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A nucleic acid base derivative tethered to a ruthenium carbene complex: hydrogen bonded dimers in both the solid state and solution?†

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A ruthenium carbene bearing a uracil (Ur) substituent has been prepared and has a dimeric structure in the solid state—the dimer being held together by hydrogen bonds between two uracil groups on neighbouring molecules: evidence for the persistence of this interaction in solution has been obtained.

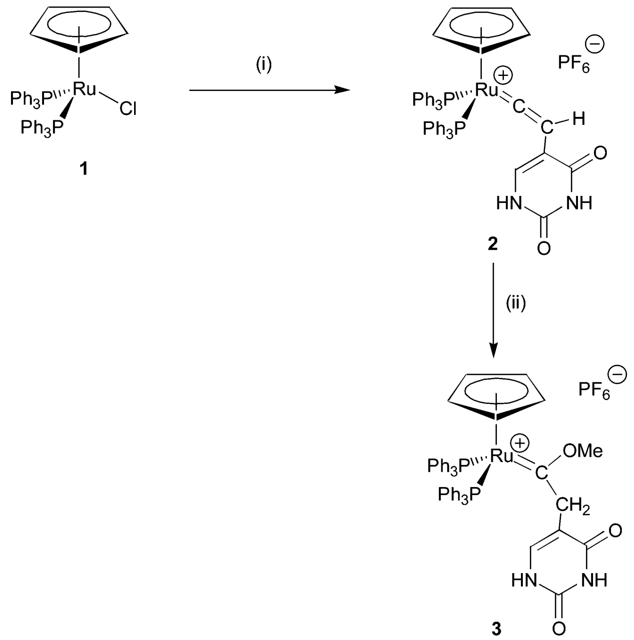
Transition metal complexes containing nucleobases are important materials in terms of their uses as probes for biological systems[1] and as precursors for supramolecular architectures.[2] The binding of metals to nucleobases within DNA is also thought to be a key step in the mechanism of anticancer drugs such as cisplatin.[3] Methods to prepare metal complexes of nucleobases typically rely on the Lewis Base properties of the nitrogen and oxygen atoms of the base.[4] More recently, however, palladium-catalysed protocols have been employed to tether the required nucleobase to a coordinated ligand.[2,5] We are currently exploring new methods to include nucleobases in the ligand environment of metals and in particular exploiting alkynes, substituted with nucleobases, as building blocks.[6] It is hoped that this approach will allow for the synthesis of new transition metal organometallic species and we wish to utilise the hydrogen bonding properties of the nucleobase as supramolecular synthons. As a starting point for these studies we decided to exploit the chemistry of the well-known $[Ru(PPh_3)_2(\eta^5\text{-}C_5H_5)]^+$ fragment which reacts with alkynes RC≡CH to give vinylidene complexes $[Ru(=C=CHR)(PPh_3)_2(\eta^5\text{-}C_5H_5)]^+$.[7]

Reaction of $[Ru(PPh_3)_2(\eta^5\text{-}C_5H_5)Cl]$, **1**, with a slight excess of the uracil-substituted alkyne UrC≡CH[8] and NH_4PF_6 in refluxing methanol solution for 24 h resulted in the formation of a bright yellow solution from which the ruthenium carbene complex **3**[PF_6], see Scheme 1, could be isolated. The NMR spectra‡ of **3**[PF_6] were consistent with its formulation as a methoxycarbene complex, notably, a resonance was observed in the $^{13}C\{^1H\}$ NMR spectrum at δ 306.6 (t, Ru=C, $^2J_{PC}$ 12.3 Hz).

A possible mechanism to account for the formation of $\mathbf{3}^+$ is shown in Scheme 1. It is proposed that initial reaction of the alkyne on the $[Ru(PPh_3)_2(\eta^5\text{-}C_5H_5)]^+$ fragment affords the vinylidene complex **2** which then reacts rapidly under the reaction conditions with the MeOH solvent to give **3**. Bruce and Swincer have shown that similar behaviour is observed for complexes $[Ru(=C=CHR)(PPh_3)_2(\eta^5\text{-}C_5H_5)]^+$ (R = Ph, Me, CO_2Me),[9] although in the case of the formation of **3** it is not possible to isolate the intermediate vinylidene complex. Presumably under the conditions employed the reaction of **2** with methanol is considerably more rapid than the reaction of **1** with UrC≡CH.

The structure of **3**[PF_6] (as a toluene solvate) was confirmed by a single crystal X-ray diffraction study,§ (Fig. 1). The short metal–carbon distance [Ru1–C11 1.946(3) Å] is consistent with the formulation as a metal carbene complex, similar bond lengths having been reported in related ruthenium carbene complexes.[10]

Further examination of the structure revealed that **3**[PF_6] does not exist as discrete units, but as dimers linked by hydrogen bonds with the overall formula $(\mathbf{3}[PF_6])_2$: one molecule of toluene is present in the structure per **3**[PF_6] unit. The dimers may be seen in the packing diagram in Fig. 2. The uracil groups on neighbouring molecules form complementary hydrogen bonds involving the N–H group in the 3-position and the oxygen in the 4-position of the uracil group with an N–H···O distance of 2.897 Å. It is interesting to note that even though a second NH and carbonyl function are present on each uracil group no further complementary hydrogen bonds are formed. Instead, the NH group in the 1-position of the uracil shows a close contact (N–H···F 3.005 Å) with one of the fluorines of the PF_6, group thus completing the overall dimeric structure. The PF_6 unit shows significant disorder, although this only appears to involve the four fluorines in a position *cis* to the



Scheme 1 (i) + HC≡CUr, + NH_4PF_6, − NH_4Cl; (ii) MeOH.

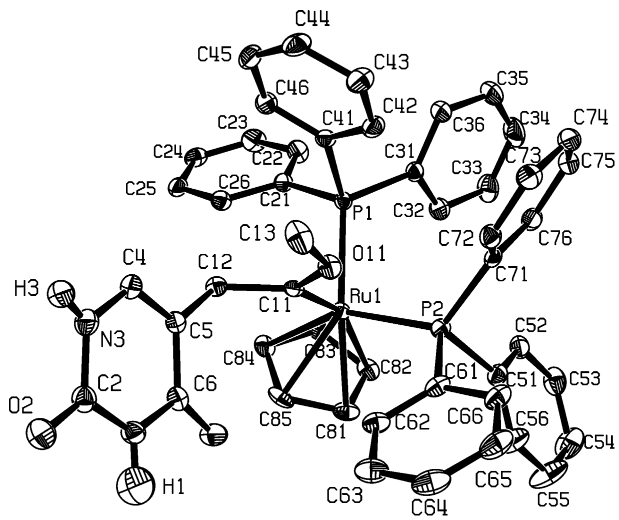


Fig. 1 Ortep representation of the cation of **3**. Thermal ellipsoids are shown at 30%. Hydrogen atoms (except H1 and H3) removed for clarity.

† Electronic supplementary information (ESI) available: details of experimental procedure and NMR spectra. See http://www.rsc.org/suppdata/cc/b4/b402592j/

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hydrogen bonded atom. It might be suspected that the formation of a second complementary hydrogen bond set on each uracil would be more energetically favoured than a single hydrogen bond to a PF_6 group, but an examination of the structure revealed that the bulky PPh_3 ligands would make such an arrangement sterically unfavourable.

We were interested to discover whether or not the dimeric structure observed in the solid state was also present in solution. In order to test this hypothesis a series of CD_2Cl_2 solutions with varying concentrations of **3**[PF_6] were prepared and their ^{1}H and ^{31}P NMR spectra recorded. As can be seen (Fig. 3) the resonances for the N–H protons of the uracil group show a marked dependence on concentration. In contrast, the resonance for the PF_6^- anion in the ^{31}P NMR spectra of the solutions of **3** did not show any marked changes on varying the concentration. This implies that in solution there is no significant cation–anion pairing and it is unlikely that the PF_6 group shows any strong interaction with the N–H function of the 1-position of the uracil—in contrast to the solid state.

It is well known, however, that concentration dependent resonances in the ^{1}H NMR spectra of nucleic acid base derivates is characteristic of the formation of hydrogen bonded dimers.[11] Therefore, one possible interpretation of our results is that, in CD_2Cl_2 solution, an equilibrium between $\mathbf{3}^+$ and a hydrogen bonded dimeric species $(\mathbf{3}_2)^{2+}$ is present.

It is interesting to compare the behaviour of **3** with the ruthenium carbene complex *fac*-, *cis*-[(PNP)RuCl(C{$NHC_4H_3N_2O_2$}{CH_2-Ph})]Cl [PNP = $CH_3CH_2CH_2N(CH_2CH_2PPh_2)_2$], **4**, prepared by Fillaut and co-workers.[12] Here the uracil unit is bound to both the carbon of the metal carbene unit (through the amino substituent) and also to the metal (through the oxygen of the carbonyl group attached to C4). In this case, no intermolecular hydrogen bonding is observed either in solution or the solid state, even though the complex has suitable donor–acceptor sites available. It is interesting to note that in the structure of **3** the carbonyl function in the 4-position of the ring is involved in the hydrogen bonding array and, in the case of **4** where no inter-base hydrogen bonds are observed, this unit is coordinated to the metal.

As well as exploring the biological activity of **3**, we are actively expanding the range of transition metal complexes containing nucleobases, nucleosides and nucleotides which may be prepared by this methodology.

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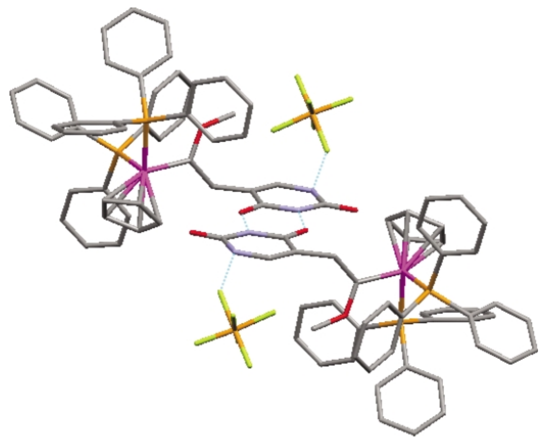

Fig. 2 Diagram showing the dimeric structure of $\mathbf{3}PF_6$ in the solid state. Nitrogen atoms shown in blue, oxygen red, phosphorus orange and ruthenium purple.

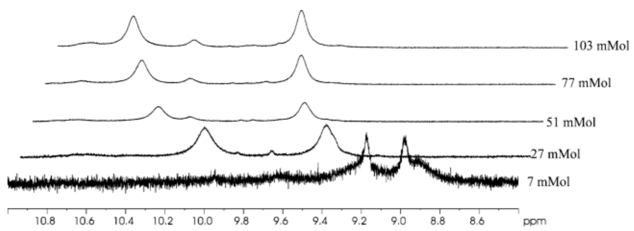

Fig. 3 ^{1}H NMR spectra of complex **3** recorded at various concentrations.

Notes and references

‡ Selected physical and spectroscopic data for **3**. ^{1}H NMR (CD_2Cl_2) δ 9.36 (br s, 1H, N*H*), δ 9.02 (br s, 1H, N*H*), δ 7.01 (C=C*H* in uracil: identified by ^{1}H–^{13}C correlation experiment), δ 4.89 (s, 5H, C_5H_5), δ 4.31 (s, 2H, CH_2), δ 3.38 (s, 3H, O*Me*), ^{31}P{^{1}H} NMR (CD_2Cl_2) δ 50.7 (s, PPh_3), δ −138.5 (sept, $^{1}J_{PF}$ = 711.6 Hz, PF_6^-), ^{13}C{^{1}H} NMR (CD_2Cl_2) δ 306.6 (t, $^{2}J_{PC}$ 12.3 Hz, Ru=*C*(OMe), δ 164.5 (s, *C*=O), δ 152.63 (s, *C*=O), δ 140.8 (s, H*C*=C), δ 138.5 (s, HC=*C*), δ 136.1 (vt, $|^{1}J_{PC}+^{3}J_{PC}|$ 46.6 Hz, P*Ph*$_3$ C1), δ 134.0 (vt, $|^{2}J_{PC}+^{4}J_{PC}|$ 10.2 Hz, P*Ph*$_3$ C2), δ 129.0 (vt, $|^{3}J_{PC}+^{5}J_{PC}|$ 9.3 Hz, P*Ph*$_3$ C3), δ 131.0 (s, P*Ph*$_3$ C4), δ 92.2 (s, C_5H_5), δ 63.9 (s, O*Me*), δ 55.1 (s, CH_2). IR (KBr) 3416 cm^{-1} (N–H), 1730 cm^{-1} (C=O), 1668 cm^{-1} (C=O), 1254 cm^{-1} (C–OMe), 841 cm^{-1} (P–F). Elemental analysis: for $\mathbf{3}PF_6.C_7H_8$ calculated C 60.27%, H 4.69%, N 2.56%; found C 59.94%, H 4.70%, N 2.66%.

§ Crystal data for complex **3**: $C_{55}H_{51}F_6N_2O_3P_3Ru$, M_r = 1095.96, triclinic, a = 11.618(2) Å, b = 14.376(2) Å, c = 16.327(2) Å, α = 94.691(3)°, β = 91.172(3)°, γ = 112.930(2)°. V = 2499.0(6) Å^3, T = 173 K, space group $P\bar{1}$, Z = 2, μ = 0.479 mm^{-1}, λ(Mo-K$_\alpha$) = 0.71073 Å. 26728 reflections measured, 11354 unique (R_{int} = 0.0467) which were used in all calculations. The final $wR(F^2)$ was 0.0815 (all data). CCDC 232408. See http://www.rsc.org/suppdata/cc/b4/b402592j/ for crystallographic data in .cif or other electronic format.

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