$Co_2(CO)_6$-induced deformation of alkynes as a reversible modulator of supramolecular interactions: controlling the synthesis of catenanes

Darren G. Hamilton and Jeremy K. M. Sanders*†

Cambridge Centre for Molecular Recognition, University Chemical Laboratory, Lensfield Road, Cambridge, UK CB2 1EW

Complexation of $Co_2(CO)_6$ clusters to the alkyne bonds of a hybrid crown macrocycle alters the dimensions of the macrocyclic cavity such that inclusion complexation and catenane formation by catalytic ring closing metathesis is prevented; since removal of the $Co_2(CO)_6$ 'protecting group' is readily achieved, this procedure provides a general method for modulation of supramolecular interactions.

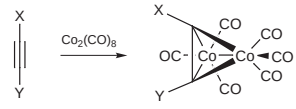
We show here that cobalt carbonyl complexation to alkyne groups provides a simple and reversible method for the modulation of molecular geometry. Since alkynes are popular linker groups that allow the precise spatial positioning of molecular components,[1] this complexation process offers a general approach for the control of supramolecular interactions. We exemplify the principle by controlling the binding properties of macrocycle **1** and hence its ability to act as a template for catenane formation under catalytic ring closing metathesis (RCM) conditions. Complexation of $Co_2(CO)_6$ clusters to the acetylene links of this hybrid crown macrocycle removes its ability to bind electron deficient substrates, while oxidative removal of the clusters restores the macrocycle's original structural form and binding capacity.

The reaction of dicobalt octacarbonyl with acetylene functions has been known for over 40 years (Scheme 1).[2] The complexes were originally of interest as some of the first characterised systems featuring multi-point attachment of an organic molecule to more than one metal atom. Complexation of an acetylene group to a cobalt carbonyl cluster has been used as a protecting group to mask the reactivity of the triple bond,[3] and also as an activating group to promote reactions requiring the stabilisation of an electron-deficient carbon centre.[4]

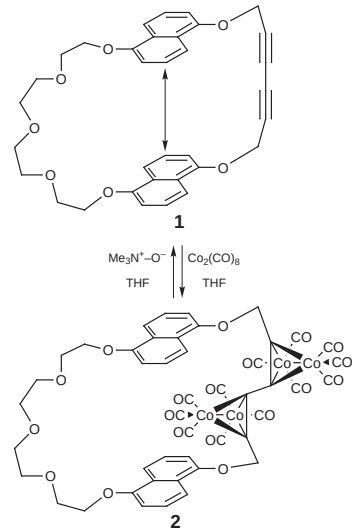
The complexation process is accompanied by a dramatic change in the geometry of the linear acetylenic carbon backbone. Complexation of $Co_2(CO)_6$ to diphenylacetylene reduces the Ph–C–C bond angles from 180 to around 138°;[5] this observation has been exploited in attempts to prepare *cyclo*-C_{18} by temporarily altering the geometry of precursors to favour cyclisation.[6] Of greatest relevance to the present discussion is the structure of the bis-$Co_2(CO)_6$ complex of diphenylbutadiyne (Ph–C≡C–C≡C–Ph).[7] The C–C–C bond angles at the four nominally sp hybridised centres of this complex fall in the range 139–145°. We predicted that if a butadiyne linker were incorporated into a macrocycle then cluster complexation to this host could induce sufficient structural change to inhibit guest binding. Hybrid macrocycle **1** appeared an ideal candidate with which to test this theory since it forms a weak donor–acceptor complex with π-deficient diimides ($K_a \approx 400$ M^{-1}), and has also been employed as a template for [2]catenane formation under kinetically controlled conditions.[8]

Treatment of a THF solution of **1** with excess $Co_2(CO)_8$ (3 equiv. per triple bond) rapidly affords a single complexed product **2** which may be obtained in near quantitative yield after chromatography on silica gel.‡ The ^{1}H NMR spectrum of **2** closely resembles that of **1** save for an aromatic doublet that shifts upfield from around 6.80 to 6.11 ppm perhaps as a result of the greater proximity of the two aromatic components. The ^{13}C NMR spectrum provides rather more information: the methylene carbons adjacent to the complexed butadiyne link are shifted downfield from around 56 to 68–70 ppm (obscured by OCH_2CH_2 resonances). The complexed acetylenic carbons are found at 96 and 93 ppm, downfield shifted from around 72 ppm in free **1**. These shifts are consistent with the introduction of strongly electron withdrawing substituents and previously reported values.[7] The electrospray ionisation mass spectrum of **2** reveals the sequential loss of CO ligands from the bis-$Co_2(CO)_6$ complexed macrocycle (M_r = 1124). Notably, the ^{1}H NMR spectrum of **2** in $CDCl_3$ was unchanged after standing in solution for several weeks; samples stored as dry solids proved similarly robust. Removal of the cobalt clusters could be achieved by treatment of **2** with iron(III) nitrate[3] in EtOH or, more conveniently, with trimethylamine oxide in THF.§ Regeneration of free **1** could be conveniently monitored by TLC. An intermediate, presumably the mono-$Co_2(CO)_6$ complex, could be discerned prior to complete conversion to **1**. Scheme 2 summarises the structural protection and deprotection steps.

We exemplify the application of this idea by controlling the formation of a π-donor/π-acceptor [2]catenane under catalytic ring closing metathesis conditions. The catalytic RCM reaction has become a familiar synthetic tool[9] and has also been employed in templated macrocycle[10] and catenane syntheses.[11] We anticipate that the reversible nature of the RCM bond-forming reaction will facilitate competition and evolution between related interlocked systems and thus provide the 'error-checking' facility necessary for the reliable assembly of higher



Scheme 1 General reaction of a functionalised acetylene with $Co_2(CO)_8$



Scheme 2 Blocking of a cyclophane receptor cavity by temporary structural modification

order interlocked molecular systems. The interlocking procedure also provides an ideal means with which to demonstrate the feasibility of our blocking principle.¶

Exposing a 2 : 1 molar ratio of diimide diolefin **3** and hybrid macrocycle **1** to Grubbs' catalyst (DCM, rt, 3 days) afforded the three isomeric forms of the corresponding [2]catenane **4**; direct hydrogenation of the reaction mixture (H_2, Pd–C) gave a single catenane product **5** in 15% overall yield.‖ Under identical reaction conditions a 2 : 1 molar ratio of diolefin **3** and complexed macrocycle **2** did not undergo interlocking, periodic analysis (LC-MS, TLC) revealing only the stubborn persistence of **2**. After three days 1 mol equiv. of free macrocycle **1** was added to the metathesis mixture and production of [2]catenane **4** commenced: this observation proves that under 'live' metathesis conditions macrocycle **2** is indeed blocked to threading by diolefin **3**. Direct hydrogenation (H_2, Pd–C) of the crude reaction mixture yielded the expected [2]catenane **5** and the protected macrocycle **2**.

The significance of the survival of **2** throughout this sequence of events lies in the realisation that this structural tool provides the means by which to prevent binding at one masked recognition site whilst the chosen reaction conditions act on a binding event elsewhere in the system or, potentially, within the same molecule. Both the olefin metathesis and hydrogenation steps are chemically orthogonal to the deprotection of **2**, the cobalt complexed macrocycle being unaffected by two distinct chemical transformations occurring within the system. We intend to exploit these observations in controlled syntheses of linear [*n*]catenanes.[12] There also exists the possibility of inhibiting a supramolecular interaction within a complex by cluster removal; an alternative view of this process is to regard the cluster as an effector for a particular interaction (Fig. 1). We also note that variations in cluster nuclearity and substitution pattern lead to subtle geometry changes in the resulting adducts, providing a means to fine tune molecular geometry.[13] In summary, it appears likely that both the specific, as described in this work, and general concepts of binding modulation through temporary structural modification will be of use in the area of host–guest chemistry.

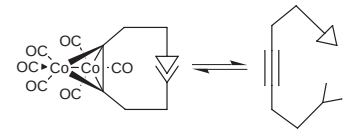


Fig. 1 Inhibition of a supramolecular interaction by cluster removal.

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Notes and references

† E-mail: jkms@cam.ac.uk

‡ **1→2**: to a solution of **1** (150 mg, 0.3 mmol) in dry THF (5 mL) was added $Co_2(CO)_8$ (560 mg, 1.6 mmol) under argon. After stirring for 30 minutes at room temperature the solvent was evaporated and the residue purified by column chromatography (SiO_2; $CHCl_3$–Et_2O–MeOH, 30 : 69 : 1) to afford **2** (R_f = 0.6) as a red–brown solid (293 mg, 96%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.88 (d, *J* 8 Hz, 2 H), 7.83 (d, *J* 8 Hz, 2 H), 7.30 (t, *J* 8 Hz, 3 H), 6.98 (t, *J* 8 Hz, 3 H), 6.84 (d, *J* 8 Hz, 2 H), 6.11 (d, *J* 8 Hz, 2 H), 5.19 (s, 4 H), 4.32 (m, 4 H), 3.98 (m, 4 H), 3.81 (m, 4 H), 3.74 (m, 4 H): ^{13}C NMR ($CDCl_3$, 100 MHz) δ 239.00, 154.45, 153.36, 125.44, 125.11, 115,16, 114.39, 106.17, 105.60, 71.36, 70.66, 69.73, 68.58, 68.37: ES–MS (positive ion) 1142.65 ($[M + NH_4]^+$, 12%), 1124.61 ($[M]^+$, 18%), 1086.66 ($[M - 2CO + NH_4]^+$, 100%), 1057.65 ($[M - 3CO + NH_4]^+$, 68%).

§ **2→1**: $Fe(NO_3)_3 \cdot 9H_2O$ (6 equiv.)–EtOH, rt, 3 days, or Me_3N^+–O^- (10 equiv.), THF, rt, 45 min; ammonium cerium(IV) nitrate (CAN) effects essentially instantaneous removal of the appended clusters[4] but also rapidly degrades the regenerated free macrocycle **1**.

¶ A preliminary experiment confirmed that **1** is unaffected by exposure to Grubbs' metathesis catalyst.

‖ M_r = 1288.29 ($[M + NH_4]^+$).

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