsonic acids; structures and spectroscopy.

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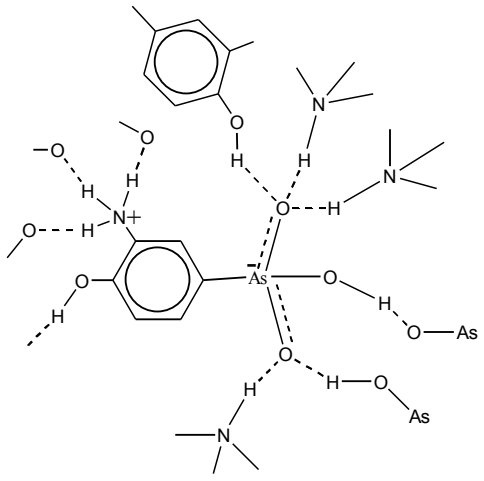
## Synopsis

Spectroscopic data for fifteen substituted phenylarsonic acids are reported, together with the X-ray structures of five examples which form extensive H-bonded networks in the crystals.

## Pictogram

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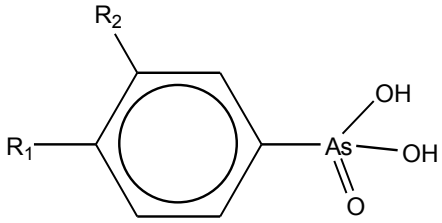
**Abstract**.

Full NMR and ESI-MS spectra, and differential scanning calorimeter data are presented for fifteen substituted phenylarsonic acids, including two new fluoro-substituted examples. X-ray crystal structure determinations of five examples (phenylarsonic acid and the 4-fluoro-, 4-fluoro-3-nitro-, 3-amino-4-hydroxy- and 3-amino-4-methoxy- substituted derivatives) were determined and the H-bonding crystal-packing patterns analysed.

## 1. Introduction.

As part of a project to re-investigate the composition and biological activity of the historically-important arsenical remedy for syphilis, Salvarsan, we required a series of substituted arylarsonic acids, $RAsO_3H_2$ [1]. There is revived interest in organo-arsenic compounds with the recognition that they are still of pharmaceutical use [2] despite their obvious toxicity, and with a developing understanding of the biological pathways for activity [3].

Since only a few examples such as phenylarsonic acid, 3-nitro-4-hydroxyphenylarsonic acid ("Roxarsone") and *o*- or *p*-aminophenylarsonic acid ("arsanilic acid") are readily available commercially, others needed to be synthesized. Much of the literature on these species is quite old [4], so we have taken the opportunity to re-examine the series **1-15** with modern spectroscopic techniques and to structurally define key examples, **1, 10, 13-15**, by single crystal X-ray diffraction.




| | | | | | |
|---|---|---|---|---|---|
| **1** | $R_1 = H$ | $R_2 = H$ | **9** | $R_1 = EtO$ | $R_2 = NO_2$ |
| **2** | $R_1 = OH$ | $R_2 = H$ | **10** | $R_1 = F$ | $R_2 = H$ |
| **3** | $R_1 = OH$ | $R_2 = NO_2$ | **11** | $R_1 = H$ | $R_2 = NO_2$ |
| **4** | $R_1 = NH_2$ | $R_2 = H$ | **12** | $R_1 = MeO$ | $R_2 = NO_2$ |
| **5** | $R_1 = NO_2$ | $R_2 = H$ | **13** | $R_1 = F$ | $R_2 = NO_2$ |
| **6** | $R_1 = MeO$ | $R_2 = H$ | **14** | $R_1 = OH$ | $R_2 = NH_2$ |
| **7** | $R_1 = Me$ | $R_2 = H$ | **15** | $R_1 = MeO$ | $R_2 = NH_2$ |
| **8** | $R_1 = EtO$ | $R_2 = H$ | | | |

## 2. Experimental Section

*2.1 General*

$PhAsO_3H_2$ (**1**) (BDH), $4\text{-}HOC_6H_4AsO_3H_2$ (**2**) (TCI), $3\text{-}NO_2\text{-}4\text{-}HOC_6H_3AsO_3H_2$ (**3**) (Aldrich) and $4\text{-}H_2NC_6H_4AsO_3H_2$ (**4**) (TCI), were commercially available.

NMR spectra were recorded on Bruker AC300 or AC400 spectrometers in $d^6$-DMSO as solvent and internal standard. Assignments were by standard proton-carbon HSQC and HMBC experiments. ESI-MS were measured on a Bruker MicrOTOF spectrometer, using MeOH or $H_2O$ as solvent. DSC data were obtained on a Perkin-Elmer DSC6 machine.

*2.2 Syntheses.*

Detailed examples of synthesis of arylarsonic acids using the Bart [5] and Scheller [6] methods are taken from the older literature, and are reproduced here for convenience.

*2.2.1 Preparation of phenylarsonic acid (**1**) using the Bart procedure [c.f. ref 7].*

Anhydrous $Na_2CO_3$ (400 g, 3.77 mol), $As_2O_3$ (200 g, 1.01 mol) and $CuSO_4.5H_2O$ (10 g, 0.06 mol) were suspended in water (800 mL) in a 5 L beaker and warmed with stirring. When most of the solid had dissolved the solution was allowed to cool.

In a separate 5 L beaker, aniline (150 g, 1.6 mol) was carefully added to a solution of concentrated HCl (320 mL), water (800 mL) and enough ice to make approximately 2.4 L. To this a saturated aqueous solution of $NaNO_2$ (112 g) was slowly added.

The resulting diazonium salt solution was slowly added over 1 h to the arsenite mixture, with cooling to keep the temperature below 15°C. Small amounts of acetone were added to minimize foaming, caused by the effervescing $N_2$ gas.

The resulting slurry was stirred overnight, to allow complete evolution of nitrogen. The mixture was filtered and the volume reduced to 1 L on a hot plate. Activated carbon was added and the mixture filtered to give a brown solution. This was acidified by adding conc. HCl until a brown oil precipitated. The mixture was filtered through Celite which absorbed the oil. The filtrate was treated again with carbon and re-filtered. More conc. HCl was slowly added, precipitating off-white crystals which were collected by filtration and dried under vacuum. On standing overnight the mother liquor precipitated a further crop of crystals. Total crude yield was 89.3 g (44%). Recrystallisation from hot water with further activated carbon treatment gave pure phenylarsonic acid (66.3 g, 32%) as white crystals. ESI-MS: *m/z* $[M-H]^-$ 200.9537 (Calc. 200.9533).

*2.2.2 Preparation of 4-nitrophenylarsonic acid (**5**) using the Scheller method [c.f. ref 6, 8, 9].*

Concentrated $H_2SO_4$ (10 g) was added to 4-nitroaniline (13.8 g, 0.1 mol) in absolute ethanol (250 mL). $AsCl_3$ (28 g, 0.16 mol) was added and the mixture cooled to < 5°C

in an ice bath. A solution of sodium nitrite (8.28 g, 0.12 mol) in water (12 mL) was added slowly to the cooled mixture with thorough stirring.

CuBr (1 g) was added to the mixture and it was warmed to 60°C for 6 hours before cooling overnight. The solution was transferred to a round-bottomed flask and steam distilled to remove solvent and unreacted aniline. The liquid residue in the still-pot was transferred to a beaker while still hot. Activated carbon (10 g) was added and the mixture boiled for 10 min and filtered. The green solution was placed in the fridge to crystallize overnight. Yellow crystals were collected and recrystallised from the minimum boiling water to give 4-nitrophenylarsonic acid as fine yellow crystals, 8.13 g, (33%). Found: C 29.40; H 2.44; N 5.38%. $C_6H_6NO_5As$ requires C 29.17; H 2.45; N 5.67%. ESI-MS: *m/z* $[M-H]^-$ 245.9414 (Calc. 245.9384)

*2.2.3 Preparation of 4-methoxyphenylarsonic acid (**6**) [c.f. 10].*

This was prepared by the Scheller procedure, as described above, from *p*-anisidine (12.3 g, 0.10 mmol). Recrystallisation from boiling water gave 4-methoxyphenylarsonic acid as white crystals (14.3 g, 61%). Found: C 36.91; H 3.92%. $C_7H_9O_4As$ requires C 36.23; H 3.91%. ESI-MS: *m/z* $[M-H]^-$ 230.9651 (Calc. 230.9639).

*2.2.4 Preparation of 4-methylphenylarsonic acid (7) [11].*

Similarly from 4-methylaniline (10.7 g, 0.10 mmol), 4-methylphenylarsonic acid was obtained as white crystals. ESI-MS: *m/z* $[M-H]^-$ 214.9697 (Calc. 214.9689).

*2.2.5 Preparation of 4-ethoxyphenylarsonic acid (**8**).*

Under the same conditions in EtOH, from 4-fluoroaniline (11.1 g, 0.10 mmol) fine yellow crystals of 4-ethoxyphenylarsonic acid were obtained. Found: C 38.94; H 4.36%. $C_8H_{11}O_4As$ requires C 39.04; H 4.51%. ESI-MS: *m/z* $[M-H]^-$ 244.9777 (Calc. 244.9795).

*2.2.6 Preparation of 4-ethoxy-3-nitro-phenylarsonic acid (**9**).*

Similarly, 4-fluoro-3-nitroaniline (15.6 g, 0.10 mmol) gave 4-ethoxy-3-nitro-phenylarsonic acid as fine yellow crystals of the monohydrate. Found: C 30.42; H 3.06; N 4.73%. $C_8H_{10}NO_6As.H_2O$ requires C 31.09; H 3.91; N 4.53%. ESI-MS: *m/z* $[M-H]^-$ 289.9669 (Calc. 289.9646).

*2.2.7 Preparation of 4-fluorophenylarsonic acid (**10**).*

Using the same general method *but with THF (220 mL) as solvent instead of EtOH*, 4-fluoroaniline (11.1 g, 0.10 mmol) gave 4-fluorophenylarsonic acid as fine white crystals (11.3 g, 51%). Found: C 33.01; H 2.77%. $C_6H_6O_3FAs$ requires C 32.75; H 2.75%. ESI-MS: *m/z* $[M-H]^-$ 218.9475 (Calc. 218.9439).

*2.2.8 Preparation of 3-nitrophenylarsonic acid (**11**) [c.f. ref 8,9].*

Phenylarsonic acid (8.08 g, 0.04 mol) was dissolved in concentrated $H_2SO_4$ (30 mL) and cooled to -8 °C in an ice/salt bath. A mixture of concentrated $HNO_3$ and $H_2SO_4$ acids (1:1, 5.6 mL) was added slowly ensuring that the temperature was <0 °C. The mixture was left to return to room temperature overnight with stirring, then poured over 200 g ice and left in the fridge for a further 24 hours. Yellow crystals were collected and recrystallised from boiling water to give 3-nitrophenylarsonic acid as pale yellow crystals. Found C 29.54; H 2.44; N 5.40%. $C_6H_8AsNO_4$ requires C 29.17; H 2.45; N 5.67%. ESI-MS: *m/z* $[M-H]^-$ 245.9399 (Calc. 245.9384).

*2.2.9 Preparation of 4-methoxy-3-nitrophenylarsonic acid (**12**).*

Similarly from 4-methoxyphenylarsonic acid (9.2 g, 0.04 mol), nitration with conc. $H_2SO_4/HNO_3$ gave pale yellow crystals from water of 4-methoxy-3-nitrophenylarsonic acid (7.21 g, 73%). Found C 30.60; H 2.90; N 4.83%. $C_7H_8AsNO_6$ requires C 30.35; H 2.91; N 5.06%. ESI-MS: *m/z* $[M-H]^-$ 275.9505 (Calc. 275.9489).

*2.2.10 Preparation of 4-fluoro-3-nitro-phenylarsonic acid (**13**).*

4-Fluorophenylarsonic acid (13.2 g, 0.06 mol) was dissolved in conc. $H_2SO_4$ (45 mL). To this solution fuming nitric acid (6 mL) was added. The mixture was heated with stirring in a water bath for approximately 6 hours. The heat was then turned off and the mixture left overnight to cool. The mixture was poured over ice ( 300 g) and stored in the fridge. The precipitate was filtered and dried.

Found C 27.42; H 1.85; N 5.06%. $C_6H_5FAsNO_5$ requires C 27.19; H 1.90; N 5.28%. ESI-MS: *m/z* $[M-H]^-$ 263.9284 (Calc. 263.9289).

*2.2.11 Preparation of 3-amino-4-hydroxyphenylarsonic acid (**14**) [c.f. ref 1,12].*

3-Nitro-4-hydroxyphenylarsonic acid (13.1g, 0.05 mol) was dissolved in a solution of aqueous NaOH (100 mL, 1 mol $L^{-1}$) and cooled to 0ºC in an ice/salt slush bath with stirring. $Na_2S_2O_4$ (30.25 g ) was added in one portion with vigorous stirring. The solution effervesced vigorously. As soon as the colour changed from orange to pale yellow, concentrated HCl (12 mL) was added. This mixture was held at <0ºC until the frothing ceased and the product had precipitated from the solution. This was filtered and washed twice with ice-cold water to give crude 3-amino-4-hydroxyphenylarsonic acid (6.50 g, 56%) as a cream coloured solid which was dried under vacuum. The crude product (6 g) was dissolved in a mixture of $H_2O$ (25 mL) and conc. HCl (2 mL) and stirred with decolourising carbon for 15 minutes before filtering. To the filtrate, sodium acetate solution (25%) was added until the solution was no longer acidic to Congo Red. The solution was cooled in a fridge for 20 min. and the precipitated crystals were collected by filtration and dried under vacuum. Yield was 4.7 g, 78%, of pure **14** as off-white microcrystals. Found C 30.76; H 3.41; N 6.32%. $C_6H_8AsNO_4$ requires C 30.90; H 3.43; N 6.01%. ESI-MS: *m/z* $[M-H]^-$ 231.9604 (Calc. 231.9591).

*2.2.12 Preparation of 3-amino-4-methoxyphenylarsonic acid (**15**).*

4-Methoxy-3-nitrophenylarsonic acid (5 g) was reduced with ferrous sulfate following the method of Jacobs *et a*l. [13]**.** Found C 34.14; H 4.05; N 5.40%. $C_7H_{11}AsNO_4$ requires C 34.03; H 4.08; N 5.67%. ESI-MS: *m/z* $[M-H]^-$ 245.9747 (Calc. 245.9748).

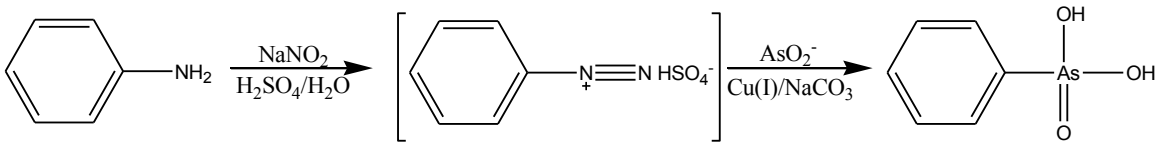
*2.3. X-ray crystallography*

X-ray intensity data for compounds **1, 10, 13-15** were obtained from a Bruker SMART CCD diffractometer, and were processed using standard software. Crystal data and refinement details are summarised in Table 1. Corrections for absorption were carried out using SADABS [14]. The structures were solved and refined using the SHELX programs [15], operating under WinGX [16]. All H atoms were located from penultimate difference maps and refined, except for **14** and **15** where only the $NH_2$ and OH hydrogen atoms were refined, and the others were placed in calculated positions. Analyses were straightforward, except for $PhAsO_3H_2$ which was refined as a racemic twin, with the twinning parameter converging to a value of 0.44.

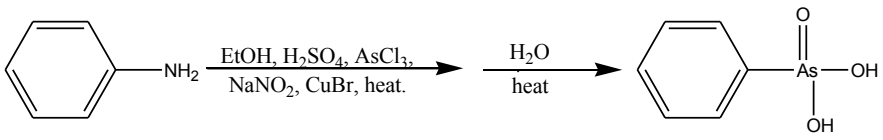
**3. Results and discussion**

*3.1 Syntheses of $RAsO_3H_2$.*

There are three general methods for the preparation of arylarsonic acids [4]. The Bart reaction [5] involves the addition of an aqueous alkaline solution of sodium arsenate to the diazonium salt of the pre-requisite amine. The reaction requires a catalyst [usually Cu(I)] and gives the maximum yield when buffered with sodium carbonate.



There are several variations of this reaction, the most useful being the Scheller [6] variation, which can be adapted into a one pot synthesis, where the diazo compound is prepared and decomposed with a cuprous bromide catalyst in the presence of arsenic trichloride in an alcoholic solution. This variation also eliminates the excessive foaming sometimes encountered in the Bart reaction.




The Bechamp reaction [4] involves heating aromatic amines, phenols or phenyl ethers with syrupy arsonic acid under reflux for several hours. The yield for this reaction is rarely over 25%, but is historically of interest as the first method to be reported.

The Bart or Scheller reactions were found to be the most convenient method of synthesis in this present study. Reasonable yields of most of the acids were achieved. However, when 4-fluoroaniline was used as a substrate for the Scheller reaction using the usual EtOH as solvent, the product of the reaction was 4-$EtOC_6H_4AsO_3H_2$ (**8**) and not the expected 4-$FC_6H_4AsO_3H_2$ (**10**), arising from efficient nucleophilic displacement of the fluorine by ethoxide from the solvent under the conditions of the reaction. Similarly 3-$NO_2$-4-F-$C_6H_3NH_2$ gave the ethoxy compound **9**, not **13.**

Aromatic C-F bonds are known to be particularly susceptible to nucleophilic substitution reactions, despite the high C-F bond energy [17]. This problem could be circumvented by carrying out the reaction in THF, when the previously uncharacterised 4-fluorophenyl arsonic acid was produced in 51% yield.

Nitro-aryl arsonic acids could be prepared either from the appropriate nitro-aniline or by direct nitration of other aryl-arsonic acids, and these in turn could be reduced to

give amino-arylarsonic acids using established methods with dithionite or ferrous sulfate as reducing agents [13].

Using these methods, arsonic acids **1-15** were prepared and were investigated in this report. Most of the acids have been reported previously, but the EtO-substituted examples **8** and **9**, and the fluorinated compounds **10** and **13,** have had only brief mention in the literature. The synthesis of 3-$NO_2$-4-$FC_6H_3AsO_3H_2$, **13**, was claimed [18] but without characterisation, and our studies would suggest that it was the 4-EtO rather than the 4-F compound that would result from the procedure used.

*3.2 Spectroscopic properties.*

$^{1}H$ and $^{13}C$ NMR data are listed in Table 2, together with their assignments, which were reasonably straightforward using standard proton-carbon HSQC and HMBC techniques.

ESI-MS was a useful technique for characterising the acids, with clean $[M-H]^-$ ions for each showing in negative ion mode when run in $H_2O$ as solvent. If MeOH was used then ions of the type $[M-OH+OMe-H]^-$ were seen through formation of methyl esters of the acid, as has been reported earlier [19].

Arylarsonic acids often decompose before melting, so were surveyed using DSC. As summarised in Table 3, these generally showed one or two endothermic feature in the range 140-180°C, presumably lattice water loss (if present) and/or water-elimination giving condensed acids, followed by an exothermic process just above 300°C which will be an oxidative degradation. A typical example is shown in Fig. 1.

*3.3 Crystal structures.*

Selected arsonic acids were subjected to single crystal structural analysis, to add to the existing bond parameter data by including new substituent patterns, and to explore the hydrogen-bonding networks formed in the crystal. A number of crystal structures of arylarsonic acids are known, dating from about 1960, but many of the earlier ones involved photographic data and consequently gave relatively imprecise refinements. Crystal and refinement data for the compounds determined in the present study are summarised in Table 3. All were low-temperature data sets with very good refinement factors, so are more precise than most of the earlier examples. None of the acids structurally investigated in the present work crystallise with water in the lattice, presumably because of strong intermolecular hydrogen bonding networks involving the -$AsO_3H_2$ group.

The individual molecular structures will be discussed initially, followed by a discussion of the crystal packing and hydrogen-bonding patterns.

*3.3.1 Individual molecules*

$PhAsO_3H_2$ (**1**)

This compound has been analysed twice before, in 1960 [20], but neither determination was precise so the structure was repeated to provide an accurate benchmark for the substituted species. $PhAsO_3H_2$ crystallises as a racemic twin (not apparent in the earlier determinations [20]), but despite this it refined cleanly, with all hydrogen atoms located (Fig.2). The As=O bond length is 1.6617(10) Å, the two As-O lengths are equal at 1.7070(10) Å and the As-C(1) bond is 1.8882(12) Å. The geometry around the As atom shows small deviations from tetrahedral, with angles in the range 106-112°. These more reliable parameters give shorter As-C and As-O, and longer As=O, bonds than those previously reported for this compound.

4-$FC_6H_4AsO_3H_2$ (**10**)

This crystallises with one molecule comprising the asymmetric unit. The structure (Fig.3) is similar to that of the unsubstituted example with the electronegative 4-F substituent having the expected effect of shortening the aryl C-C bonds adjacent to the 4-position, but having no significant effect on the bond lengths around the As atom, where the As=O [1.6567(11) Å], As-OH [1.7121(12) Å], and As-C [1.8974(16) Å] bonds are essentially the same as in $PhAsO_3H_2$. There is a wider variation in the angles around the As atom (105-115°) but this is presumably to accommodate the different H-bonding network in the crystal.

3-$NO_2$-4-F-$C_6H_3AsO_3H_2$ (**13**)

This crystallises with two independent molecules in the asymmetric unit, but they differ only in small details (Fig.4). The most apparent are the degree of twisting of the plane of the $–NO_2$ group from the plane of the phenyl ring (35° and 30°) and the displacement of the As atom from the phenyl plane (0.18 and 0.83 Å) respectively. Otherwise the individual bond parameters are indistinguishable from the corresponding ones in the 4-F example **10**.

3-$NH_2$-4-MeO-$C_6H_3AsO_3H_2$ (**15**).

This has a complicated structure with three independent molecules in the asymmetric unit. Interestingly they are all molecular species (Fig.5), in contrast to the closely related 3-$NH_2$-4-HO-$C_6H_3AsO_3H_2$ which packs in the zwitterionic form (see below). The three independent molecules show only small variations in bond parameters, so the discussion here is based on average values. The As=O [1.664(2) Å] and As-OH [1.719(2) Å] bonds are essentially the same as in the simpler examples, as is the As-C

[1.899(2) Å]. The most noticeable effect of the substituents is bond alternation within the aryl ring – the C(3)-C(4) bond between the two adjacent groups is the longest (1.419 Å), presumably because of steric crowding, and this has induced significantly longer C(1)-C(2) (1.405 Å) and C(5)-C(6) (1.399 Å) bonds than the C(1)-C(6) (1.392 Å), CC(2)-C(3) (1.390 Å) and C(4)-C(5) (1.394 Å) ones. This effect is much more noticeable here than for the 3-$NO_2$-4-F example **13** discussed above.
The angles around the As atoms are again within the 103-113° range.

3-$NH_2$-4-HO-$C_6H_3AsO_3H_2$ (**14**).

This structure is quite different from the others discussed, in that it packs in the crystal as zwitterions, 3-$^{+}H_3N$-4-HO-$C_6H_3AsO_3H^{-}$ (Fig.6). This is readily seen from the pattern of two shorter As=O bonds [1.677(2) Å] and one long As-OH [1.728(2) Å], and from the location in the penultimate difference map of the three H atoms on the nitrogen. There is no immediately apparent reason why this compound should pack in this form, while the analogous methoxy compound does not, since the substitution of an –OH group for a –OMe is not expected to change the pKa values of the acid nor the $pK_b$ value for the $–NH_2$ group. Presumably it is simply a consequence of accommodating the optimum H-bonding interactions in the crystal. It may be significant that the –OH group in the zwitterion is involved in H-bonding, whereas the –OMe in the previous example has no intermolecular interactions. One consequence of the zwitterion packing is a relatively high density for this compound (2.07 g $cm^{-3}$) compared with the methoxy analogue (1.83 g $cm^{-3}$) which indicates a tighter packing for the ionic arrangement. 4-$H_2NC_6H_4AsO_3H_2$ is the only other arsonic acid reported to be a zwitterion in the solid state [21], while the corresponding 2- and 3-

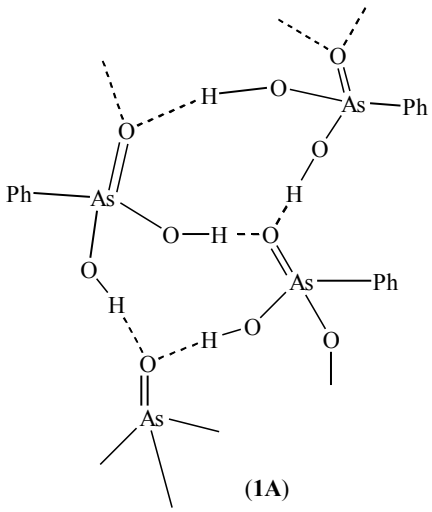
$H_2NC_6H_4AsO_3H_2$ pack in their molecular forms [22, 23], so there is no obvious predictability.

Overall, these arsonic acid structures show very little variation with substitution patterns. The As-C (1.888-1.895 Å), As=O (1.657-1.664 Å) and As-O (1.707-1.719 Å) bonds cover a narrow range for the compounds with molecular packing, and these conform to the other examples in the literature. For the zwitterionic compound **14** the As-C (1.904 Å), As=O (1.677 Å) and As-O (1.728 Å) are all longer than the equivalent bonds in the molecular examples, possibly because of the stronger participation of hydrogen bonding in the charged species. The tetrahedral geometry around the As atoms in all of the examples shows some flexibility with angles ranging between 103 and 115°, presumably to accommodate the hydrogen bonding, as discussed below.

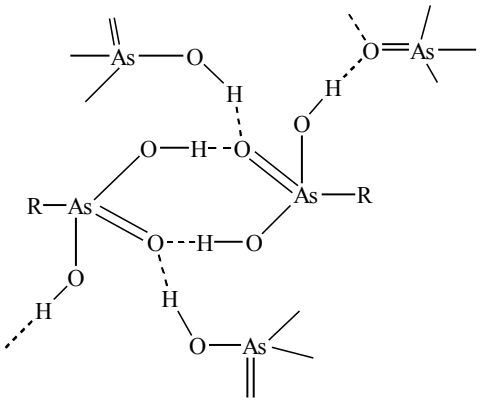
*3.3.2 Hydrogen bonding networks.*

The arsonic acids described here have many possibilities for H-bonding interactions in the crystals. In addition to those involving the $AsO_3H_2$ moieties, the $–NH_2$, -OH or $–NO_2$ groups on the phenyl rings are also likely to act as donors or acceptors.

For $PhAsO_3H_2$, molecules pack in the crystal so they form single chains parallel to the *a* axis. Each of the two As-O-H groups acts as a donor to the As=O of two adjacent molecules, with each As=O acting as an acceptor to two separate O-H donors, forming 10-membered rings as shown in **1A**. The O….O distances between donor and acceptor are all about 2.57 Å, making them on the strong/moderate borderline using Jeffrey's classification [24, 25]. This arrangement is also further stabilised by allowing the phenyl rings to π-stack parallel to each other at 3.4 Å apart. There are only Van der Waals interactions cross-linking these chains. This particular H-bonding arrangement was also found for 2-$H_2NC_6H_4AsO_3H_2$ [22].




(**1A**)




(**10A**)

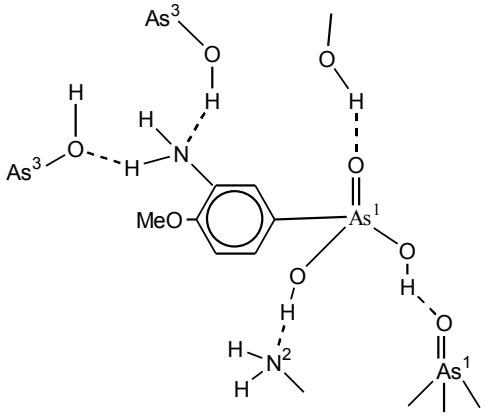
For 4-$FC_6H_4AsO_3H_2$, (**10**), there are no significant interactions involving the fluoride atom, which is not unexpected since C-F groups are known to be weak H-bond acceptors [17]**.** The basic motif is a dimer, about a crystallographic inversion centre, reminiscent of those commonly formed by carboxylic acids [24, 25] with As-O-H…O=As interactions characterised by an O….O distance of 2.58 Å. These generate nearly planar 8-membered rings, as shown in **10A**. These dimers are further linked into 2-dimensional sheets perpendicular to the c axis, by the remaining As-O-H bonding to an As=O of an adjacent molecule, so that each As=O acts as an acceptor to As-O-H from two separate molecules.

This same basic arrangement is also seen for 3-$NO_2$-4-$FC_6H_3AsO_3H_2$, where the two independent molecules in the lattice form a dimer with each other. This gives an eight-membered ring with 2.60 Å O…O separations, but this is distinctly chair-shaped. The remaining As-O-H…O=As linkages again generate a two dimensional sheet in the *ab* plane, as in (**10A**). There is no H-bonding involvement of either the F or $NO_2$ substituents, although there is a relatively close O…O (2.98 Å) contact between one of the oxygen atoms of the $NO_2$ group and an As=O group. This

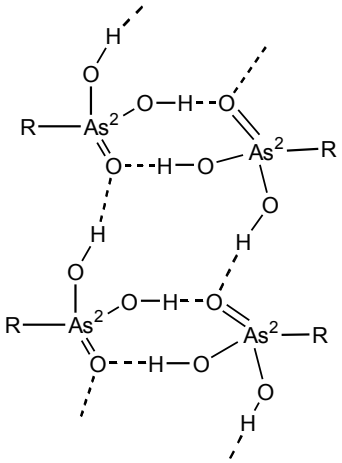
contrasts with the reported structure of 3-$NO_2$-4-$MeOC_6H_3AsO_3H_2$ where strong H-bonding between an As-O-H and an adjacent $NO_2$ group links molecules nose-to-tail, with additional As-O-H…O=As interactions completing the network [26]. The basic eight-membered ring dimer motif is common for arylarsonic acids, with at least seven other examples known [27,28], however the way these dimers stack varies in each case. For example, 4-$HOC_6H_3AsO_3H_2$ also has the chair-shaped dimer unit, further linked into tetrameric units held by alternating H-bonds between the C-O-H group acting as both a donor and acceptor, and As=O and As-O-H groups acting as acceptors and donors respectively, giving 12-membered rings [26].

For 3-$NH_2$-4-$MeOC_6H_3AsO_3H_2$ (**15**) the packing is very complicated. There are three independent molecules in the asymmetric unit, and each of these is involved in different H-bonding arrangements to generate three cross-linked strands, each parallel to the short *a* axis.

The As(1) molecules form a simple strand based on strong As-O-H…O=As links, with the remaining As-O-H donating to the $NH_2$ group of As(2) molecules as in **15A**.



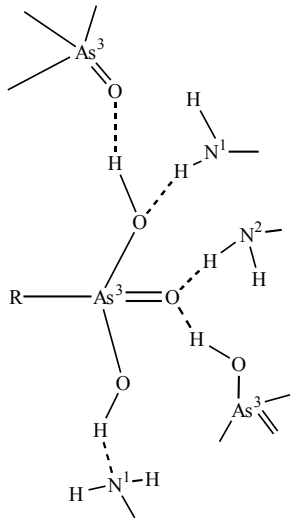

(**15A**)



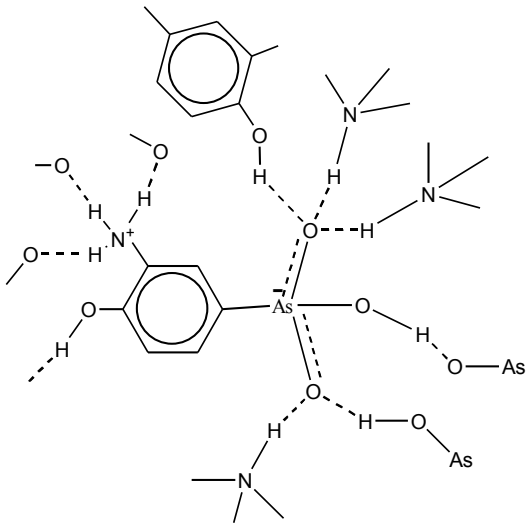

(**15B**)

The As(2) molecules form a double chain based on slightly chair-shaped eight-membered dimers, formed about an inversion centre, similar to the arrangement **10A** found for compounds **10** and **13**, with O…O distances of 2.57 Å. These stack up the *a* axis, with further 2.52 Å O…O links between the remaining As-O-H and the As=O of adjacent molecules to give 12-membered rings, with each As=O acting as acceptor to two As-O-H groups, as shown in (**15B**). The $–NH_2$ group acts as an acceptor to an As-OH from As(1) molecules, and as an N-H donor to the O of an As-O-H of As(3) molecules. The 8/12-membered alternating ring motif was also found for 4-$NO_2$-$C_6H_4AsO_3H_2$, though with a small variation in the 12-membered ring [28].

The As(3) strand links the others together through a variety of interactions. The single chain is based on As-O-H groups H-bonding as a donor to the As=O group of the adjacent molecules (O…O 2.52 Å), as also found for the As(1) molecules. This –OH further acts as an acceptor from an -$NH_2$ group of an As(1) molecule (N…O 2.94 Å). The As=O also accepts a H-bond from the -$NH_2$ group of an As(2) molecule (N…O 2.97 Å), while the remaining As(3)-O-H acts as an H-bond donor to the -$NH_2$ group of an As(1) molecule. This is summarised in **15C**. For this As(3) molecule the $–NH_2$ group does not participate in any H-bonding interactions.



(**15C**)



(**14A**)

For the zwitterionic 3-$^{+}H_3N$-4-$HOC_6H_3AsO_3H^{-}$ compound **14**, there is a strong H-bonding network, as shown in **14A**. Each of the three N-H hydrogens is linked to the As-O groups of three different molecules (N…O 2.77-2.82 Å), with the phenolic –OH also bonded to an As-O of another one (O…O 2.60 Å). At the other end of the molecule, the As-O-H is donating to an As-O with O…O 2.64 Å, one of the As-O groups accepts an H-bond from both an N-H and an As-O-H, while the other As-O is involved as an acceptor in three hydrogen bonds; one from the phenolic –O-H (O…O 2.60 Å), and two from two different N-Hs (N…O 2.78 and 2.82 Å). This arrangement accommodates an offset π-stacking arrangement of the phenyl rings, 3.57 Å apart. All these strong interactions undoubtedly give rise to the higher density of this compound compared with the others.

**Supplementary material**

Crystallographic data for the structural analyses have been deposited with the Cambridge Crystallographic Data Centre, CCDC 678806-678810. Copies of this information may be obtained free of charge from the Director, CCDC, 12 Union Rd.,

Cambridge CB2 1EZ, UK (Fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk.

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## Table 1

**Crystal data and refinement details for aryl arsonic acids.**

| | **$PhAsO_3H_2$ (1)** | **$4\text{-}FC_6H_4AsO_3H_2$ (10)** | **$3\text{-}NO_2\text{-}4\text{-}F\text{-}C_6H_3AsO_3H_2$ (13)** | **$3\text{-}NH_2\text{-}4\text{-}MeO\ C_6H_3AsO_3H_2$ (15)** | **$3\text{-}NH_2\text{-}4\text{-}HO\text{-}C_6H_3AsO_3H_2$ (14)** |
|---|---|---|---|---|---|
| Formula | $C_6H_7AsO_3$ | $C_6H_6AsFO_3$ | $C_6H_5AsFNO_5$ | $C_7H_{10}AsNO_4$ | $C_6H_8AsNO_4$ |
| $M_r$ | 202.04 | 220.03 | 265.03 | 247.08 | 233.05 |
| T(K) | 93(2) | 84(2) | 84(2) | 84(2) | 84(2) |
| crystal system | orthorhombic | orthorhombic | orthorhombic | monoclinic | monoclinic |
| space group | $P2_12_12_1$ | Pbca | $Pca2_1$ | $P2_1/n$ | $P2_1/c$ |
| *a* (Å) | 4.6854(1) | 8.4575(3) | 10.4661(2) | 4.6581(1) | 7.1511(2) |
| *b*(Å) | 10.3540(3) | 10.7817(3) | 7.5937(1) | 28.2798(4) | 15.8277(4) |
| *c*(Å) | 14.8614(4) | 16.5150(5) | 21.3387(3) | 20.4669(3) | 7.3779(2) |
| α(deg) | 90 | 90 | 90 | 90 | 90 |
| β(deg) | 90 | 90 | 90 | 90.33(1) | 116.25(1) |
| γ(deg) | 90 | 90 | 90 | 90 | 90 |
| V($Å^3$) | 720.97(3) | 1505.94(8) | 1695.92(5) | 2696.06(8) | 748.93(3) |
| Z | 4 | 8 | 8 | 12 | 4 |
| ρ(g $cm^{-3}$) | 1.861 | 1.941 | 2.076 | 1.826 | 2.067 |
| μ($mm^{-1}$) | 4.66 | 4.48 | 4.02 | 3.76 | 4.51 |
| Size ($mm^3$) | 0.80x0.58x0.40 | 0.34x0.26x0.22 | 0.32x0.28x0.18 | 0.46x0.12x0.12 | 0.26x0.11x0.05 |
| F(000) | 400 | 864 | 1040 | 1488 | 464 |
| $\theta_{max}$(deg) | 29.6 | 26.4 | 26.5 | 26.3 | 26.3 |

| | | | | | |
|---|---|---|---|---|---|
| Reflns collected | 9541 | 10803 | 9640 | 15644 | 4408 |
| Tmax, min | 0.257, 0.118 | 0.440, 0.333 | 0.451, 0.295 | 0.719, 0.537 | 0.696, 0.416 |
| Unique reflns | 2028(Rint 0.025) | 1544 ($R_{int}$ 0.020) | 3257 ($R_{int}$ 0.0269) | 5435 ($R_{int}$ 0.0245) | 1526 ($R_{int}$ 0.0302) |
| Parameters | 121 | 331 | 293 | 392 | 129 |
| $R_1$ [$I > 2\sigma(I)$] | 0.0117 | 0.0173 | 0.0173 | 0.0243 | 0.0286 |
| $wR_2$ (all data) | 0.0332 | 0.0465 | 0.0420 | 0.0523 | 0.0745 |
| GOF on $F^2$ | 1.004 | 1.151 | 1.046 | 1.107 | 1.034 |
| Flack x parameter | 0.441(8) | | 0.010(6) | | |

Table 2. NMR Data for Arylarsonic Acids **1-15**.

$^{1}$H NMR data (δ).

| Compound | H-2 | H-3 | H-4 | H-5 | H-6 | $CH_2$ | $CH_3$ | OH |
|---|---|---|---|---|---|---|---|---|
| **1** | 7.78(d) | 7.59(m) | 7.65(m) | 7.59(m) | 7.78(d) | | | 5.45 |
| **2** | 7.59(d) | 6.97(d) | - | 6.97(d) | 7.59(d) | | | 4.79 |
| **3** | 8.19 | - | - | 7.31(d) | 7.84(d) | | | 4.35 |
| **4** | 7.40 | 6.71 | - | 6.71 | 7.40 | | | |
| **5** | 8.04(d) | 8.40(d) | - | 8.40(d) | 8.04(d) | | | 4.37 |
| **6** | 7.70(d) | 7.13(d) | - | 7.13(d) | 7.70(d) | | 3.79 | 5.06 |
| **7** | 7.64(d) | 7.41(d) | - | 7.41(d) | 7.64(d) | | 2.37 | 3.93 |
| **8** | 7.67(d) | 7.11(d) | - | 7.11(d) | 7.67(d) | 4.08(q) | 1.32(t) | 3.95 |
| **9** | 8.17(d) | - | - | 7.54(d) | 7.96(d) | 4.27(q) | 1.33(t) | 4.84 |
| **10** | 7.83(dd) | 7.42(t) | - | 7.42(t) | 7.83(dd) | | | 4.52 |
| **11** | 8.48(s) | - | 8.17(d) | 7.90(t) | 8.46(d) | | | 4.56 |
| **12** | 8.18(s) | - | - | 7.57(d) | 7.99(d) | | 3.99 | 4.43 |
| **13** | 8.41(d) | - | - | 7.78(m) | 8.14(m) | | | 4.51 |
| **14** | 6.98(s) | | | 6.84(d) | 6.84(d) | | | |
| **15** | 7.01(s) | | | 6.96(d) | 6.94(d) | | 3.80 | |

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$^{13}$C NMR data (δ).

| Compound | C-1 | C-2 | C-3 | C-4 | C-5 | C-6 | $CH_2$ | $CH_3$ |
|---|---|---|---|---|---|---|---|---|
| **1** | 133.2 | 130.4 | 129.9 | 133.5 | 129.9 | 130.4 | | |
| **2** | 122.3 | 132.7 | 117.0 | 162.2 | 117.0 | 132.7 | | |
| **3** | 123.2 | 128.3 | 137.7 | 156.2 | 121.0 | 136.6 | | |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **4** | 116.8 | 131.5 | 113.8 | 153.2 | 113.8 | 131.5 | | |
| **5** | 140.3 | 132.1 | 124.5 | 150.5 | 124.5 | 132.1 | | |
| **6** | 124.2 | 132.2 | 115.3 | 163.1 | 115.3 | 132.3 | | 55.8 |
| **7** | 130.4 | 130.2 | 130.2 | 143.5 | 130.2 | 130.2 | | 21.4 |
| **8** | 124.4 | 132.2 | 115.5 | 162.2 | 115.5 | 132.2 | 63.8 | 14.6 |
| **9** | 124.9 | 127.2 | 139.7 | 154.8 | 116.5 | 136.4 | 66.2 | 14.4 |
| **10**[a] | 129.5 | 133.5 | 117.3 | 165.4 | 117.3 | 133.5 | | |
| **11** | 135.5 | 125.0 | 148.2 | 136.6 | 131.7 | 127.9 | | |
| **12** | 124.9 | 127.2 | 139.5 | 155.5 | 115.9 | 136.5 | | 57.5 |
| **13**[b] | 130.7 | 128.7 | 137.7 | 157.7 | 120.8 | 138.5 | | |
| **14** | 122.7 | 115.4 | 137.9 | 148.8 | 114.9 | 119.6 | | |
| **15** | 124.3 | 114.1 | 138.9 | 149.9 | 110.9 | 118.8 | | 55.8 |

---

[a] $J_{F\text{-}C}$ (Hz): C-1 3.1; C-2,6 9.2; C-3,5 22.0; C-4 251.6.

[b] $J_{F\text{-}C}$ (Hz): C-1 4.2; C-2 1.8; C-3 7.1; C-4 268.6; C-5 21.6; C-6 10.3.

Table 3. DSC Data for arsonic acids **1-15**.

| Compound | 1st endo /°C | 2nd endo /°C | final exo /°C |
|---|---|---|---|
| **1** | 160 | | 392 |
| **2** | 175 | 188 | 332 |
| **3** | 184 | | 320 |
| **4** | 165 | | 250 |
| **5** | 162 | 245 | 332 |
| **6** | 165 | 180 | 352 |
| **7** | 160 | | 380 |
| **8** | 170 | | 355 |
| **9** | 148 | 225 | 303 |
| **10** | 175 | 182 | none <400 |
| **11** | 160 | 175 | 330 |
| **12** | 170 | 245 | 315 |
| **13** | 145 | | 310 |
| **14** | 200 | 240 | ----- |
| **15** | 180 | | ----- |

**Captions to figures:**

Figure 1. The DSC trace for 4-$O_2NC_6H_4AsO_3H_2$.

Figure 2. The structure of $PhAsO_3H_2$ (**1**) (50% ellipsoids) showing numbering scheme. Selected bond lengths (Å): As(1)-C(1) 1.8882(12); As(1)-O(1) 1.6617(10); As(1)-O(2) 1.7074(10); As(1)-O(3) 1.7065(10).

Figure 3. The structure of 4-$FC_6H_4AsO_3H_2$ (**10**) (50% ellipsoids) showing numbering scheme. Selected bond lengths (Å): As(1)-C(1) 1.8974(16); As(1)-O(1) 1.6567(11); As(1)-O(2) 1.7076(12); As(1)-O(3) 1.7167(12).

Figure 4. The structure of one of the two independent molecules of 3-$O_2N$-4-$FC_6H_3AsO_3H_2$ (**13**).Selected bond lengths (Å): As(1)-C(1) 1.893(2), 1.893(2); As(1)-O(1) 1.6539(14), 1.6598(13); As(1)-O(2) 1.7165(19), 1.7110(18); As(1)-O(3) 1.7096(15), 1.7110(18).

Figure 5. The structure of one of the three independent molecules of 3-$NH_2$-4-$MeOC_6H_3AsO_3H_2$ (**15**). Selected bond lengths (Å): As-C(1) 1.915(2), 1.888(2), 1.895(2); As-O(1) 1.654(2),1.675(2), 1.663(2); As-O(2) 1.712(2), 1.705(2), 1.719(2); As-O(3) 1.733(1), 1.716(2), 1.730(2).

Figure 6. The zwitterionic structure of 3-$NH_2$-4-$HOC_6H_3AsO_3H_2$ (**14**). Selected bond lengths (Å): As(1)-C(1) 1.904(3), As(1)-O(1) 1.670(2), As(1)-O(2) 1.684(2), As(1)-O(3) 1.728(2).

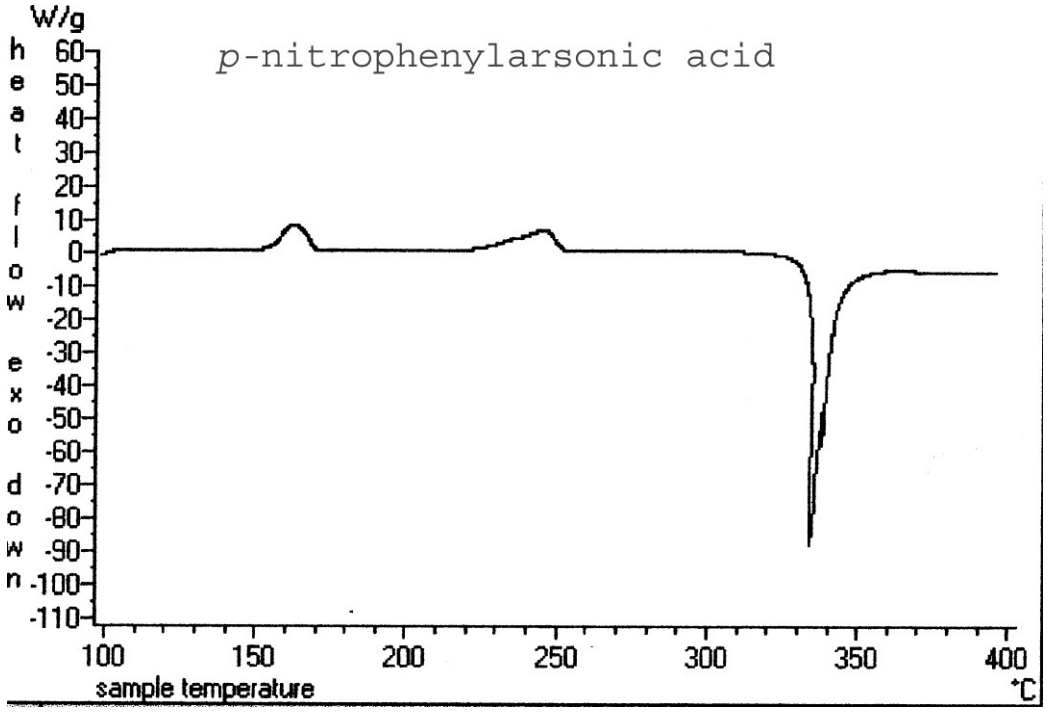
W/g
heat flow exo down
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
p-nitrophenylarsonic acid
100
150
200
250
300
350
400
sample temperature
°C

Figure 1

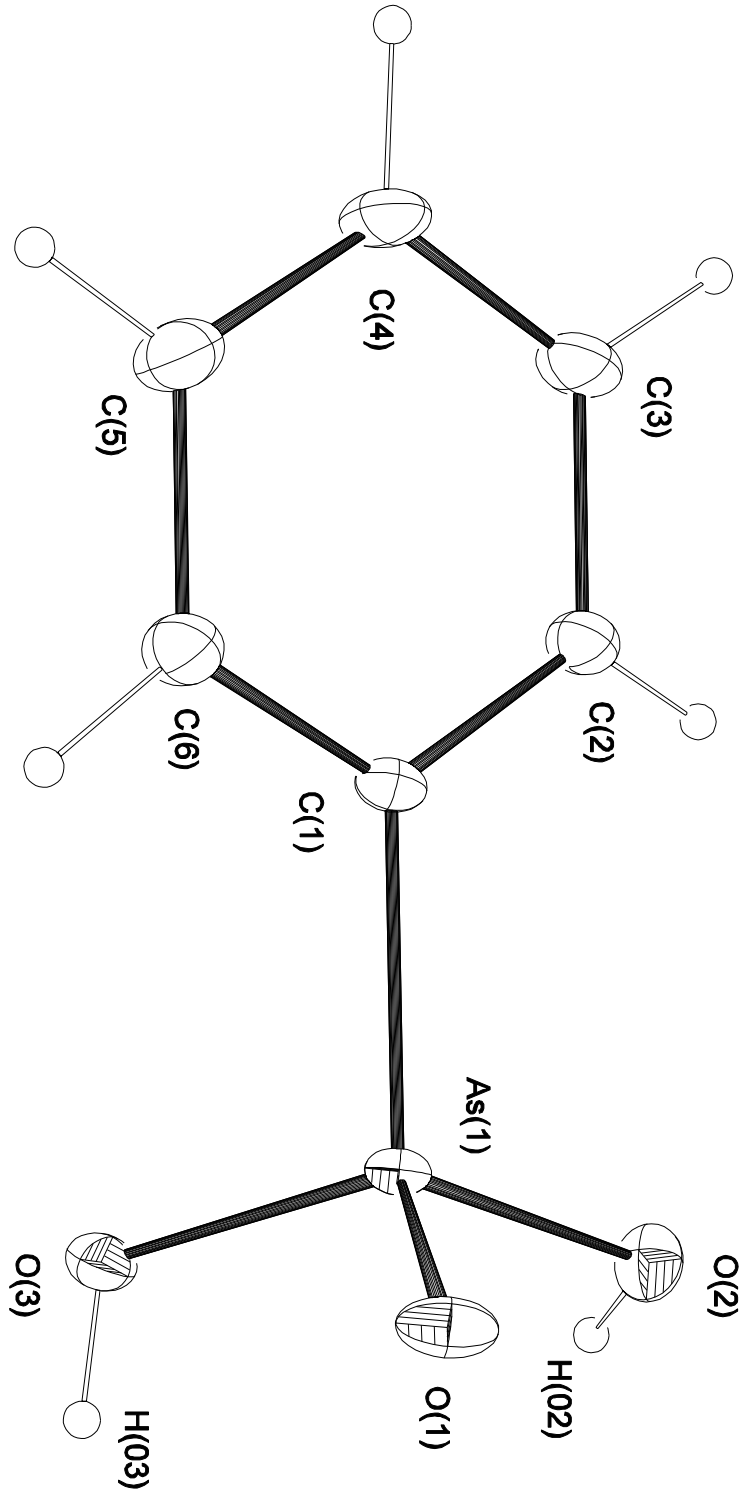


Figure 2

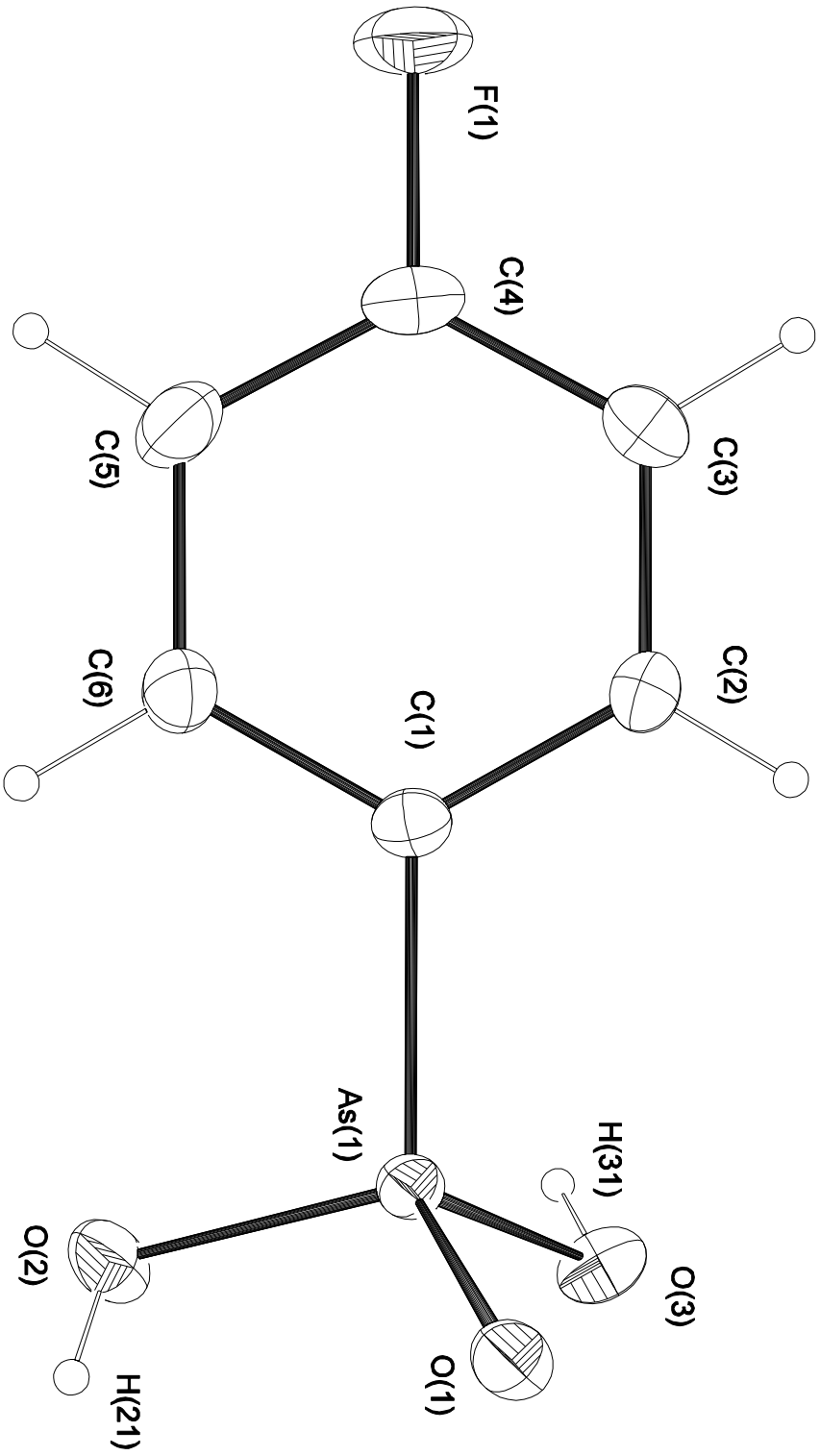


Figure 3

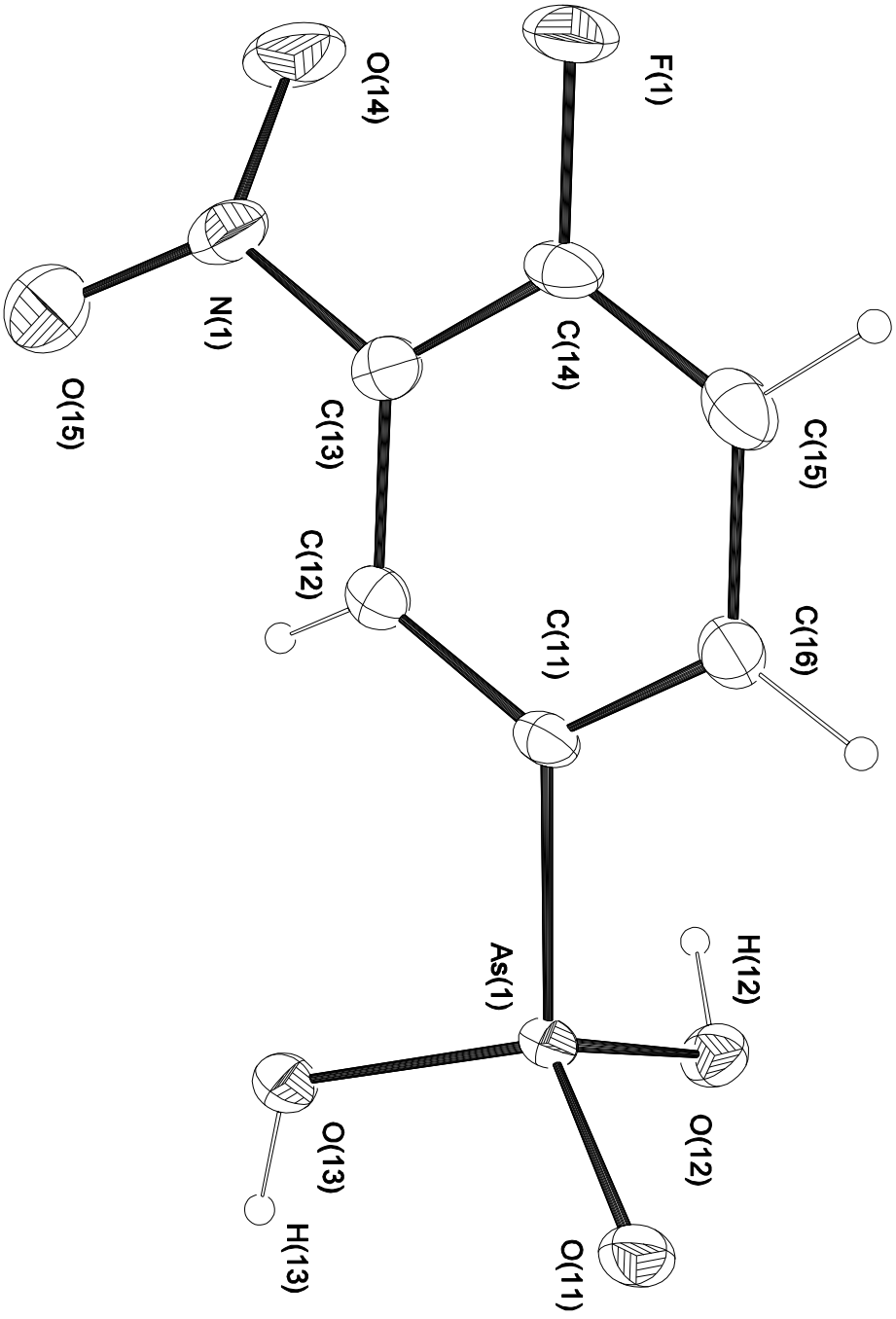


Figure 4

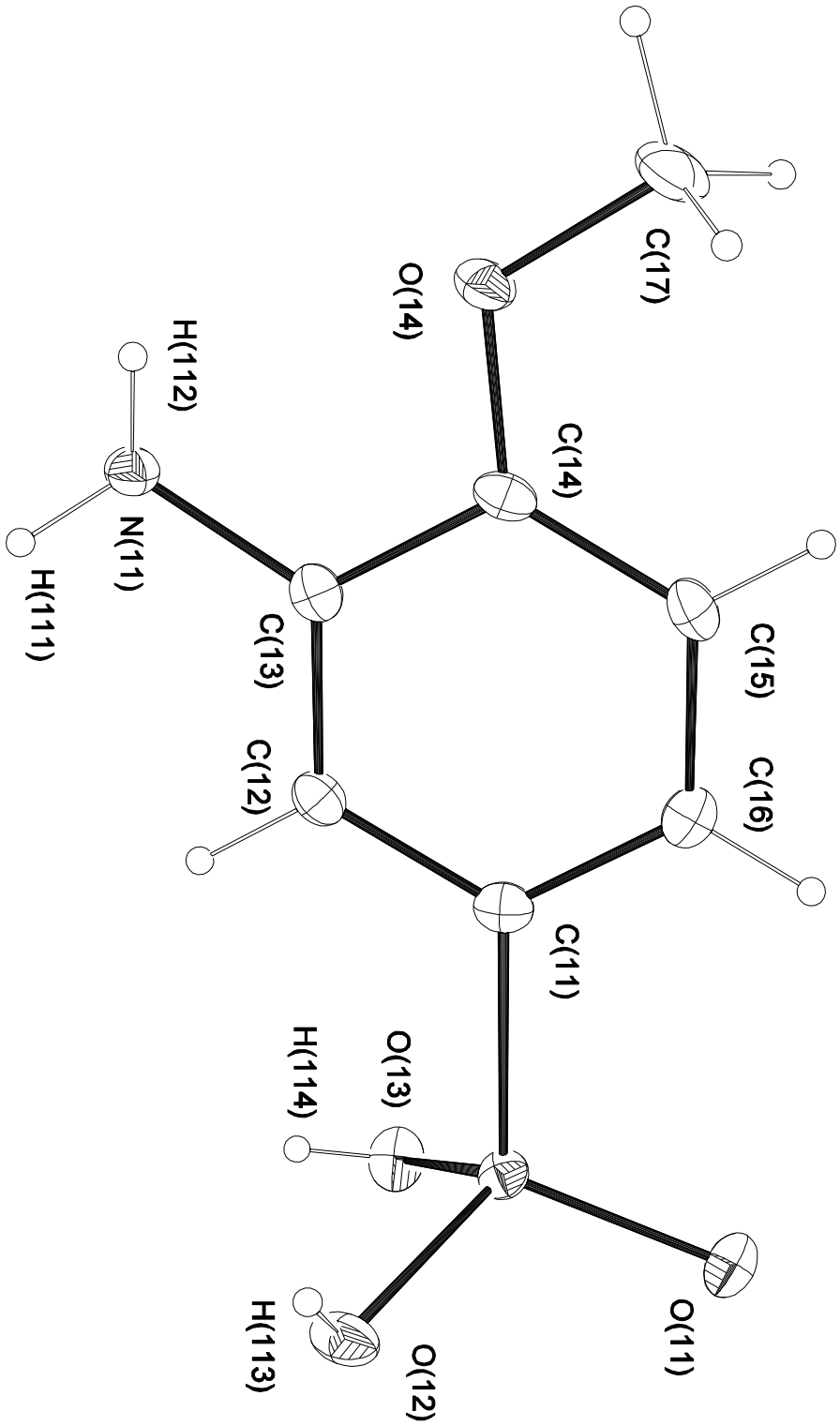
C(17)
O(14)
H(112)
C(14)
N(11)
H(111)
C(13)
C(15)
C(12)
C(16)
C(11)
H(114)
O(13)
H(113)
O(12)
O(11)

Figure 5

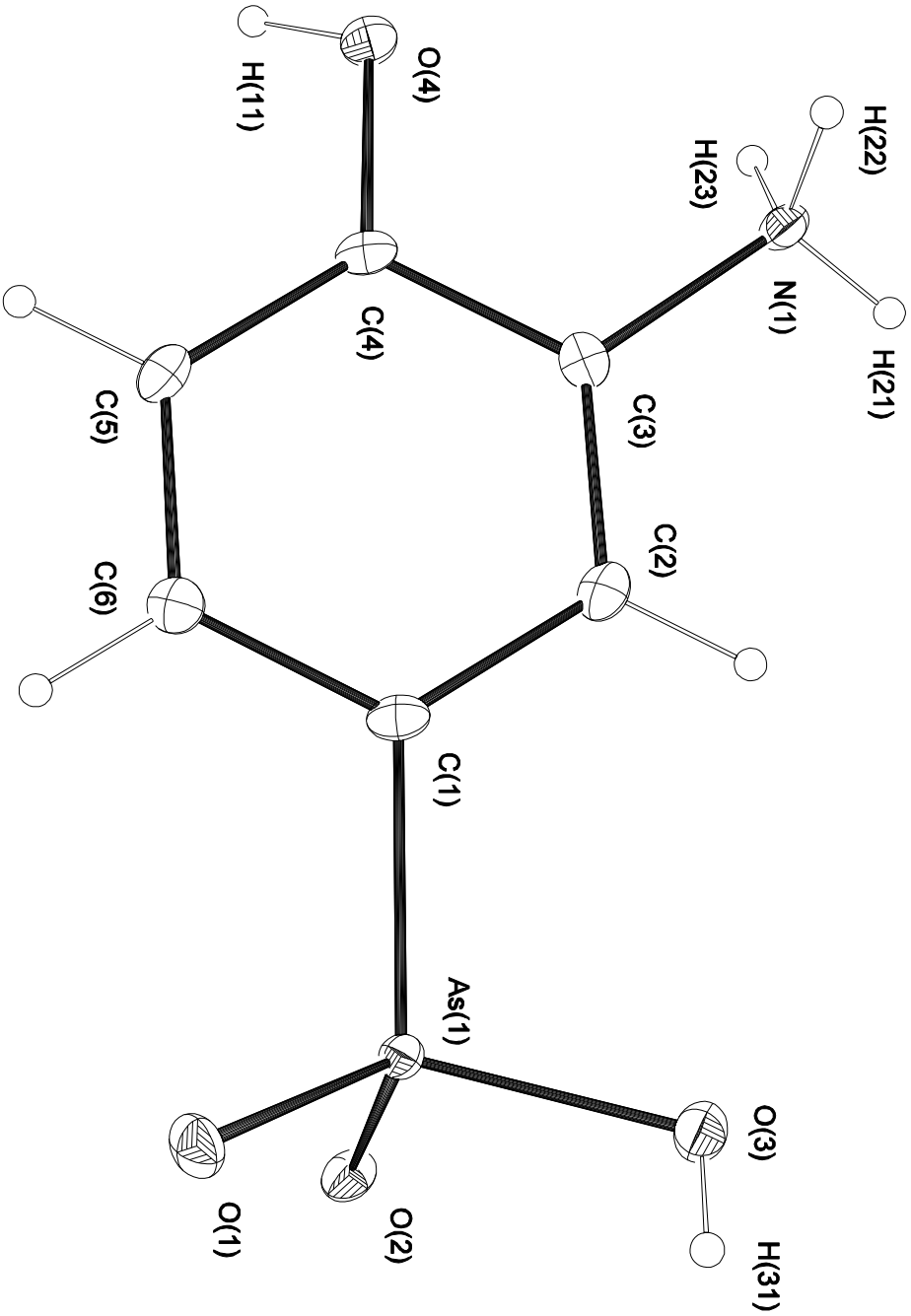


Figure 6