Orientational Selectivity for the Inclusion of Acetonitrile in Tailor-made Macrobicyclic Host Molecules

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The first σ–π-interaction between a C–H acidic acetonitrile methyl group and and a 'π-basic' host cavity is described based on the X-ray structure of the complex between the host **3** and MeCN; comparison with the structure of the complex between **1** and MeCN shows orientational selectivity for MeCN in the two hosts.

The first inclusion of acetonitrile in a non-crown ether-like molecular cavity† was described recently:[1] the acetonitrile guest is enclosed selectively *inside* the macrobicyclic host **1**. The phenylene rings of host **1** could be responsible for the orientation of the nitrile group inside the host cavity owing to donor–acceptor interactions.

We now describe the second example of inclusion of acetonitrile, inside a new macrobicyclic cavity of structure **3**. The acetonitrile molecule here is enclosed in the opposite direction compared to that in the previously described host **1**.

For the synthesis of **3** (Scheme 1) phloroglucinol was treated with prop-2-ynyl bromide–K_2CO_3 in refluxing acetone whereby the tris-propynylic ether **2** could be obtained (12% yield after separation by column chromatography; etherification of all three OH groups of phloroglucinol is known only in few cases and the resulting tris-ethers are accessible only in poor

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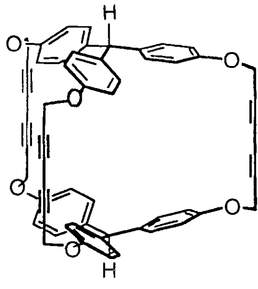
† Acetonitrile as a guest molecule until recently was reported only in complexes of crown ether compounds and as a clathrate with hydroquinone. The acetonitrile therein is mostly bonded by (weak) hydrogen bridges between its methyl group and the oxygen bridge atoms of the crown ether counterpart (single crystal X-ray structural analyses of such complexes are cited in ref. 1). *Cf.* also the MeCN adduct in ref. 2.



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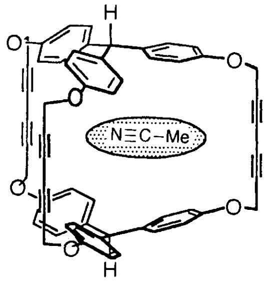
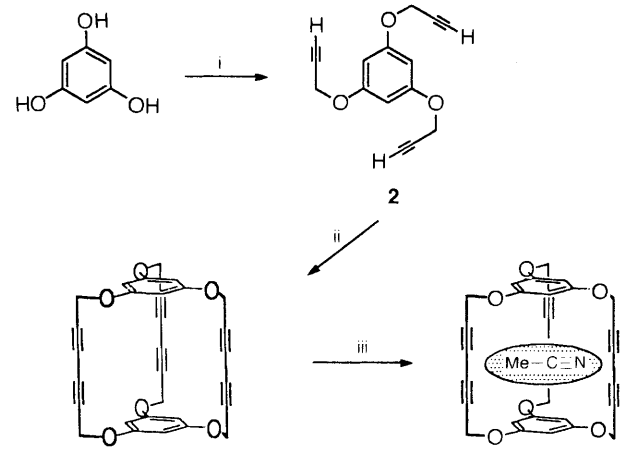


1 • MeCN



Scheme 1 *Reagents and conditions*: i, prop-2-ynyl bromide, K_2CO_3, acetone, reflux 5 h, chromatography (12%); ii, $Cu(OAc)_2{\cdot}H_2O$, pyridine, 60 °C, 1 h, chromatography (8%); iii, recrystallization from acetonitrile

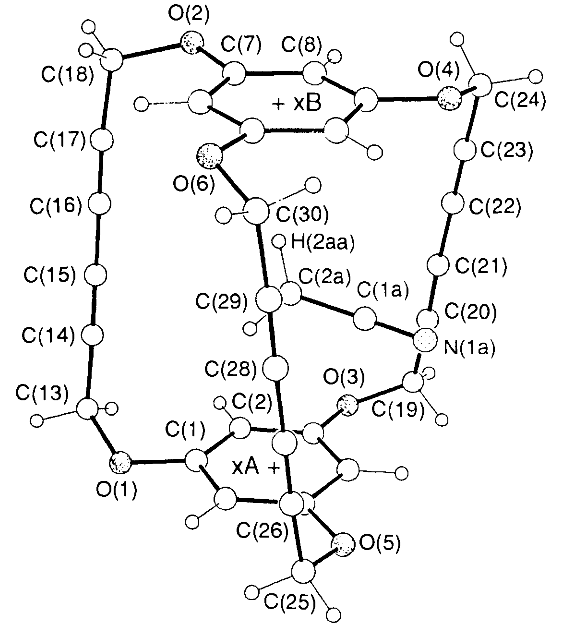


Fig. 1 Structure of 3·MeCN in the crystal. Selected distances (pm) and angles (°): C(1a)–C(2a) 143.6(5), C(1a)–N(1a) 112.7(5), N(1a)–C(1a)–C(2a) 179.0(3), xA–xB 712, C(2a)–xA 361, C(2a)–xB 354, H(2aa)–xA 261, xA–C(2a)–xB 172, xB–H(2aa)–C(2a) 162.

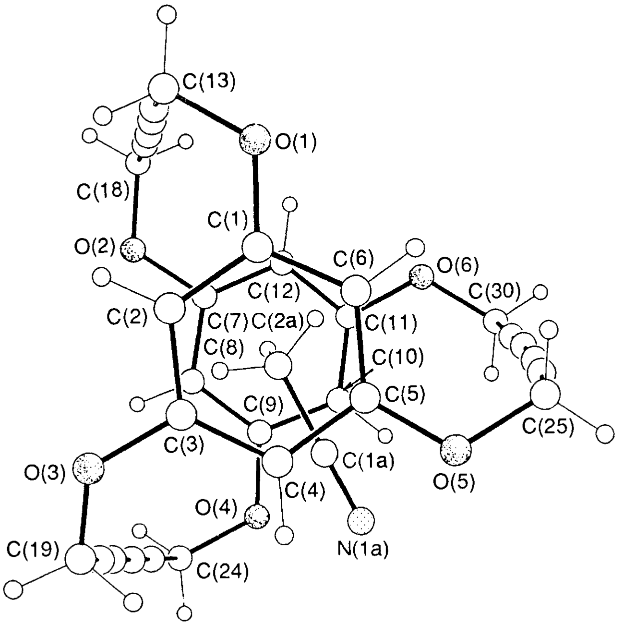


Fig. 2 View of complex 3·MeCN along its pseudo-C_3 axis

yields).‡ The tris-propyne **2** was cyclodimerized with $Cu(OAc)_2{\cdot}H_2O$ in pyridine under normal atmosphere and gave the desired macrobicyclic **3** in 8% yield after separation by column chromatography (cyclohexane–diethyl ether, 1 : 3).‡ Recrystallisation from acetonitrile yielded the crystalline 1 : 1 inclusion complex **3**·MeCN.

In contrast to the relatively weak interactions in the 18-crown-6–acetonitrile adduct from which the acetonitrile could be removed under high vacuum conditions (0.1–0.5 mmHg; 2–3 h) with gentle heating (≤40 °C)[3] the new inclusion complex **3**·MeCN did *not* release its enclosed acetonitrile by heating the powdered crystals to 40 °C (0.2 mmHg; 3 h).

As observed for the complex **1**·MeCN, the IR spectrum of the crystalline complex **3**·MeCN in a KBr matrix also shows a

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‡ Satisfactory analytical and spectroscopic data have been obtained for compounds **2, 3** and **3**·MeCN. Compound **2**, 1,3,5-tris-(prop-2-ynyl)benzene, m.p. 83 °C, colourless fine needles (from ethanol); R_f 0.61 [hexane–diethyl ether, 1 : 4, silica gel 60 (Riedel No. 37333)]; ^1H NMR (90 MHz, $CDCl_3$, *J* values in Hz): δ 2.49 (t, *J* 2.5, 3H, ≡C–H), 4.60 (d, *J* 2.5, 6H, OCH_2) and 6.22 (s, 3H, HC-2,4,6); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 55.96 (t, 3C, OCH_2), 75.83 (d, 3C, ≡C–H), 78.27 (s, 3C, ≡*C*-CH_2), 95.40 (d, 3C, C-2,4,6) and 159.34 (s, 3C, C-1,3,5); MS (70 eV, EI): *m/z* 240.0790 (calc. 240.0786; $C_{15}H_{12}O_3$, M^+, 30%), 201 (M^+ $-C_3H_3$, 100), 185 (M^+ $-$ C_3H_3O, 39), 173 (201 − CO, 75), 159 (185 − C_2H_2, 70), 145 (173 − CO, 48), 131 (185 − C_3H_3O, 50), 121 (99), 117 (42) and 115 (84); (Found: C, 74.45; H, 5.0; $C_{15}H_{12}O_3$ requires C, 75.0; H, 5.0%); IR (KBr): ν_{max}/cm^{-1} 3279s, 3269s, 3259s, 2975w, 2935w, 2925w, 2908w, 2874w, 2864w, 2134m, 2115m, 1617vs, 1471s, 1450m, 1369s, 1272s, 1157vs, 1062s, 1015m, 975w, 956m, 950m, 909m and 814s.

Compound **3**, 4,11,17,24,27,34-hexaoxapentacyclo[12.12.8.1^{3,25}.1^{12,16}]hexatriaconta-1,3(35),12,14,16(36),25-hexaene-6,8,19,21,29,31-hexayne, m.p. > 250 °C, colourless solid; R_f 0.48 [hexane–diethyl ether, 1 : 4, silica gel 60 (Riedel No. 37333)]; ^1H NMR (400 MHz, $CDCl_3$, *J* values in Hz): δ 4.72 (s, 12H, OCH_2) and 6.09 (s, 6H, HC-2,4,6); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 55.19 (t, 6C, OCH_2), 70.97 (s, 6C, ≡C–C≡), 73.71 (s, 6C, ≡*C*–CH_2), 96.30 (d, 6C, C-2,4,6) and 157.94 (s, 6C, C-1,3,5); FAB MS *m/z* 475.1 ($C_{30}H_{18}O_6$, $[M + H]^+$); IR (KBr): ν_{max}/cm^{-1} 3102w, 2924w, 2872w, 2854w, 2252w, 1604vs, 1471s, 1330w, 1286m, 1258m, 1145vs, 1065s, 1026m, 1008w, 993w, 925w, 903w and 819m.

Compound **3**·MeCN, m.p. > 250 °C, slightly brown crystals; MS (70 eV, EI): no molecular peak, *m/z* 41.0305 (CH_3CN^+, 100%); FAB MS *m/z* 475.1 ($C_{30}H_{18}O_6$, $[M + H]^+$); IR (KBr): ν_{max}/cm^{-1} 3102w, 2924w, 2871w, 2252w, 2218.5vw ($\nu_{C\equiv N}$), 1604vs, 1472s, 1330w, 1287m, 1258m, 1146vs, 1065s, 1026m, 1008w, 993w, 927w, 903w and 820m.

significant shift of the nitrile band, $\Delta\nu = 35\ \text{cm}^{-1}$, towards smaller wavenumbers with nearly identical positions of the other IR bands compared to those of the guest-*free* host **3** in KBr matrix.§

The ^{1}H NMR spectra of the complex **3**·MeCN measured in C_6D_6, CD_2Cl_2 and $CDCl_3$ shows signals due to both the free host **3** and free acetonitrile in a 1 : 1 ratio, again analogous to the complex **1**·MeCN.

In striking contrast to the **1**·MeCN-complex, the geometry of the complex **3**·MeCN, which was established by a single crystal X-ray structural analysis, turned out to be completely different with respect to the orientation of the acetonitrile guest (Figs. 1 and 2).¶ The host **3**, which was tailored on the basis of consideration of models, is twisted along its pseudo-threefold axis (an analogous twisting was found in the structure of **1**·MeCN[1]). The aromatic rings approach each other to 712 pm which is almost the ideal distance for the inclusion of aromatic guests. The host benzene rings are exactly planar and stacked almost parallel to each other (the normals of the planes of the two aromatic rings are inclined by 178.3° to each other); they are twisted along the pseudo-C_3 axis by about 13° (Fig. 2).

Acetonitrile is enclosed exclusively *inside* the molecular cavity of **3**; intermolecular empty spaces in the crystal lattice are unoccupied. This behaviour was also found for the inclusion complex **1**·MeCN. The enclosed acetonitrile guest is fixed at the equatorial level perpendicular to the pseudo-C_3 axis. One of the disordered acetonitrile guest molecules in **1**·MeCN, like the enclosed acetonitrile in **3**·MeCN, is centred in the middle of the host cages. In striking contrast to **1**·MeCN, **3**·MeCN shows a completely different and, for acetonitrile, new kind of complexation. The acetonitrile proton H-2aa (electron density is found for it in the corresponding region) projects nearly perpendicularly towards the centre of gravity of the benzene ring B (xB) located above (Fig. 1). The distance C2a–xB is determined to 354 pm.||

There is a weak repulsive interaction between the π-electrons of the nitrile group and those of the two neighbouring diyne bridges ($ArOCH_2C_4CH_2OAr$). This results in a slightly larger bending of these [angle C(20)≡C(21)–C(22)≡C(23) 7.1°; C(26)≡C(27)–C(28)≡C(29) 5.0°] than for the remaining diyne bridge [angle C(14)≡C(15)–C(16)≡C(17) 1.2°]; the shortest distances between the centre of the C≡N bond and the diyne bridges are in the region of 340–350 pm.

We interpret this arrangement as a consequence of an attractive σ–π interaction between the acidic methyl proton of acetonitrile with the 'π-basic' 1,3,5-tris-alkoxybenzene donor of the host compound.

A comparison of the two inclusion complexes **1**·MeCN and **3**·MeCN exhibits a remarkable reversed selectivity with respect to the orientation of acetonitrile. The host phenylene rings in **1**· MeCN interact with the *nitrile* group of MeCN whereas in **3**·MeCN there is an interaction between the *methyl* group of MeCN and the host phenyl rings.

We suggest that **3** could act as a sensor compound for acetonitrile.

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References

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§ For comparison: acetonitrile in a KBr matrix shows ν 2254 cm^{-1}. The host **1**·MeCN shows likewise a shift of the nitrile vibration, $\Delta\nu = 35\ \text{cm}^{-1}$, towards smaller wavenumbers. The same value was found in the case of **3**·MeCN.[1] In the case of the 18-crown-6-acetonitrile adduct no such shift is observed; Knöchel *et al.* reported that there is 'no significant changing' in the adduct IR spectrum in relation to the IR spectrum of 18-crown-6

¶ *Crystal data*: $C_{30}H_{18}O_6 \cdot CH_3CN$, monoclinic, $P2_1/c$ (No. 14), $a = 10.553(2)$, $b = 17.548(1)$, $c = 14.680(1)$ Å, $\beta = 107.12(2)°$, $V = 2600.9(5)$ Å^3, $Z = 4$, $D_c = 1.316\ \text{g cm}^{-3}$, $\lambda(\text{Mo-K}\alpha) = 0.71073$ Å. $F(000) = 1072$, $T = 298$ K. In the range of $4° < 2\theta < 50°$ a total of 4934 intensity data were measured on an Enraf-Nonius CAD4 diffractometer (graphite monochromatized Mo-Kα radiation) using the ω–θ scan mode. From 4570 symmetry-independent reflections, 3654 with $|F| > 4\sigma(F)$ were used for all calculations. The structure was determined by direct methods (SHELXTL-Plus) and refined by full-matrix least-squares methods minimizing 353 parameters. An extinction correction was applied. Anisotropic thermal parameters were refined for all non-H atoms. Hydrogen atoms (localized by difference electron density determination) were refined by a riding model. Electron density was found for H(2aa) at the corresponding region. Using the coordinates of H(2aa) and C(2a) an ideal tetrahedral geometry was calculated and refined for the acetonitrile methyl group. Final $R = 0.063$ and $R_w = 0.074$ [$w^{-1} = \sigma^2(F) + 0.0004F^2$]; residual electron density 0.58 e Å^{-3}. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

|| An amazingly similar geometry between a benzene ring and acetonitrile as complexation partner was proposed in 1989 by Kollman *et al.*;[5] they studied the benzene–acetonitrile complex theoretically and minimized its energy by molecular mechanics methods. The distance between the centre of gravity of benzene and the acetonitrile methyl group in their complex was calculated to be 341 pm; we have found 354 pm in our host–guest complex. However, they found a slightly favourable complexation enthalpy for a coplanar arrangement of acetonitrile relative to benzene compared with a perpendicular arrangement ($\Delta H = -2.5$ compared with $-1.6\ \text{kcal mol}^{-1}$ respectively; 1 cal = 4.184 J; in both cases the methyl group is pointing towards the centre of the benzene ring). The angle between the aromatic plane and the C≡N axis was calculated as 99°; we have found 93° in our structure. For our sandwich-like arrangement in the new inclusion complex **3**·MeCN the complexation enthalpy can be estimated to 5 kcal mol^{-1}. The participation of σ–π-interactions between an acetonitrile methyl proton and a host aromatic ring as well as the electronic contributions of six alkoxy groups in the aromatic rings of host **3** remain unconsidered. We thank Professor Kollman and Dr Grootenhuis for perusing their calculated data and for fruitful discussions.