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Reactions of *eq,eq*-$Re_2(CO)_8(MeCN)_2$ with phenylacetylene and α-ethynylestradiol. A new synthesis of acetylide complexes

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Abstract

The complex *eq*,,*eq*-$Re_2(CO)_8(MeCN)_2$ reacts with phenylacetylene and α-ethynylestradiol to give the acetylide complexes (μ-H)(μ-C≡CR)$Re_2(CO)_7$(MeCN) [**1**, R = Ph; **2**, R = α-ethynylestradiol] and not the expected compounds (μ-H)(μ-C≡CR)$Re_2(CO)_8$. The products were identified from their spectroscopic properties and by an X-ray structural determination in the case of **1**. The α-ethynylestradiol complex exists in two diastereomeric forms.

There is a current interest in the development of bioligand tagging methods for units containing ^{186}Re and ^{188}Re isotopes owing to their potential as radioactive imaging and therapeutic agents [1]. The usual sources of these radioactive species are perrhenate $[Re^{\star}O_4]^-$ compounds, which can be readily transformed into $Re_2^{\star}(CO)_{10}$ [2] derivatives of which the non-radioactive form is commercially available. In addition, alkyne groups are often either already present or easy to attach to bioligands [3]. In this context, we thought it of interest to study the reactions of rhenium carbonyl complexes with alkyne derivatives.

To our knowledge, this type of chemistry has received scarce attention in the literature. Complexation of disubstituted alkynes by rhenium carbonyl reagents has been brought about thermally by using a high boiling point alkane as a solvent. However, this method leads to rhenium complexes in which the alkyne is dimerized and tetramerized [4]. The preparation of (μ-hydrido)(μ-phenylacetylido)dirhenium octacarbonyl, (μ-H)(μ-C≡CPh)$Re_2(CO)_8$, was reported by Nubel and Brown [5a]: in their work $Re_2(CO)_{10}$ in toluene was photolyzed in the presence of propylene for 20 h and the (μ-H)(μ-*trans*-CH=CHCH$_3$)$Re_2(CO)_8$ was allowed to react with an excess of phenylacetylene for 10 h. The resulting oil was kept under dynamic vacuum for 1–2 days to remove the residual alkyne. Direct treatment of $Re_2(CO)_{10}$ with

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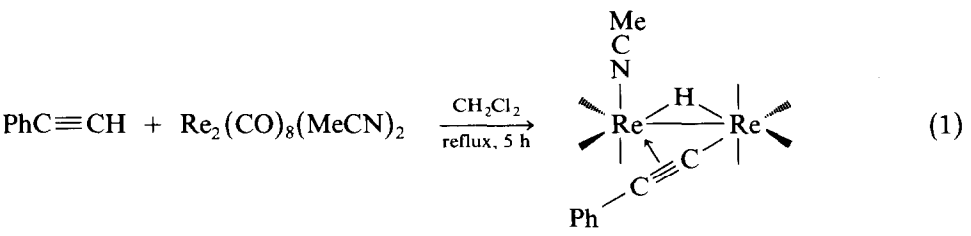
phenylacetylene afforded the same complex, but in undetermined yield because of decomposition during the work-up [5b]. Since these procedures were not suitable for our purposes, we devised another approach complexing phenylacetylene with rhenium carbonyl moieties and 17α-ethynylestradiol to give model systems.

As mentioned above, thermal activation of *eq,eq*-$Re_2(CO)_{10}$ requires extreme conditions, unlikely to be compatible with the use of fragile alkynes for direct replacement of carbonyl groups. A strategy developed for both triosmium carbonyl [6] and triruthenium carbonyl [7] clusters involves replacement of one or two carbonyl groups by more labile ligands such as acetonitrile (CH_3CN) under relatively mild conditions, thus allowing subsequent reactions to take place smoothly with a variety of organic ligands.

The relevant $Re_2(CO)_9(MeCN)$ [8] and $Re_2(CO)_8(MeCN)_2$ [9] complexes, prepared by removal of CO ligands by oxidation with Me_3NO and replacement by MeCN, have been previously described. However, their reactions with alkynes have not previously been investigated.

The reaction of $Re_2(CO)_9(MeCN)$ in refluxing dichloromethane with phenylacetylene was found not to lead to a rhenium alkyne complex, since the monosubstituted rhenium reagent not being sufficiently activated for reaction with this substrate. When a solution of phenylacetylene and *eq,eq*-$Re_2(CO)_8(MeCN)_2$ in dichloromethane was refluxed, however, the disubstituted acetonitrile reagent completely disappeared during 5 h heating. Compound **1** was isolated by TLC on silica in 54% yield (eq. 1).



(1)

(1)

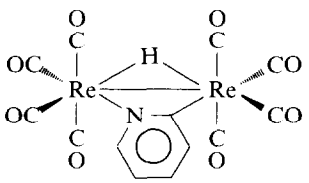
The IR, ^1H- and ^{13}C-NMR, and mass spectral data are consistent with the formulation (μ-H)(μ-C≡CPh)$Re_2(CO)_7(MeCN)$, and not with the expected complex (μ-H)(μ-C≡CPh)$Re_2(CO)_8$. Compound **1** showed a methyl peak of the MeCN ligand at 2.20 ppm and a hydride peak at −11.45 ppm *.

The facile removal of MeCN from *eq,eq*-$Re_2(CO)_8(MeCN)_2$ accounts for the formation of the alkyne complex **1**. Activation of the rhenium reagent allows coordination of phenylacetylene at one Re center and subsequent intramolecular oxidative addition of acetylenic C–H at the other. The σ–π binding mode of the

* Selected spectroscopic data for **1**: IR (CH_2Cl_2): ν(C=O) and ν(C≡C) = 2100 w, 2034 s, 2000s, 1987 sh, 1955 s, 1929 sh cm^{-1}. ^1H NMR (CD_2Cl_2, 250 MHz), δ 7.56 (dd, *o*), 7.45 (m, *p*), 7.39 (m, *m*) (Ph), 2.20 (s, Me), −11.45 (s, μ-H). ^{13}C NMR (CD_2Cl_2, 62.5 MHz) δ: 189.84 (m, 3), 187.27 (1), 185.38 (1), 182.75 (1), 181.54 (1) (CO), 131.75 (*m*), 128.80 (*ip*), 128.71 (*o*), 128.35 (*p*) (Ph), 119.63 (CN), 101.78 (C≡), 98.85 (≡C–Ph), 3.29 (Me). EI MS (70 eV): *m/z* calculated for Re_2 = 372 : 670 (M^+ − MeCN), 642 (M^+ − MeCN − CO), 614 (M^+ − MeCN − 2CO), 586 (M^+ − MeCN − 3CO), 558 (M^+ − MeCN − 4CO), 532 (M^+ − MeCN − 5CO), 502 (M^+ − MeCN − 6CO), 474 (M^+ − MeCN − 7CO).

acetylide ligand was clearly revealed by the structural determination (Fig. 1). The incorporation of MeCN into the final product **1** may be due to the remarkably facile thermal substitution of the axial CO group in the postulated intermediate (μ-H)(μ-C≡CPh)$Re_2(CO)_8$ in the presence of MeCN. It has been hypothetized that the acetylide ligand can labilize *cis* CO ligands of octahedral complexes through stabilisation of the coordinatively unsaturated transition state species, since it possesses two pairs of π electrons [5a]. One pair is involved in the coordination whereas the other is available for π donation in the unsaturated transition state.

The solid-state molecular structure of **1** * shows a degree of similarity to that of complex **2** isolated by Brown et al. [10]. Complex **2** has an eclipsed structure, in



(2)

contrast to the staggered structure of $Re_2(CO)_{10}$. The Re–Re distance is 3.0788 Å, slightly longer than that of $Re_2(CO)_{10}$ (3.0413 Å) [11] but shorter than that of **2** (3.2324 Å) [10]. The MeCN ligand is perpendicular to the mean plane determined by Re(1), Re(2), C(3) and H(1); the C–N–Re angle is 178.5°. The phenylacetylido ligand is clearly bound to Re in a μ-η^1,η^2 mode. The bond length between Re(2) and C(3) is 2.307 Å, while the triple bond length C≡C (1.216 Å), is close to that in the free ligand (1.200 Å). The results show that there is a little difference in the Re–Re and C≡C bond lengths of the phenylacetylido ligand from those in the starting molecules.

When a solution of α-ethynylestradiol and $Re_2(CO)_8(MeCN)_2$ was refluxed in dichloromethane for 15 h (eq. 2), the reaction gave one major compound, **3**, in 58% yield. Compound **3** exhibits six bands in the carbonyl region in the IR spectrum. The ^{1}H-NMR spectrum shows the characteristic steroid signals as well as peaks in the hydride region at −11 ppm.

$$\alpha\text{-ethynylestradiol} + Re_2(CO)_8(MeCN)_2 \xrightarrow[\text{reflux, 15 h}]{CH_2Cl_2} \mathbf{3} \qquad (2)$$

Comparison of the IR spectrum of **3** with that of **1** in the carbonyl region (see Fig. 2) clearly shows that the organometallic moiety in these two compounds is

* Crystal data: $C_{17}H_9O_7NRe_2$, $M = 711.66$, monoclinic, space group $P2_1/n$, $Z = 4$, $a = 7.2462$ (7), $b = 16.146$ (2), $c = 17.060$ (3) Å, $\beta = 101.13$ (1)°, $D_c = 2.41$ g cm^{-3}. 4723 data collected at room temperature on a Nonius CAD4 diffractometer. An absorption correction was applied (DIFABS). Anomalous dispersion terms and a correction for secondary extinction were applied. The structure was solved by standard Patterson–Fourier techniques and refined by least squares using anisotropic thermal parameters for all non-hydrogen atoms. H atoms were located from a difference Fourier map and their coordinates refined with an overall isotropic thermal parameter, except for the phenyl H which were kept in calculated positions. 3301 reflection with $I > 3\sigma(I)$ were used to solve and refine the structure to $R = 0.023$ and $R_w = 0.025$ (258 least-squares parameters). The programs used were CRYSTALS and ORTEP-2. Lists of atomic coordinates bond lengths, angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre.

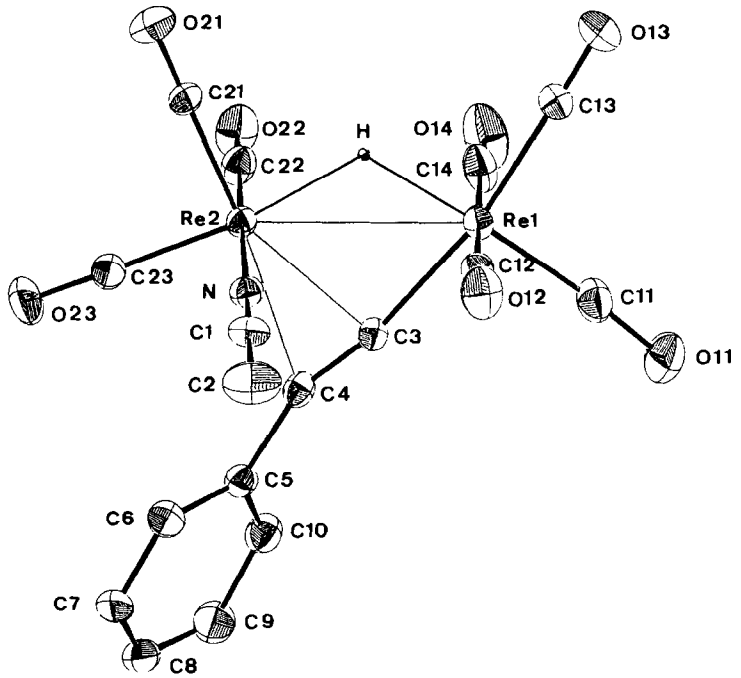
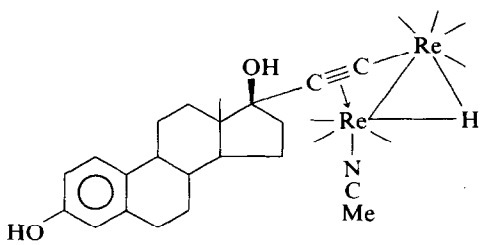


Fig. 1. ORTEP drawing of (μ-H)(μ-C≡CPh)$Re_2(CO)_7$(MeCN), **1**. Selected bond lengths (Å): Re(1)–Re(2), 3.0788(4); Re(1)–C(3), 2.095(7); Re(2)–C(4), 2.446(7); Re(1)–C(11), 1.881(9); Re(1)–H(1), 1.6(1); Re(2)–N(1), 2.151(5); Re(2)–C(3), 2.307(6); Re(2)–C(21), 1.907(7); Re(2)–H(1), 1.9(1); N(1)–C(1), 1.121(8); C(3)–C(4), 1.216(9); C(4)–C(5), 1.450(9); C(5)–C(6), 1.38(1); C(11)–O(11), 1.19(1); C(21)–O(21), 1.142(8).

almost the same. Hence, the structure of **3** is similar to that of **1**, and can be represented as shown below.



(3)

The ^{13}C-NMR spectrum of **3** exhibits two singlets at 3.38 and 3.17 ppm corresponding to the coordinated MeCN, as well as two peaks corresponding to each of the carbons C5, C≡C and C17. In addition, the ^{1}H-NMR spectrum shows two signals at 2.18 and 2.14 ppm with about the same integration for the Me group

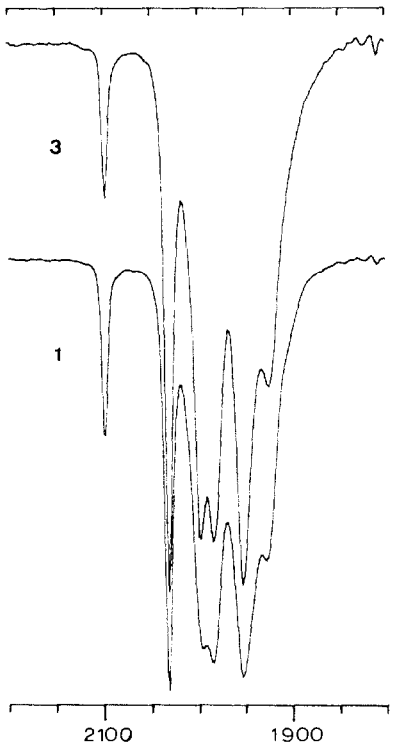
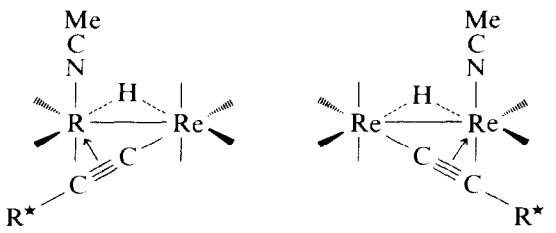


Fig. 2. IR spectra of **1** and **3** in the carbonyl region (CH_2Cl_2).

of MeCN *. We attribute this result to the formation of two diastereomers, as shown below



(3a) **(3b)**

* Selected spectroscopic data for **3**: IR (CH_2Cl_2): ν(C=O) and ν(C≡C) = 2099 w, 2033 s, 1999 s, 1984 sh, 1953 s, 1925 cm^{-1} sh. ^1H NMR (CD_2Cl_2, 250 MHz) δ: 7.20 (d, H1), 6.61 (dd, H2), 6.56 (d, H4), 5.38 and 5.08 (s, s, OH), 2.83 (m, H6), 2.18 and 2.14 (s, s, MeCN), 1.05 (s, Me-13), −11.75 and −11.76 (d, μ-H). ^{13}C NMR (CD_2Cl_2, 62.5 MHz) δ: 189.75 (m, 3), 187.27 (1), 185.26 (1), 182.65 (1), 181.42 (1) (CO), 153.67 (C3), 138.60, 138.42 (C5), 132.78 (C10), 126.67 (C1), 119.37 (CN), 115.25 (C4), 112.69 (C2), 109.84, 109.44, 98.55, 98.14 (C≡C), 84.90, 84.65 (C17), 14.32, 14.20, (Me-13), 3.38, 3.17 (MeCN).

Attempts to separate these two diastereomers by TLC or fractional crystallisation were unsuccessful owing to the similarity of their physical properties. The reactivity and biological activity of these complexes are currently under investigation. The apical MeCN ligand is very labile and can be easily replaced by CO at atmospheric pressure and by amines at room temperature. The potential of such substitution is currently under investigation from both the chemical and biochemical viewpoints.

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