CHAPTER 3

PURIFICATION OF ORGANIC CHEMICALS

The general principles, techniques and methods of purification in Chapters 1 and 2 are applicable in this chapter. Most organic liquids and a number of solids can readily be purified by fractional distillation, usually at atmospheric pressure. Sometimes, particularly with high boiling or sensitive liquids, or when in doubt about stability, distillation or fractionation under reduced pressure should be carried out. To save space, the present chapter omits many substances for which the published purification methods involve simple distillation. Where boiling points are given, purification by distillation is another means of removing impurities. Literature references are omitted for methods which require simple recrystallisation from solution if the correct solvent can be guessed readily, and where no further information is given, e.g. spectra. Substances are listed alphabetically, usually with some criteria of purity, giving brief details of how they can be purified. Also noted are the molecular weights (to the first decimal place), melting points and/or boiling points together with the respective densities and refractive indexes for liquids, and optical rotations when the compounds are chiral. When the temperatures and/or the wavelengths are not given for the last three named properties then they should be assumed to be 20°C and the average of the wavelengths of the sodium D lines respectively; and densities are relative to water at 4°C.

The present chapter includes commercially available organic chemicals. Most of the organo-phosphorus, boron, silicon, alkali metal compounds and metal ion salts are in Chapter 4. Naturally occurring commercially available organic compounds of use in biochemistry, molecular biology and biology are included in Chapter 5.

Abbreviations of words and some journal names are listed in Chapter 1, pages 1 and 2.

As a good general rule all low boiling (<100°C) organic liquids should be treated as highly flammable and the necessary precautions should be taken.

Abietic acid [514-10-3] M 302.5, m 172-175°C, [α]D 25° -116° (-106°C)(c 1, EtOH). Crystd by dissolving 100g of acid in 95% EtOH (700ml), adding to H2O (600ml) and cooling. Filter, dry in a vacuum (over KOH or CaSO4) store in an O2-free atmosphere.

Abiscic acid [21293-39-8] M 264.3, m 160-161°C (sublimation), [α]D 287° + 24,000°, [α]D 245° -69,000° (c 1-50µg/ml in acidified MeOH or EtOH). Crystd from CCl4-pet.ether.

Acenaphthene [208-96-8] M 152.2, m 92-93°C. Dissolved in warm redistd MeOH, filtered through a sintered glass funnel and cooled to -78°C to ppte the material as yellow plates [Dainton, Invin and Walmsley TFS 56 1784 1960]. Alternatively can be sublimed in vacuo.

Acenaphthoquinone [82-86-0] M 182.2, m 260-261°C. Extracted with, then recrystd twice from C6H6. [LeFevre, Sundaram and Sundaram JCS 974 1963].

Acenaphthene [83-32-9] M 154.2, m 94.0°C. Crystd from EtOH. Purified by chromatography from CCl4 on alumina with benzene as eluent [McLaughlin and Zainal JCS 2485 1960].
**RS-Acenaphthenol**  [6306-07-6] M 170.2, m 144.5-145.5°, 146°, 148°. If highly coloured (yellow), dissolve in boiling benzene (14g in 200ml), add charcoal (0.5g), filter through a heated funnel, concentrate to 100ml and cool to give almost colourless needles. Benzene vapour is **TOXIC** use good fumecupboard. The acetate has b 166-168°/5mm (bath temp 180-185°). [Org Synth Col. Vol. III 3 1955]. It can also be recrystd from C6H6 or EtOH [Fieser and Cason JACS 62 432 1940]. It forms a brick-red crystalline complex with 2,4,5,7-tinitrofluoren-9-one which is recrystd from AcOH and dried in a vacuum over KOH and P2O5 at room temp. m 170-172° [Newman and Lutz JACS 78 2469 1956].

**Acetal**  [105-57-7] M 118.2, b 103.7-104°, d 0.831, n 1.38054, n25 1.3682. Dried over Na to remove alcohols and water, and to polymerise aldehydes, then fractionally distd. Or, treat with alkaline H2O2 soln at 40-45° to remove aldehydes, then the soln is saturated with NaCl, separated, dried with K2CO3 and distd from Na [Vogel JCS 616 1948].

**Acetamide**  [60-35-5] M 59.1, m 81°. Crystd by soln in hot MeOH (0.8ml/g), dilted with Et2O and allowed to stand [Wagner J Chem Ed 7 1135 1930]. Alternate crystns are from acetone, benzene, chloroform, dioxane, methyl acetate or from benzene-ethyl acetate mixture (3:1 and 1:1). It has also been recrystd from hot water after treating with HCl-washed activated charcoal (which had been repeatedly washed with water until free from chloride ions), then cryst again from hot 50% aqu. EtOH and finally twice from hot 95% EtOH [Christoffers and Kegeles JACS 85 2562 1963]. Final drying is in a vacuum desiccator over P2O5. Acetamide is also purified by distn (b 221-223°) or by sublimation in vacuo. Also purified by recrystn twice from cyclohexane containing 5% (v/v) of benzene. Needle-like crystals separated by filtn, washed with a small volume of distl H2O and dried with a flow of dry N2. [Slebocka-Tilk et al. JACS 109 4620 1987].
p-Acetamidobenzensulphonyl chloride \([121-60-8]\) M 233.7, \(m 149^\circ\)(dec). Crystd from toluene, CHCl₃, or ethylene dichloride.

\(\alpha\)-Acetamidocinnamic acid \([5469-45-4]\) M 205.2, \(m 185-186^\circ\) (\(2H_2O\)), \(190-191^\circ\)(anhydr), 193-195°. Recrystd from \(H_2O\), ethyl acetate, or toluene.

\(Z\)-O-(2-Acetamido-2-deoxy-\(D\)-glycopyranosylideneamino)\(N\)-phenylcarbamate (PUGNAC) \([132489-69-1]\) M 335.3, \(m 171-174^\circ\)(dec), \(174-180^\circ\)(dec), \(\alpha\)\(_D^\circ +67.5^\circ\) (c 0.2, MeOH). Purified by flash chromatography (silica gel and eluted with AcOEt-hexane 3:2) evaporated, and the foam recrystallised from AcOEt-MeOH. TLC on Merck SiO₂ gel 60 F254 and detected by spraying with 0.025M I₂ in 10% aqueous H₂SO₄ and heat at 200° gave RF 0.21. The acetate is hydrolysed with NH₃-MeOH.

2-Acetamidofluorene \([53-96-3]\) M 223.3, \(m 194^\circ\), 196-198°. Recrystd from toluene (1.3mg in 100ml). Solubility in \(H_2O\) is 1.3mg/L; \(UV A_{max} nm(log \varepsilon)\): 288(4.43), 313(4.13). [JOC 21 271 1956]. It can also be recrystd from 50% AcOH and sol in \(H_2O\) is 1.3mg/100ml at 25°. [B 99 3204 1966; A 343 265 1905].

\(5\)-Acetamido-1,3,4-thiadiazole-2-sulphonamide \([59-66-5]\) M 222.3, \(m 144-146^\circ\), 146-147°. Dissolve in \(CH_2Cl_2\), wash with saturated \(K_2CO_3\), then saturated aqueous \(NaCl\), dry (\(N_2SO_4\)), filter and evaporate. The red solid is recrystd from aqueous MeOH, \(m 147.5^\circ\). [JOC 56 6110 1991; BASU 15 1422 1966].

\(N\)-(2-Acetamido)iminodiacetic acid (ADA) \([26239-55-4]\) M 190.2, \(m 219^\circ\)(dec). Dissolved in water by adding one equivalent of NaOH soln to (final pH of 8-9), then acidified with HCl to ppte the free acid. Filtered and washed with water.

Acetamidomethanol \([625-51-4]\) M 89.1, \(m 47-50^\circ\), 54-56°, 55°. Recryst from freshly distd Me₂CO, wash the crystals with dry Et₂O and dry in a vacuum desiccator over \(P_2O_5\). RF 0.4 on paper chromatography with \(CHCl_3-EtOH\) (2:8) as solvent and developed with ammoniacal AgNO₃. Also crystallises in needles from EtOAc containing a few drops of Me₂CO. It is hygroscopic and should be stored under dry conditions. [JACS 73 2775 1951; B 99 3204 1966; A 343 265 1905].

2-Acetamido-5-nitrothiazole \([140-40-9]\) M 187.2, \(m 264-265^\circ\). Recrystd from EtOH or glacial acetic acid.

2-Acetamidophenol \([614-80-2]\) M 151.2, \(m 209^\circ\). Recrystd from water or aqueous EtOH.

3-Acetamidophenol \([621-42-1]\) M 151.2, \(m 148-149^\circ\). Recrystd from water.

4-Acetamidophenol \([103-90-2]\) M 151.2, \(m 169-170.5^\circ\). Recrystd from water or EtOH.

4-Acetamido-2,2,6,6-tetramethylpiperidine-1-oxyl (acetamidoTEMPO) \([14691-89-5]\) M 213.3, \(m 144-146^\circ\), 146-147°. Dissolve in \(CH_2Cl_2\), wash with saturated \(K_2CO_3\), then saturated aqueous \(NaCl\), dry (\(N_2SO_4\)), filter and evaporate. The red solid is recrystd from aqueous MeOH, \(m 147.5^\circ\). [JOC 56 6110 1991; BASU 15 1422 1966].

5-Acetamido-1,3,4-thiadiazole-2-sulphonamide \([59-66-5]\) M 222.3, \(m 256-259^\circ\)(dec). Recrystd from water.

Acetanilide \([103-84-4]\) M 135.2, \(m 114^\circ\). Recrystd from water, aqueous EtOH, benzene or toluene.

Acetic acid (glacial) \([64-19-7]\) M 60.1, \(m 16.6^\circ\), \(b 118^\circ\), \(d 1.049\), \(n 1.37171\), \(n^2O \ 1.36995\). Usual impurities are traces of acetaldehyde and other oxidisable substances and water. (Glacial acetic acid is very hygroscopic. The presence of 0.1% water lowers its \(m\) by 0.2°.) Purified by adding some acetic anhydride to react with water present, heating for 1h to just below boiling in the presence of 2g \(CrO_3\) per 100ml and then
fractionally distilling [Orton and Bradfield *JCS* 960, 1924, 983, 1927]. Instead of CrO₃, 2-5% (w/w) of KMnO₄, with boiling under reflux for 2-6h, has been used.

Traces of water have been removed by refluxing with tetraacetyl diborate (prepared by warming 1 part of boric acid with 5 parts (w/w) of acetic anhydride at 60°, cooling, and filtering off), followed by distn [Eichelberger and La Mer *JACS* 55, 3633, 1933].

Refluxing with acetic anhydride in the presence of 0.2g % of 2-naphthalenesulphonic acid as catalyst has also been used [Orton and Bradfield *JCS* 983, 1927]. Other suitable drying agents include CuSO₄ and chromium triacetate: P₂O₅ converts some acetic acid to the anhydride. Azeotropic removal of water by distn with thiophene-free benzene or with butyl acetate has been used [Birdwhistell and Griswold *JACS* 77, 873, 1955]. An alternative purification uses fractional freezing. Acetic acid has a pKa₂ of 4.76 in water.

**Acetic anhydride** [108-24-7] M 102.1, b 138°, d 1.082, n 1.3904. Adequate purification can usually be obtained by fractional distn through an efficient column. Acetic acid can be removed by prior refluxing with CaC₂ or with coarse Mg filings at 80-90° for 5days, or by distn from synthetic quinoline (1% of total charge) at 75mm pressure. Acetic anhydride can also be dried by standing with Na wire for up to a week, removing the Na and distilling from it under vacuum. (Na reacts vigorously with acetic anhydride at 65-70°).

Dippy and Evans [JOC 15, 451, 1950] let the anhydride (500g) stand over P₂O₅ (50g) for 3h, then decanted it and stood it with ignited K₂CO₃ for a further 3h. The supernatant liquid was distd and the fraction b 136-138°, was further dried with P₂O₅ for 12h, followed by shaking with ignited K₂CO₃, before two further distns through a five-section Young and Thomas fractionating column. The final material distd at 137.8-138.0°. Can also be purified by azeotropic distn with toluene: the azeotrope boils at 100.6°. After removal of the remaining toluene, the anhydride is distd [sample had a specific conductivity of 5 x 10⁻⁹ ohm⁻¹cm⁻¹].

**Acetin Blue** Crystd from 1:3 benzene-methanol.

**Acetoacatamide** [5977-14-0] M 101.1, m 54-56°, 54-56°. Recrystallise from CHCl₃, or Me₂CO/pet ether. Crystals from pyridine with 4mol of solvent. Slightly soluble in H₂O, EtOH and AcOH but insoluble in Et₂O.

**Acetoacetanilide** [102-01-2] M 177.2, m 86°. Crystd from H₂O, aqueous EtOH or pet ether (b 60-80°).

**Acetoacetyl piperidide** [1128-87-6] M 169.2, b 88.9°/0.1mm, n₂ 1.4983. Dissolved in benzene, extracted with 0.5M HCl to remove basic impurities, washed with water, dried, and distd at 0.1mm [Wilson JOC 28, 314, 1963].

**α-Acetobromoglucose** [572-09-8] M 411.2, m 88-89°, [α]D₂⁵ +199.3° (c 3, CHCl₃). Crystd from isopropyl ether or pet ether (b 40-60°).

**Acetoin** see 3-hydroxy-2-butanone.


**β-Acetonaphthene** see 2-acetonaphthene.

**Acetone** [67-64-1] M 58.1, b 56.2°, d 0.791, n 1.35880. The commercial preparation of acetone by catalytic dehydrogenation of isopropyl alcohol gives relatively pure material. Analytical reagent quality generally contains less than 1% organic impurities but may have up to about 1% H₂O. Dry acetone is appreciably hygroscopic. The main organic impurity in acetone is mesityl oxide, formed by the aldol condensation. It can be dried with anhydrous CaSO₄, K₂CO₃ or type 4A Linde molecular sieves, and then distd. Silica gel and alumina, or mildly acidic or basic desiccants cause acetone to undergo the aldol condensation, so that its water content is increased by passage through these reagents. This also occurs to some extent when
P₂O₅ or sodium amalgam is used. Anhydrous MgSO₄ is an inefficient drying agent, and CaCl₂ forms an addition compound. Drierite (anhydrous CaSO₄) offers the minimum acid and base catalysis of aldol formation and is the recommended drying agent for this solvent [Coetzee and Siao Inorg Chem 14v 2 1987; Riddick and Bunger Organic Solvents Wiley-Interscience, N.Y., 3rd edn, 1970]. Acetone was shaken with Drierite (25g/L) for several hours before it was decanted and distd from fresh Drierite (10g/L) through an efficient column, maintaining atmospheric contact through a Drierite drying tube. The equilibrium water content is about 10⁻²M. Anhydrous Mg(ClO₄)₂ should not be used as drying agent because of the risk of EXPLOSION with acetone vapour.

Organic impurities have been removed from acetone by adding 4g of AgNO₃ in 30ml of water to 1L of acetone, followed by 10ml of M NaOH, shaking for 10min, filtering, drying with anhydrous CaSO₄ and distilling [Werner Analyst 58 335 1933]. Alternatively, successive small portions of KMnO₄ have been added to acetone at reflux, until the violet colour persists, followed by drying and distn. Refluxing with chromic anhydrate has also been used. Methanol has been removed from acetone by azetrope distn (at 35°) with methyl bromide, and treatment with acetyl chloride.

Small amounts of acetone can be purified as the NaI addition compound, by dissolving 100g of finely powdered NaI in 400g of boiling acetone, then cooling in ice and salt to -50°. Crystals of NaI·3Me₂CO are filtered off, and, on warming in a flask, acetone distils off readily. [This method is more convenient than the one using the bisulphite addition compound]. Also purified by gas chromatography on a 20% free fatty acid phthalate (on Chromosorb P) column at 100°.

For efficiency of desiccants in drying acetone see Burfield and Smithers [JOC 43 3966 1978]. The water content of acetone can be determined by a modified Karl Fischer titration [Koupparis and Malmstadt AC 54 1914 1982].

**Acetone cyanohydrin** [75-86-5] M 85.1, b 48°/2.5mm, 68-70°/11mm, 78-82°/15mm, d₁₀⁰ 0.93. Dry with Na₂SO₄ and dist as rapidly as possible under vacuum to avoid decomposition. Discard fractions boiling below 78-82°/15mm. Store in the dark. **USE AN EFFICIENT FUME HOOD as HCN (POISONOUS) is always present.** [Org Synth Col.Vol. II 7 1940].

**Acetonedicarboxylic acid** [542-05-2] M 146.1, m 187°. Crystd from ethyl acetate and stored over P₂O₅.

**Acetone semicarbazone** [110-20-3] M 115.1, m 187°. Crystd from water or from aqueous EtOH.

**Acetonitrile** [75-05-8] M 41.1, b 81.6°, dᵢ²⁵ 0.77683, n 1.3441, n₂⁵ 1.34163. Commercial acetonitrile is a byproduct of the reaction of propylene and ammonia to acrylonitrile. The procedure that significantly reduces the levels of acrylonitrile, allyl alcohol, acetone and benzene was used by Kiesel [AC 52 2230 1988]. Methanol (300ml) is added to 3L of acetonitrile fractionated at high reflux ratio until the boiling temperature rises from 64° to 80°, and the distillate becomes optically clear down to λ = 240nm. Add sodium hydride (1g) free from paraffin, to the liquid, reflux for 10min, and then distil rapidly until about 100ml of residue remains. Immediately pass the distillate through a column of acidic alumina, discarding the first 150ml of percolate. Add 5g of CaH₂ and distil the first 50ml at a high reflux ratio. Discard this fraction, and collect the following main fraction. The best way of detecting impurities is by gas chromatography.

Usual contaminants in commercial acetonitrile include H₂O, acetamide, NH₄OAc and NH₃. Anhydrous CaSO₄ and CaCl₂ are inefficient drying agents. Preliminary treatment of acetonitrile with cold, satd aq KOH is undesirable because of base-catalysed hydrolysis and the introduction of water. Drying by shaking with silica gel or Linde 4A molecular sieves removes most of the water in acetonitrile. Subsequent stirring with CaH₂ until no further hydrogen is evolved leaves only traces of water and removes acetic acid. The acetonitrile is then fractionally distd at high reflux, taking precaution to exclude moisture by refluxing over CaH₂ [Coetzee PAC 13 429 1966]. Alternatively, 0.5-1% (w/w) P₂O₅ is often added to the distilling flask to remove most of the remaining water. Excess P₂O₅ should be avoided because it leads to the formation of an orange polymer. Traces of P₂O₅ can be removed by distilling from anhydrous K₂CO₃.

Kolthoff, Bruckenstein and Chantooni [JACS 83 3297 1961] removed acetic acid from 3L of acetonitrile by shaking for 24h with 200g of freshly activated alumina (which had been reactivated by heating at 250° for 4h). The decanted solvent was again shaken with activated alumina, followed by five batches of 100-150g of anhydrous CaCl₂. (Water content of the solvent was then less than 0.2%). It was shaken for 1h with 10g of
P2O5, twice, and distd in a 1m x 2cm column, packed with stainless steel wool and protected from atmospheric moisture by CaCl2 tubes. The middle fraction had a water content of 0.7 to 2mM.

Traces of unsaturated nitriles can be removed by an initial refluxing with a small amount of aq KOH (1ml of 1% solution per L). Acetonitrile can be dried by azeotropic distn with dichloromethane, benzene or trichloroethylene. Isonitrile impurities can be removed by treatment with conc HCl until the odour of isonitrile has gone, followed by drying with K2CO3 and distn.

Acetonitrile was refluxed with, and distd from alkaline KMnO4 and KHSO4, followed by fractional distn from CaH2. (This was better than fractionation from molecular sieves or passage through a type H activated alumina column, or refluxing with KBH4 for 24h and fractional distn)[Bell, Rodgers and Burrows *JCSFT* I 73 315 1977; Moore et al. *JACS* 108 2257 1986].

Material suitable for polarography was obtained by refluxing over anhydrous AlCl3 (15gL) for lh, distilling, refluxing over Li2CO3 (lo&); for lh and redistg. It was then refluxed over CaH2 (2gL) for lh and fractionally distd, retaining the middle portion. The product was not suitable for UV spectroscopy use. A better purification used refluxing over anhydrous AlCl3 (15gL) for lh, distg, refluxing over alkaline KMnO4 (log KMn04, log Li2C03L) for 15min, and distg. A further reflux for lh over KHSO4 (15g/L), then dist, was followed by refluxing over CaH2 (2g/L) for lh, and fractional distn. The product was protected from atmospheric moisture and stored under nitrogen [Walter and Ramalay *AC* 45 165 1973].

Acetonitrile has been distd from AgN03, collecting the middle fraction over freshly activated A12O3. After standing for two days, the liquid was distd from the activated A12O3. Specific conductivity 0.8-1.0 x 10⁻⁸ mhos [Harkness and Daggett *Canad J Chern* 43 12 15 1965].

Acetonitrile 14C was purified by gas chromatography and is water free and distd at 81°. [J.Mol.Biol. 1974, 87, 541].


### Acetophenone [98-86-2] M 120.2, m 19.6°, b 54°/2.5mm, 202°/760mm, d²⁵ 1.0238, n²⁵ 1.5322. Dried by fractional distn or by standing with anhydrous CaSO4 or CaCl2 for several days, followed by fractional distn under reduced pressure (from P2O5, optional), and careful, slow and repeated partial crysfts from the liquid at 0° excluding light and moisture. It can also be crystd at low temperatures from isopentane. Distn can be followed by purification using gas-liquid chromatography [Earls and Jones *JCSFT* I 71 2186 1975].

### Acetoxime [127-06-0] M 73.1, m 63° b 135°/760mm. Crystd from pet ether (b 40-60°). Can be sublimed.

### Acetonylacetone (hexane-2,5-dione) [110-13-4] M 114.2, m -9°, b 76-78°/13 mm, 88°/25mm, 137°/150mm, 188°/atm, d₄ 0.9440, n₄ 1.423. Purified by dissolving in Et₂O, stirred with K2CO3 (a quarter of its bulk), filtered, dried over anhydrous Na₂SO₄ (not CaCl₂), filtered, evapd and distd in a vacuum. It is then redistd through a 30cm Vigreux column (oil bath temp 150°). It is miscible with H₂O and EtOH. The dioxime has m 137° (plates from C₆H₆), mono-oxime has b 130°/11mm, and the 2,4-dinitrophenylhydrazone has m 210-212° (red needles from EtOH). [B 22 2100 1989; for enol content see *JOC* 19 1960 1954].

### Acetonyl triphenyl phosphonium chloride [1235-21-8] M 354.8, m 237-238°, 244-246° (dec). Recryst from CHCl₃ + C₆H₆ + pet ether (b 60-80°) and by dissolving in CHCl₃ and running the soln into dry Et₂O. λmax nm(e) 255(3,600), 262(3,700), 268(4,000) and 275(3,100). The iodide salt crystallises from H₂O and has m 207-209°. [JOC 22 41 1957]. IR: max (cm⁻¹) 1529 (s), 1470 (m), 1425 (s), 1374 (m), 1105 (s) and 978 (s). [JOC 22 41, 44 1957].

### Aceto-o-toluidide [120-66-1] M 149.2, m 110°, b 296°/760mm,

### Aceto-m-toluidide [537-92-8] m 65.5°, b 182-183°/14mm, 307°/760mm. Crystd from H₂O, EtOH or aqueous EtOH.
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Aceto-p-toluidide [103-89-9] M 149.2, m 146°, b 307°/760mm. Crystd from aqueous EtOH.

Acetoxyacetone (acetol acetone) [592-20-1] M 149.2, m 146°/760mm, 307°/760mm, 174-176°/atm, d4 1.0757, nD 1.4141. Distil under reduced pressure, then redistil at atm pressure. It is miscible with H2O but is slowly decomposed by it. Store in dry atmosphere. The 2,4-dinitrophenylhydrazone has m 115-119° (from CHCl3/hexane).

Acetoxyacetone [(1R)-1-(tert-butylmethylsiloxy)ethyl]-2-azetidinone see Chapter 4.

1-Acetoxy-2-butoxyethane [112-07-2] M 160.2, b 61-62°/0.2mm, 75-76°/12mm, 185.5°/740mm, 188-192°/atm, d0 0.97, nD 1.406. Shake with anhyd Na2CO3, filter and distil in vac. Redistn can then be carried out at atm pressure. [JOC 21 1041 1956].


R-(-)-a-Acetoxyphenylacetic acid [51019-43-3] M 194.2, m 96-98°, [α]D -153.7° (c 2.06, Me2CO), [α]D -194° (c 2.4, Me2CO). Recrysts from H2O with 1mol of solvent which is removed on drying. [JCS 22 1943].

21-Acetoxypregnalone M 374.5, m 184-185°. Crystd from Me2CO.

Acetoxyacetone [123-54-6] M 100.1, b 45°/30mm, d20 0.9630, n18.5 1.45178. Small amounts of acetic acid were removed by shaking with small portions of 2M NaOH until the aqueous phase remained faintly
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alkaline. The sample, after washing with water, was dried with anhydrous Na₂SO₄, and distd through a modified Vigreux column [Cartledge JACS 73 4416 1951]. An additional purification step is fractional crystn from the liquid. Alternatively, there is less loss of acetylacetone if it is dissolved in four volumes of benzene and the soln is shaken three times with an equal volume of distd water (to extract acetic acid); the benzene is then removed by distn at 43-53o and 20-30mm through a helices-packed column. It is then refluxed over P₂O₅ (10gL) and fractionally distd under reduced pressure. The distillate (sp conductivity 4 x 10⁻⁸ ohm⁻¹cm⁻¹) was suitable for polarography [Fujinaga and Lee Talanta 24 395 1977]. To recover used acetylacetone, metal ions were stripped from the soln at pH 1 (using 100ml 0.1M H₂SO₄/L of acetylacetone). The acetylacetone was washed with (1:10) ammonia soln (100mVL), and with distd water (100mL, twice), then treated as above.


Acetyl-α-amino-n-butyric acid [34271-24-4] M 145.2. Crystd twice from water (charcoal) and air dried [King and King JACS 78 1089 1956].

2-Acetylaminofluorene see N-2-fluorenylacetamide.


N-Acetylanthranilic acid [89-52-1] M 179.1, m 182-184°, 185-186°, 190°(dec). Wash with distilled H₂O and recrystallise from aqueous AcOH, dry and recrystallise again from EtOAc. Also recryst from water or EtOH. Its pKa is 3.61 at 20°. [JCS 2495 1931; JACS 77 6698 1955].

2-Acetylbenzoic acid [577-56-0] M 164.2, m 115-116°, 116-118°. Recrystallises from C₆H₆ and H₂O (15g/100ml). It has pKa in H₂O of 4.10 at 25°, and the oxime has m 156-157°, and the 2,4-dinitrophenylhydrazone has m 185-186°(needles from EtOH). [JACS 69 1547 1947].

4-Acetylbenzoic acid [586-89-0] M 164.2, m 207.5-209.5°, 208.6-209.4°. Dissolve in 5% aqueous NaOH, extract with Et₂O, and acidify the aqueous soln. Collect the ppte, and recrystallise from boiling H₂O (100 parts) using decolorising charcoal. It has a pKa of 3.70 in H₂O at 25°, and a pKa of 5.10 in 50% aq EtOH. [JOC 24 504 1959; JCS 265 1957; JACS 72 2882 1050, 74 1058 1952].


4-Acetylphenol [92-91-1] M 196.3, m 120-121°, b 325-327°/760mm. Crystd from EtOH or acetone.


2-Acetylbutyrolactone [517-23-7] M 128.1, b 105°/5mm, 120-123°/11mm, 142-143°/30mm, d₄¹ 1.1846, nD¹ 1.459. Purified by distillation, which will convert any free acid to the lactone, alternatively dissolve in Et₂O, wash well with 0.5N HCl, dry the organic layer and distil. The
solubility in H$_2$O is 20% v/v. The 2,4-dinitrophenylhydrazone forms orange needles from MeOH, m 146$^\circ$. The dipropylamine salt has m 68-70$^\circ$, from which the lactone is formed on acidification. The liquid is a skin irritant. [J Pharm Soc Japan 62 417(439) 1942; HCA 35 2401 1952].


Acetyl chloride [75-36-5] M 78.5, b 52$^\circ$, d 1.1051, n 1.3897. Refluxed with PCl$_5$ for several hours to remove traces of acetic acid, then distd. Redistd from one-tenth volume of dimethylaniline or quinoline to remove free HCl. A.R. quality is freed from HCl by pumping it for 1h at -78$^\circ$ and distg into a trap at -196$^\circ$.

Acetylcholine bromide [66-23-9] M 226.1, m 146$^\circ$. Crystd from EtOH.

Acetylcyclohexane (cyclohexyl methylketone) [823-76-7] M 126.2, b 64°/11mm, 76.2-77°/25mm, d$_2^0$ 0.9178, n$_D^2$ 1.4519. Dissolve in Et$_2$O, shake with H$_2$O, dry, evaporate and fractionate under reduced pressure. [UV: JACS 74 518 1952; JCS 2384 1956]. The semicarbazone has m 174$^\circ$ and the 2,4-dinitrophenylhydrazone has m 139-140$^\circ$ [HCA 39 1290 1956].

2-Acetylcyclohexanone [874-23-7] M 140.2, m -11°, b 62-64°/2.5mm, 95-98°/10mm, 111-112°/18mm, d$_4^2$ 1.08, n$_D^2$ 1.51. Dissolve in ligroin (b 30-60$^\circ$), wash with saturated aqueous NaHCO$_3$, dry over Drierite and fractionate in a vacuum. [JACS 75 626, 5030 1953; B 87 108 1954]. It forms a Cu salt which crystallises in green leaflets from EtOH, m 162-163$^\circ$ [UV: JCS 4419 1957].

2-Acetylcyclopentanone [1670-46-8] M 126.2, b. 72-75°/8mm, 82-86°/12mm, 88°/18mm, d$_4^2$ 1.043, n$_D^2$ 1.490. Dissolve in pet ether (b 30-60$^\circ$), wash with satd aq NaHCO$_3$, dry over Drierite and fractionate in a vacuum. It gives a violet colour with ethanolic FeCl$_3$ and is only slowly hydrolysed by 10% aq KOH but rapidly on boiling to yield 6-oxoheptanoic acid. [JACS 75 5030 1953; JCS 4232 1956; UV: JACS 81 2342 1959]. It gives a gray green Cu salt from Et$_2$O-pentane, m 237-238$^\circ$ [JACS 79 1488 1957].

N$^4$-Acetylcytosine [14631-20-0] M 153.1, m >300$^\circ$, 326-328$^\circ$. If TLC or paper chromatography show that it contains unacetylated cytosine then reflux in Ac$_2$O for 4h, cool at 3-4$^\circ$ for a few days, collect the crystals, wash with cold H$_2$O, then EtOH and dry at 100$^\circ$. It is insoluble in EtOH and difficulty soluble in H$_2$O but crystallises in prisms from hot H$_2$O. It is hydrolysed by 80% aq AcOH at 100$^\circ$/1h. [Amer Chem J 29 500 1903; UV: JCS 2384 1956; JACS 80 5164 1958]. It forms an Hg salt [JACS 79 5060 1957].

Acetyldigitoxin-α M 807.0, m 217-221°, [α]$_D^{20}$+5.0 (c 0.7, pyridine). Crystd from MeOH as plates.

Acetylene [74-86-2] M 26.0, m -80.8$^\circ$, b -84$^\circ$. Purified by successive passage through spiral wash bottles containing, in this order, satd aq NaHSO$_4$, H$_2$O, 0.2M iodine in aq KI (two bottles), sodium thiosulphate soln (two bottles), alkaline sodium hydrosulphite with sodium anthraquinone-2-sulphonate as indicator (two bottles), and 10% aqueous KOH soln (two bottles). The gas was then passed through a Dry-ice trap and two drying tubes, the first containing CaCl$_2$, and the second, Dehydrite [Conn, Kistiakowsky and Smith JACS 61 1868 1939]. Acetone vapour can be removed from acetylene by passage through two traps at -65$^\circ$. Sometimes contains acetone and air. These can be removed by a series of bulb-to-bulb distns, e.g. a train consisting of a conc H$_2$SO$_4$ trap and a cold EtOH trap (-73$^\circ$), or passage through H$_2$O and H$_2$SO$_4$, then over KOH and CaCl$_2$.

Acetylenedicarboxamide [543-21-5] M 112.1, m 294$^\circ$/(dec). Crystd from MeOH.

Acetylenedicarboxylic acid [142-43-0] M 114.1, m 179$^\circ$/(anhydrous). Crystd from aqueous ether as dipicrate.
Acetylenedicarboxylic acid monopotassium salt [928-04-1] M 152.2. Very soluble in H₂O, but can be crystallized from small volume of H₂O in small crystals. These are washed with EtOH and dried over H₂SO₄ at 125°C. [B 10 841 1877; A 272 133 1893].

N-Acetylenehexadienamidine [1001-53-2] M 102.1, m 50-51⁰, 51⁰, b 128⁰/3mm, 125-130⁰/5mm, 133-139⁰/27mm. It has been fractionated under reduced pressure and fraction b 125-130⁰/5mm was re-refractionated; fraction b 132-135⁰/4mm was collected and solidified. It is a low melting hygroscopic solid which can be recrystallized from dioxane-Et₂O. It is soluble in H₂O, Et₂O and C₆H₆. The p-toluene sulphonate salt can be recrystallized from EtOH-EtOAc 1:8, has m 125-126⁰ but the free base cannot be recovered from it by basifying and extracting with CH₂Cl₂. The pication has m 175⁰ (from EtOH). The pKa is 9.28 in H₂O at 25⁰. [JACS 63 853 1941; 78 2570 1956].

2-Acetylfluorene [781-73-7] M 208.3, m 132⁰. Crystallizes from EtOH.


N-Acetyltartaric acid [1188-37-0] M 189.2, m 185⁰ (RS); 201⁰ (S), [α]₁₅₄₆ +152.4⁰ (c 2, acetone); [α]₁₃₈₆ +150.4⁰ (c 2, acetone). Crystallizes from boiling water.


N-Acetylglycine [543-24-8] M 175.2, m 206-208⁰. Treated with acid-washed charcoal and recrystallizes three times from water or EtOH/Et₂O and dried in vacuo over KOH [King and King JACS 78 1089 1956].


N-Acetylhistidine (H₂O) [39145-52-3] M 171.2, m 148⁰ (RS); 169⁰ (S), [α]₂₅ +25 -16.6⁰ (in H₂O). Likely impurity is glutamic acid. Crystallizes from boiling water.


3-Acetylindole [703-80-0] M 159.2, m 188-190⁰, 191-193⁰, 194⁰. Recrystallizes from MeOH or C₆H₆ containing a little EtOH. The phenylureido derivative has m 154⁰. [JCS 461 1946].

Acetyl iodide [507-02-8] M 170.0, m 108⁰/760mm. Purified by fractional distillation.


Acetyl mandelic acid (R-) [51019-43-3] M 194.2, m 98-99⁰ [α]₁₃₈₆ -152.4⁰ (c 2, acetone); (S+) [7322-88-5] m 97-99⁰ [α]₁₃₈₆ +150.4⁰ (c 2, acetone). Crystallizes from benzene or toluene.
**Purification of Organic Chemicals**

**S-β-(Acetylmercapto)isobutyric acid** [7649-39-7] M 162.2, m 40-40.5°, b ca 120°/1.25mm. Distill under vacuum and recrystd from C6H6. [Chem Abs 38 3616 1944].


**Acetymethionine nitrile** [538-14-7] M 172.3, m 44-46°. Cryst from ethyl ether.

**5-Acetyl-2-methoxybenzaldehyde** [531-99-7] M 166.2, m 144°.

**5-Acetyl-N'-methyl-L-alaninamide** [1901-83-8] M 144.2. Crystd from EtOAc-Et2O, then from EtOH and Et2O.

**Acetymethylcarbinol** see 3-hydroxy-2-butanone.

**4-Acetyl-1-methyl-1-cyclohexene** [6090-09-1] M 138.2, 73-75°/7.5mm, 85-86°/13mm, 94-94.7°/20mm, 204.5-206°/747mm, d4 1.0238, nD 1.4690. Purified by fractionation under reduced pressure in vacuo, and when almost pure it can be fractionated at atmospheric pressure, preferably in an inert atm. Forms two semicarbazones one of which is more soluble in C6H6, and both can be recryst from EtOH, more soluble has m 149° (15lo), and the less soluble has m 172-175° (1910). 4-Nitrophenylhydrazone has m 166-167° and the 2,4-dinitrophenylhydrazone has m 114-115°. [HCA 17 129, 140 1934; A 564 109 1949].

**4-Acetylmorpholine** M 129.2, m 13.8-14°, 14°, 14.5°, b 96-97°/6mm, 113-128°/22mm, 242-247°/760mm, d4 1.0963, nD 1.4830. Distd through an 8inch Fenske column with a manual take-off head. Purified by fractional distn. The hydrobromide has m 172-175°. [JACS 75 357 1953, JOC 21 1072 1956].

**N-Acetyl-6N'-methylglycinamide** [7606-79-3] M 130.2. Recrystd from EtOH/Et2O mixture.


**1-Acetylnaphthalene** [941-98-0] M 170.1, m 10.5°, b 93-95°/0.1mm, 167°/12 mm, 302°/atm, d4 1.12. If the NMR spectrum indicates the presence of impurities, probably 2-acetylnaphthalene, convert the substance to its picrate by dissolving in benzene or EtOH and adding excess of satd picric acid in these solvents until separation of picrates is complete. Recryst the picrate till m is 118°. Decompose the picrate with dil NaOH and extract with Et2O and evaporation gives purer 2-acetylnaphthalene. If this residue solidifies it can be recrystd from pet ether. Purity should be checked by high field NMR spectroscopy. Oxime has m 145° dec, and the semicarbazone has m 235°. [A 300 95 1911; JACS 61 3438 1939].

**2-Acetylnaphthalene** (2-acetonaphthenone) [93-08-3] M 170.2, m 52-53°, 55°, 55.8°, b 164-166°/8mm, 171-173°/17mm, 301-303°/atm. Separated from the 1-isomer by fractional crystall of the picrate in EtOH (see entry for the 1-isomer) m 82°. Decomposition of the picrate with dil NaOH and extraction with Et2O and evaporation gives purer 2-acetylnaphthalene. If this residue solidifies it can be recrystd from pet ether. Purity should be checked by high field NMR spectroscopy. Oxime has m 145° dec, and the semicarbazone has m 235°. [A 300 95 1911; JACS 72 753 and 5626 1950, JOC 25 512 1940].

**N-Acetyl-D-penicillamine** [15537-71-0] M 191.3, m 189-190° (dec), [α]D +18° (c 1, in 50% EtOH). Cryst from water.


**1-Acetyl-2-phenylhydrazine** [114-83-0] M 150.2, m 128.5°. Cryst from aqueous EtOH.
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1-Acetyl-4-piperidone [350-33-8] M 121.1, m 13-14°, b 65-66°/1mm, 92-95°/8-9 mm, 105°(113°)/16mm, 219-221°/760mm, d\textsubscript{4} 1.1065, n\textsubscript{D} 1.5023. Purified by fractional distn through a short Vigreux column (15mm). The 2,4-dinitrophenylhydrazone has m 212-213° (from EtOH). It is freely soluble in H\textsubscript{2}O but insoluble in Et\textsubscript{2}O. [JACS 79 4226 1957].

2-Acetylthiazole [24295-03-2] M 127.2, b 89-91° (90-95°)/12mm, 95-105°/15mm, d\textsubscript{4} 1.23, n\textsubscript{D} 1.55. Check NMR spectrum, if not too bad, distil through an efficient column in a vacuum. The oxime sublimes at 140-145°, m 159° (cryst from H\textsubscript{2}O) has m 163-165.5°; [JACS 79 4524 1957; HCA 31 1142 1948]. [HCA 40 554 1957].

3-Acetylthiophene (methyl 3-thienyl ketone) [1468-83-3] M 126.2, m 57°, 60-63°, b 106-107°/25 mm, 208-210°/748mm. Recryst from pet ether (b 30-60°) or EtOH. 2,4-dinitrophenylhydrazone crystallises from CHCl\textsubscript{3}, m 265°, and the semicarbazone crystallises from EtOH, m 174-175°. [JACS 70 1555 1948].
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N-Acetyltryptophan M 246.3, [α]D ~87-32-1 m 206° (RS); [2128-34-4] m 188° (S), [α]D +30.1° (aq NaOH). Likely impurity is tryptophan. Crystd from EtOH by adding water.


N-Acetylurea [591-08-2] M 118.2, m 164-165°, 165-168°. Recrystd from AcOH, the solid is washed with Et2O and dried in air then at 100°. [Coll Czech Chem Comm 24 3678 1959].


trans-Aconitic acid (1,2,3-propenetriscarboxylic acid) [4023-65-8] M 174.1, m 195°(dec), m 198-199°(dec), 204-205°(dec). Purified by dissolving in AcOH (77g/150ml), filtering and cooling. The acid separates (55g) as colourless needles. A further quantity (log) can be obtained by reducing the vol of the filtrate. The acid is dried in air then in a vacuum desiccator over NaOH. The acid can be recrystd from Me2CO-CHCl3. The highest m is obtained with the very dry acid. [JACS 52 3128 1930]. The acid has a pKa (H2O) at 20° of 2.88. [Org Synth Coll Vol II 12 1943].

cis-Aconitic anhydride [6318-55-4] M 156.1, m75°, 76-78°, 78-78.5°. Reflux in xylene (7.5 parts) for 1h, then evaporate and recrystallise the residue from C6H6. Alternatively, reflux in Ac2O, evaporate and recrystallise from C6H6. It is sensitive to moisture. [IR: Acta Chem Scand 21 291 1967, B 61 2523 1928; NMR: Biochemistry 5 2335 1966].


Aconitine hydrobromide M 726.7, m 207°. Crystd from water or EtOH/ether.

Acraldehyde see acrolein

Acridine [260-94-6] M 179.2, m 111°, b 346°. Crystd twice from benzene/cyclohexane, or from aqueous EtOH, then sublimed, removing and discarding the first 25% of the sublimate. The remainder was again crystallized and sublimed, discarding the first 10-15% [Wolf and Anderson JACS 77 1608 1955]. Acridine can also be purified by crystallizing from n-heptane and then from ethanol/water after pre-treatment with activated charcoal, or by chromatography on alumina with pet ether in a darkened room. Alternatively, acridine can be precipitated as the hydrochloride from benzene solution by adding HCl, after which the base is regenerated, dried at 110°/50mm, and crystallized to constant melting point from pet ether [Cumper, Ginman and Vogel JCS 4518 1962]. The regenerated free base may be recrystallized, chromatographed on basic alumina, then vac-sublimed and zone-refined. [Williams and Clarke, JCSFT 173 514 1977].

Acridine Orange [494-38-2] M 349.94, m 181-182° (free base). The double salt with ZnCl3 (6g) was dissolved in water (200ml) and stirred with four successive portions (12g each) of Dowex-50 ion-exchange resin (K+ form) to remove the zinc. The soln was then concentrated to vacuum to 20ml, and 100ml of ethanol was added to ppt KCl which was removed. Ether (160ml) was added to the soln from which, on chilling, the dye crystallizes as its chloride. It was separated by centrifuging, washed with chilled ethanol and ether, and dried under vac, before being recryst from ethanol (100ml) by adding ether (50ml), and chilling. Yield 1g. [Pal and Schubert JACS 84 4384 1962]. It was recrystd twice as the free base from ethanol or methanol/water by dropwise addition of NaOH (less than 0.1M). The ppt was washed with water and dried under vacuum. It was dissolved in CHCl3 and chromatographed on alumina: the main sharp band was collected, concentrated and cooled to -20°. The ppt was
filtered, dried in air, then dried for 2h under vacuum at 70°. [Stone and Bradley JACS 83 3627 1961; Blauer and Linschitz JPC 66 453 1962].

**Acridine Yellow** [135-49-9] M 237.8, m 325°. Crystd from 1:1 benzene/methanol.

**Acridinol** see 4-hydroxyacridine.

**Acridine [578-95-0]** M 195.2, m >300°. Dissolve in ca 1% NaOH (100ml), add 3M HCl to pH 4 when acridone separates as a pale yellow solid with m just above 350° (sharp). It can be recrystd from large vols of H2O to give a few mg. It is soluble in 160 parts of boiling EtOH (540 parts at 22°) [JCS 1294 1956]. A few decigrams are best crystallised as the HCl from 400 parts of 10N HCl (90% recovery) from which the free base is obtained by washing the salt with H2O. A small quantity can be recrystd (as the neutral species) from boiling AcOH. Larger quantities are best recrystallised from a mixture of 5 parts of freshly distd aniline and 12.5 parts of glacial acetic acid. Acridone distills unchanged at atmospheric pressure, but the boiling point was not recorded, and some sublimation occurs below 350°. It has a basic pKa of -0.32 and an acidic pKa of 14. UV: $\lambda_{max}$ 399nm. [see Albert, The Acridines Arnold Press p372, 201 1966].

**N-(9-Acridinyl)maleimide (NAM) [49759-20-8] M 274.3, m 248°, 255-258°. Purified by chromatography on silica gel using CH2C12 as eluant. Evaporation of pooled fractions that gave the correct NMR spectra gave a solid which was recrystd from Me2CO as pale yellow prisms. IR $\nu$ (nujol): 1710 (imide); UV (MeOH): $\lambda_{max}$ (nm), $\epsilon$ (M$^{-1}$cm$^{-1}$): 251 (159 500), 343 sh (7 700), 360 (12 400) and 382sh (47 000). [Chem Pharm Bull, Japan 26 596 1978; Eur J Biochem 25 64 1972].

**Acriflavin [8048-52-0]** M 196.2. Treated twice with freshly ppted AgOH to remove proflavine, then recrystd from absolute methanol [Wen and Hsu JPC 66 1353 1962].

**Acriflavin Mixture (Euflavin, 3,6-diamino-10-methylacridinium chloride) [8048-52-0] M 259.7, m 179-181°. Purified by dissolving in 50 parts of H2O, shake with a small excess of freshly ppted and washed Ag2O. The mixture is set aside overnight at 0° and filtered. The cake is not washed. The pH of the filtrate is adjusted to 7.0 with HCl and evaporated to dryness. The residue is then crystd twice from MeOH, twice from H2O and dried at 120°. $\lambda_{max}$ at 452nm has a loge value of 4.67. It is a red powder which readily absorbs H2O. The solubility is increased in the presence of proflavin. The diHCl is a deep red crystn powder. It is available as a mixture of 3,6-diaminoacridinium chloride (35%) and its 10-metho chloride (65%). [see Albert, The Acridines Arnold Press p346 1966; B 45 1787 1912].

**Acrolein [107-02-8]** M 56.1, b 52.1°, n 1.3992, d 0.839. Purified by fractional distn. under nitrogen, drying with anhydrous CaSO4 and then distilling under vac. Blacet, Young and Roof [JACS 59 608 1937] distd under nitrogen through a 90cm column packed with glass rings. To avoid formation of diacryl, the vapour was passed through an ice-cooled condenser into a receiver cooled in an ice-salt mixture and containing 0.5g catechol. The acrolein was then distd twice from anhydrous CuSO4 at low pressure, catechol being placed in the distilling flask and the receiver to avoid polymerization. [Alternatively, hydroquinone (1% of the final soln) can be used].

**Acrolein diacetyl acetal (1,1-diacetoxy-2-propene). [869-29-4] M 158.2, b 75°/10mm, 184°/atm, d$_D$ 1.08, n$_D$ 1.4203. Check the NMR spectrum. If it is not satisfactory then add Ac$_2$O and a drop of cone H$_2$SO$_4$ and heat at 50° for 10min. Then add anhydrous NaOAc (ca 3g/ 100g of liquid) and fractionate. Note that it forms an azeotrope with H$_2$O, so do not add H$_2$O at any time. It is a highly flammable and TOXIC liquid, keep away from the skin. [JACS 73 5282 1951].

**Acrolein diethyl acetal [3054-95-3] M 130.2, b 120-125°/atm, $n_D$ 1.398-1.407. Add Na$_2$CO$_3$ (ca 3.5%) and distil using an efficient column, or better a spinning band column. [Org Synth 25 1 1945].

**Acrolein dimethyl acetal (1,1-dimethoxy-2-propene) [6044-68-4] M 102.1, b 87.5-88°/750mm, 89-90°/760mm, d$_D$ 0.86, n$_D$ 1.3962. Fractionally distil (after adding 0.5g of hydroquinone) under reduced press through an all glass column (40cm x 2.5 cm) packed with glass helices and provided with a heated jacket and a total reflux variable take-off head. Stainless steel Lessing rings (1/8 x 1/8
in) or gauze have been used as packing. It is a **highly flammable and TOXIC** liquid, keep away from the skin. [JCS 2657 1955].

**Acrolein semicarbazone** [6055-71-6] M 113.1, m 171°. Crystd from water.

**Acrylamide** [79-06-1] M 71.1, m 84°, b 125°/25mm. Crystd from acetone, chloroform, ethyl acetate, methanol or benzene/chloroform mixture, then vac dried and kept in the dark under vac. Recryst from CHCl₃ (200g dissolved in 1L heated to boiling and filtered without suction in a warmed funnel through Whatman 541 filter paper. Allowed to cool to room temp and kept at -15° overnight). Crystals were collected with suction in a cooled funnel and washed with 300ml of cold MeOH. Crystals were air-dried in a warm oven. [Dawson et al. *Data for Biochemical Research*, Oxford Press 1986 p 449].

**CAUTION:** Acrylamide is extremely **TOXIC** and precautions must be taken to avoid skin contact or inhalation. Use gloves and handle in a well ventilated fume cupboard.

**Acrylic acid** [79-10-7] M 72.1, m 13°, b 30°/3mm, d 1.051. Can be purified by steam distn, or vacu distn through a column packed with copper gauze to inhibit polymerisation. (This treatment also removes inhibitors such as methylene blue that may be present.) Azeotropic distn of the water with benzene converts aqueous acrylic acid to the anhydrous material.

**Acrylonitrile** [107-13-1] M 53.1, b 78°, d 0.806, n² 1.3886. Washed with dilute H₂SO₄ or dilute H₃PO₄, then with dilute Na₂CO₃ and water. Dried with Na₂SO₄, CaCl₂ or (better) by shaking with molecular sieves. Fractionally distd under nitrogen. Can be stabilised by adding 10ppm tert-butyl catechol. Immediately before use, the stabilizer can be removed by passage through a column of activated alumina (or by washing with 1% NaOH soln if traces of water are permissible in the final material), followed by distn. Alternatively, shaken with 10% (w/v) NaOH to extract inhibitor, and then washed in turn with 10% H₂SO₄, 20% Na₂CO₃ and distd water. Dried for 24h over CaCl₂ and fractionally distd under N₂ taking the fraction boiling at 75.0 to 75.5°C (at 734mm Hg). Stored with 10ppm tert-butyl catechol. Acrylonitrile is distilled off as required. [Burton et al., *JACS* 72 2299 1950].

**Acrylic acid chloride** [814-68-6] M 90.5, b 72-74°/740mm, 74°/760mm, d₂⁰ 1.1127, n² 1.4337. Distil rapidly through an efficient 25cm column after adding 0.5g of hydroquinone/200g of chloride, and then redistil carefully at atmospheric pressure preferably in a stream of dry N₂. [JACS 72 2299 1950].

The liquid is an irritant and is **TOXIC**.

**Actidione** see cycloheximide.

**Actinomycin D** [50-76-0] M 1255.5. Crystd from ethyl acetate or from MeOH.

**Adamantane** [281-23-2] M 136.2, m 269.6-270.8° (sublimes). Crystd from acetone or cyclohexane, sublimed in a vacuum below its melting point. [Butler et al. *JCSFT* 1 82 535 1986]. Adamantane was also purified by dissolving in n-heptane (ca 10ml/g of adamantane) on a hot plate, adding activated charcoal (2g/100g of adamantane), and boiling for 30min, filtering the hot sofn through a filter paper, concentrating the filtrate until crystn just starts, adding one quarter of the original volume n-heptane and allowing to cool slowly over a period of hours. The supernatant was decanted off and the crystals were dried on a vacuum line at room temperature. [Walter et al. *JACS* 107 793 1985].


1-Adamantane carboxylic acid [828-51-3] M 180.3, m 175-176.5°, 177°. Possible impurities are trimethylacetic acid and C₉ and C₁₃ acids. Dissolve 15g of acid in CCl₄ (300ml) and shake with 110ml of 15N aqueous NH₃ and the ammonium salt separate and is collected. Acid impurities form soluble ammonium salts. The salt is washed with cold Me₂CO (20ml) and suspended in H₂O (250ml). This is treated with 12N HCl and extracted with CHCl₃ (100ml). The dried (Na₂SO₄) is evaporated and the residue recrystd from a mixture of
MeOH (30ml) and H2O (ca 10ml) to give the pure acid (10-11g). [Org Synth Col. Vol. V 20 1973]. Also recryst from absolute EtOH and dried under vacuum at 100°.
Alternatively, the acid (5g) is refluxed for 2h with 15ml of MeOH and 2ml of 98% H2SO4 (cool when mixing this soln). Pour into 10 volumes of H2O and extract with the minimum volume of CHC13 to give clear separation of phases. The extract is washed with H2O and dried (CaCl2) and distd. The methyl ester is collected at 77-79°/1mm, m 38-39°. The ester is hydrolysed with the calculated amount of N KOH and refluxed until clear. Acidification with HCI provides the pure acid with 90% recovery. [Org Synth 4 1 1964]. The amide crystallizes from cyclohexane, m 189°. [B 93 1366 1960].

1,3-Adamantane diamine dihydrochloride [26562-81-2] M 239.2, m >310°. Dissolve in boiling conc HCl (400mg in 15ml) and evaporate to dryness. Dissolve in absolute EtOH and add dry Et2O to crystallise the HCl. [B 93 1366 1960].

1,3-Adamantane dicarboxylic acid [39269-10-8] M 224.3, m 276°, 276-278°, 279°. Dissolve in aq NaOH, treat with charcoal, filter and acidify with dilute HCI. Recryst from MeOH. [B 93 1366 1960].

1,3-Adamantane dicarboxylic acid [39269-10-8] M 224.3, m 276°, 276-278°, 279°. Dissolve in aq NaOH, treat with charcoal, filter and acidify with dilute HCI. Recryst from MeOH. [B 93 1366 1960].

1-Adamantane methylamine [768-95-6] M 152.4, m 288.5-290°. If 2-adamantanol is a suspected impurity then dissolve substance (2g) in acetone (100ml) and Jones’ reagent (CrO3 (10.3g) in H2O (30ml)) is added dropwise (turns green in colour) until excess reagent is present (slight red colour). Allow to stir overnight, decant the acetone soln from the Cr salts and adamant-2-one, and dry (Na2SO4) and evaporate to dryness. The residue (ca 7g) is chromatographed through A1203 (250g) and washed with 50% benzene-pet ether (b 40-60°), then 100% Et2O (to remove any adamant-2-one present) and the 1-adamantanol is then eluted with 5% MeOH in Et2O. The eluate is evaporated, and the residue is recrystallized from pet ether (b 30-60°), m 287.2-288.5°. It has characteristic IR, v 3640, 14, 1086, 982 and 930cm⁻¹. [JACS 83 182 1961]. Alternatively, if free from the 2-isomer, dissolve in tetrahydrofuran, dilute with H2O to precipitate the alcohol. Collect, dry and sublimate in a vacuum at 130°. [B 92 1629 1959].

2-Adamantanol [700-57-2] M 152.4, m 296.2-297.7°. Can be purified by chromatography as for the 1-isomer. It crystallises from cyclohexane and has characteristic IR, v 3600, 1053, 1029 and 992cm⁻¹ [JACS 8 182 1961].


2-Adamantylamine hydrochloride [10523-68-9] M 187.7, m >300°. The free amine in Et2O, liberated by the action of alkali in H2O, is dried over KOH, filtered, evap and sublimed at 110°/12Torr, m 230-236°. The base is dissolved in EtOH and crystd by the addition of Et2O, and dried in vac. [B 93 226 1960].

1-Adamantyl bromide [768-90-1] M 215.1, m 117-119°, 118°, 119.5-120°. If coloured, dissolve in CCl4, wash with H2O, treat with charcoal, dry (CaCl2), filter, evap to dryness. Dissolve in a small volume of MeOH and cool in a CO2-trichloroethylene bath and collect the crystals. Sublime at 90-100%/water pump vacuum. [B 92 1629 1959; JACS 83 2700 1961].
1-Adamantyl bromomethylketone \([5122-82-7]\) \(M \, 257.2, m \, 76-79^\circ\), \(m \, 78-79^\circ\). Dissolve in \(Et_2O\), wash with \(H_2O\), dry (\(MgSO_4\)), evaporate and crystallise residue from small volumes of \(MeOH\). **LACHRYMATORY.** [B 93 2054 1960].

1-Adamantyl chloride \([935-56-8]\) \(M \, 170.7, m \, 164.3-165.6^\circ\). Crystd from aqueous \(MeOH\) and sublimed at 100°/12Torr. Also crystd from \(MeOH\) at -70O. [B 92 1629 1959; JACS 83 2700 1961].

1-Adamantyl fluoride \([1768-92-3]\) \(M \, 154.2, m \, 210-212^\circ\) (dec), 259-260° (dec). Dissolve in \(Et_2O\), dry over \(Na_2SO_4\), evaporate to dryness and sublime the residue at 90-100°/12mm. Recryst sublimate from \(MeOH\), \(m \, 259-260^\circ\). [ZPC 35 1647 1976; JACS 88 1988 1966].

1-Adamantyl fluoroformate \([62087-82-5]\) \(M \, 198.2, m \, 31-32^\circ\). Dissolve in \(n\)-hexane (ca 10g in 150 ml) and keep at 0° for 24h. Any 1-adamantanol present will separate. Filter and evaporate to dryness. Crystalline residue has \(m \, 31-32^\circ\) (v 1242, 1824 and 2340 cm\(^{-1}\)). There should be no OH str band above 2500 cm\(^{-1}\). [ZPC 35 1647 1976; JACS 88 1988 1966].

1-Adamantyl iodide \([768-93-4]\) \(M \, 262.1, m \, 75.3-76.4^\circ\). Dissolve in \(Et_2O\), shake with aqueous \(NaHSO_3\), aqueous \(K_2CO_3\), and \(H_2O\), dry (\(Na_2SO_4\)), evaporate and recrystallise from \(MeOH\) at -70° (to avoid alcoholysis) giving white crystals. [JACS 83 2700 1961; lit \(m \, of 151-152.5^\circ\) is incorrect]. Also purified by recrystn from pet ether (40-60°C) followed by rigorous drying and repeated sublimation.

1-Adamantyl isocyanate \([4411-25-0]\) \(M \, 177.3, m \, 144-145^\circ\). Recryst from \(n\)-hexane and sublume. Irritant. [B 95 2302 1962].

1-Adamantyl isothiocyanate \([4411-26-1]\) \(M \, 193.3, m \, 168-169^\circ\). Dissolve in \(Et_2O\), wash with \(H_2O\), dry (\(Na_2SO_4\)), evaporate and sublime the residue in a vacuum at 140°, and recryst from \(MeOH\). Irritant. [B 95 2302 1962].

1-Adamantylmethanol see 1-hydroxymethyladamantine.

\(N\)-(1-Adamantyl)urea \([13072-69-0]\) \(M \, 194.2, m \, >250^\circ\) (dec), 268-272° (dec). Wash with \(H_2O\) and dioxane and recryst from EtOH. [B 95 2302 1962].

Adenine \([73-24-5]\) \(M \, 135.1, m \, 360-365^\circ\) (dec rapid heating). Crystd from distd water.

Adenosine \([58-61-7]\) \(M \, 267.3, m \, 234-236^\circ\), \([\alpha]_{546} \, -85^\circ\) (c 2, 5% \(NaOH\)). Cryst from distilled water.

Adenosine-3'-phosphoric acid \([84-21-9]\) \(M \, 365.2, m \, 210^\circ\) (dec), \([\alpha]_{546} \, 50^\circ\) (c 0.5, 0.5M \(Na_2HPO_4\)). Cryst from a large volume of distilled water, as the monohydrate.

Adenosine-5'-phosphoric acid monohydrate \([18422-05-4]\) \(M \, 365.2, m \, 196-200^\circ\) (dec), \([\alpha]_{546} \, -56^\circ\) (c 2, 2% \(NaOH\)). Cryst from \(H_2O\) by addition of acetone. Purified by chromatography on Dowex 1 (in formate form), eluting with 0.25M formic acid. It was then adsorbed onto charcoal (which had been boiled for 15min with M \(HCl\), washed free of chloride and dried at 100°C), and recovered by stirring three times with isooamyl alcohol/\(H_2O\) (1:9 v/v). The aqueous layer from the combined extracts was evaporated to dryness under reduced pressure, and the product was crystallised twice from hot \(H_2O\). [Morrison and Doherty BJ 79 433 1961]. See entry in Chapter 5.

Adenosine-5'-triphosphate \([56-65-5]\) \(M \, 507.2, [\alpha]_{546} \, -35.5^\circ\) (c 1, 0.5 \(M\) \(Na_2HPO_4\)). Ppted as its barium salt when excess barium acetate soln was added to a 5% soln of ATP in water. After filtering off, the ppte was washed with distd water, redissolved in 0.2M \(HNO_3\), and again pptd with barium acetate. The ppte, after several washings with distd water, was dissolved in 0.2M \(HNO_3\) and slightly more 0.2M \(H_2SO_4\) than was