The 1:1 adduct of Kemp's triacid with 2-aminopyridine

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The crystal structure determination of the molecular proton-transfer adduct of Kemp's triacid (*cis-cis*-1,3,5-trimethylcyclohexane-1,3,5-tricarboxylic acid, KTA) with 2-aminopyridine (2-APY), namely 2-aminopyridinium 3,5-dicarboxy-1,3,5-trimethylcyclohexanecarboxylate, 2-APY$^+$·KTA$^-$ or C$_5$H$_7$N$_2$$^+$·C$_{12}H_{17}O_6$$^-$, has revealed a centrosymmetric hydrogen-bonded cyclic KTA homodimer repeating unit [O···O 2.524 (4) Å] linked into a polymer structure through the pyridinium and amino groups of the 2-APY molecule [O···N 2.736 (4), 2.989 (4) and 2.999 (4) Å].

Comment

Kemp's triacid (*cis-cis*-1,3,5-trimethylcyclohexane-1,3,5-tricarboxylic acid, KTA; Kemp & Petrakis, 1981; Hazell & Toftlund, 1999, at 120 K) is a unique triprotic acid having all of its carboxylic acid groups axially oriented. The crystal structure analysis (Rebek *et al.*, 1985; Chan *et al.*, 1991) also indicated that the molecules had no intramolecular hydrogen-bonding associations between the carboxylic acid groups, as might have been expected with this configuration. Instead, the molecules formed into an unusual convoluted hydrogen-bonded chain structure made up of intermolecular head-to-tail cyclic hydrogen bonds [graph set $R_2^2(8)$; Etter, 1990; Etter & MacDonald, 1990], with two at the head and one at the tail. This is also found in the acetonitrile solvate structure (Hirose *et al.*, 1998). This same framework structure is found in the 2:1 adduct of KTA with 8-aminoquinoline (8-AQ), where the chains are linked peripherally by hydrogen bonds through the hetero-N atom and the amino group of the substituted quinoline molecules (Smith *et al.*, 2000). No proton transfer is found in this compound [pK_{a1} = 3.3 (KTA) and pK_{a2} (hetero-N) = 4.0 (8-AQ)]. This is in contrast with the 1:1 adduct with the analogous compound quinolin-8-ol (8-HQ; Smith *et al.*, 2000), where proton transfer is found [pK_{a2} = 5.0 (hetero-N)] in a structure which no longer retains the KTA chain backbone. Instead, the singly deprotonated KTA molecules form centrosymmetric dimer interactions, which differ from conventional hydrogen-bonded cyclic dimers in that they involve both *cis*-related carboxylic acid groups. One of these O

atoms then links to the protonated hetero-N atom of the 8-HQ molecule, while the 8-hydroxy group of 8-HQ completes the polymer link to an adjacent dimer unit. In addition, a single intermolecular hydrogen bond is found between two of the carboxylic acid groups. This work indicated that Kemp's triacid has particular affinity for the 8-amino-substituted quinoline system, and reinforced the potential of KTA in molecular recognition processes (Bencini *et al.*, 1992, 1994). In a continuation of this work on the self-assembly of KTA in the presence of Lewis bases, the title 1:1 adduct, (I), of KTA with 2-aminopyridine was synthesized and the structure determined.

(I)
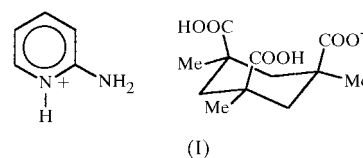
The structure of (I) reveals a proton-transfer complex (Fig. 1), which is analogous to the complex with 8-HQ in having cyclic centrosymmetric hydrogen-bonded dimers [O4—H4···O2^i 2.524 (4) Å and O—H—O 179 (3)°; symmetry code: (i) 1 − x, 1 − y, 1 − z] (Fig. 2). A similar short intramolecular hydrogen bond is also found [O5—H5···O1 2.552 (4) Å and O—H—O 162 (3)°]. The same carboxylate O atom is then linked to the protonated pyridinium N atom of 2-APY [O1···H12—N12 2.736 (4) Å and O—H—N 161 (3)°], while the 2-amino substituent gives a bidentate linkage to a second carboxylate O atom [N22—H2···O3 2.999 (4) Å and N—H—O 162 (3)°]. The second H atom of the amino group provides the peripheral linkage between dimer units in the chain polymer structure [N22—H1···O6^{ii} 2.989 (4) Å and N—H—O 158 (3)°; symmetry code: (ii) 1 − x, 1 − y, −z].

Although no further examples of Lewis base adducts with KTA have been isolated, the examples characterized so far
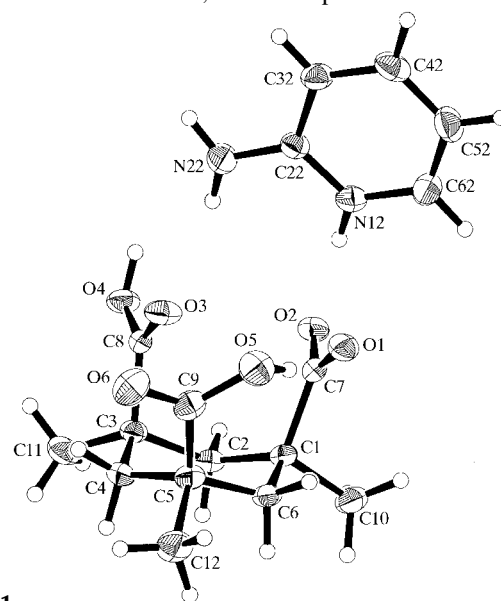

Figure 1
The molecular configuration and atom-labelling scheme for the individual Kemp's triacid anion and the pyridinium cation in (I). Displacement ellipsoids are shown at the 30% probability level and H atoms are drawn as small spheres of arbitrary radii.

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organic compounds

indicate that there is a critical minimum pK_a difference (ΔpK_a) between the first dissociation constant for KTA and that for the hetero-N atom of the Lewis base, which determines which structure type exists (chain or dimer variant) [for 8-AQ, ΔpK_a = 0.7 (no proton transfer, chain structure); for 8-HQ, ΔpK_a = 1.7; and for 2-APY, ΔpK_a = 3.4 (both proton transfer, both dimer structures)]. This threshold value appears to be considerably smaller than the corresponding ΔpK_a minimum for the unsubstituted pyridine system (3.5; Johnson & Rumon, 1965). By analogy, the relatively strong nitro-substituted aromatic carboxylic acids [2,4-dinitrobenzoic acid (pK_a = 3.7), 5-nitrosalicylic acid (pK_a = 2.2) and 3,5-dinitro-salicylic acid (pK_a = 2.1)] readily protonate the hetero-N atom in both 8-AQ and 8-HQ, giving 1:1 adducts based on cyclic hydrogen-bonded *A*–*B* heterodimers (Smith *et al.*, 2000; unpublished data).
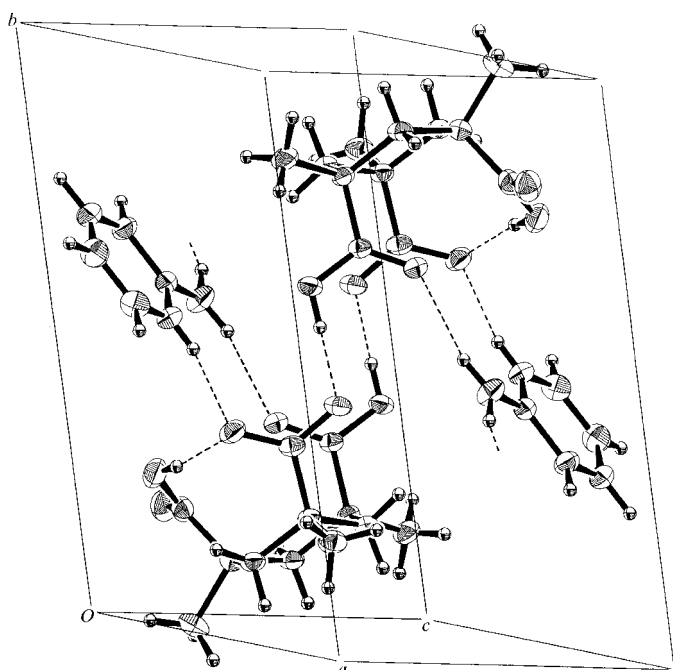

Figure 2
The dimeric KTA anion units and the crosslinking 2-aminopyridinium cations in (I), with the hydrogen-bonding scheme shown as broken lines.

Experimental

The synthesis of (I) was carried out by refluxing equimolar amounts (1 mmol) of 2-aminopyridine and *cis-cis*-1,3,5-trimethylcyclohexane-1,3,5-tricarboxylic acid for 15 min at *ca* 350 K in 50% aqueous ethanol (20 ml). Crystals of (I) were obtained by evaporation of the solvent at room temperature.

Crystal data

$C_5H_7N_2^+ \cdot C_{12}H_{17}O_6^-$	$Z = 2$
$M_r = 352.39$	$D_x = 1.321$ Mg m^{-3}
Triclinic, $P\bar{1}$	Mo $K\alpha$ radiation
$a = 8.767$ (2) Å	Cell parameters from 25
$b = 12.228$ (2) Å	reflections
$c = 8.600$ (3) Å	$\theta = 19.4$–$19.9°$
$\alpha = 94.12$ (2)°	$\mu = 0.100$ mm^{-1}
$\beta = 90.07$ (3)°	$T = 293$ K
$\gamma = 105.44$ (1)°	Plate, colourless
$V = 886.2$ (4) Å^3	$0.3 \times 0.2 \times 0.1$ mm

Data collection

Rigaku AFC-7R diffractometer	$h = 0 \rightarrow 10$
$\omega/2\theta$ scans	$k = -14 \rightarrow 14$
3350 measured reflections	$l = -10 \rightarrow 10$
3128 independent reflections	3 standard reflections
1699 reflections with $I > 2\sigma(I)$	every 150 reflections
$R_{int} = 0.029$	intensity decay: 1.8%
$\theta_{max} = 25.02°$	

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o{}^2) + (0.08P)^2$
$R(F) = 0.049$	$+ 0.369P]$
$wR(F^2) = 0.168$	where $P = (F_o{}^2 + 2F_c{}^2)/3$
$S = 1.024$	$(\Delta/\sigma)_{max} < 0.001$
3128 reflections	$\Delta\rho_{max} = 0.36$ e Å^{-3}
242 parameters	$\Delta\rho_{min} = -0.36$ e Å^{-3}
H atoms treated by a mixture of	Extinction correction: *SHELXL*97
independent and constrained	(Sheldrick, 1997)
refinement	Extinction coefficient: 0.022 (5)

Only the positional parameters for those H atoms involved in hydrogen bonding (H1, H2, H4, H5 and H12) were refined [N—H = 0.81 (4)–0.89 (3) Å and O—H = 0.81 (3) and 0.86 (3) Å]. All other H atoms were constrained, with C—H = 0.95 Å and $U_{iso} = 1.2U_{eq}$ of the bonded C atom.

Data collection: *MSC/AFC Diffractometer Control Software* (Molecular Structure Corporation, 1994); cell refinement: *MSC/AFC Diffractometer Control Software*; data reduction: *TEXSAN for Windows* (Molecular Structure Corporation, 1997–1999); program(s) used to solve structure: *SIR*92 (Altomare *et al.*, 1994); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); software used to prepare material for publication: *TEXSAN for Windows*.

References

Altomare, A., Cascarano, M., Giacovazzo, C. & Guagliardi, A. (1994). *J. Appl. Cryst.* **26**, 343–350.
Bencini, A., Bianchi, A., Burguete, M. I., Dapporto, P., Domenech, A., Garcia-Espana, E., Luis, S. V., Paoli, P. & Ramirez, J. (1994). *J. Chem. Soc. Perkin Trans.* 2, pp. 569–577.
Bencini, A., Bianchi, A., Burguete, M. I., Garcia-Espana, E., Luis, S. V. & Ramirez, J. (1992). *J. Am. Chem. Soc.* **114**, 1919–1921.
Chan, T.-L., Cui, Y.-X., Mak, T. C. W., Wang, R.-J. & Wong, H. N. C. (1991). *J. Crystallogr. Spectrosc. Res.* **21**, 297–303.
Etter, M. C. (1990). *Acc. Chem. Res.* **23**, 120–126.
Etter, M. C. & MacDonald, J. C. (1990). *Acta Cryst.* B**46**, 256–262.
Hazell, A. & Toftlund, H. (1999). *Acta Cryst.* C**55**, IUC9900079.
Hirose, T., Baldwin, B. W., Wang, Z.-H. & Kennard, C. H. L. (1998). *Acta Cryst.* C**54**, 1143–1144.
Johnson, J. L. & Rumon, K. A. (1965). *J. Phys. Chem.* **69**, 74–86.
Kemp, D. S. & Petrakis, K. S. (1981). *J. Org. Chem.* **46**, 5140–5143.
Molecular Structure Corporation (1994). *MSC/AFC Diffractometer Control Software*. MSC, 3200 Research Forest Drive, The Woodlands, TX 77381, USA.
Molecular Structure Corporation (1997–1999). *TEXSAN for Windows*. Version 1.06. MSC, 9009 New Trails Drive, The Woodlands, TX 77381, USA.
Rebek, J. Jr, Marshall, L., Wolak, R., Parris, K., Killoran, M., Askew, B., Nameth, D. &. Islam, N. (1985). *J. Am. Chem. Soc.* **107**, 7476–7481.
Sheldrick, G. M. (1997). *SHELXL*97. University of Göttingen, Germany.
Smith, G., Wermuth, U. D. & White, J. M. (2000). *J. Chem. Soc. Chem. Commun.* Accepted.