of mass collision energy (421 eV) for these $C_{60}^{\bullet+}$ collisions with argon.

Capture of simple molecular gases undergoing high-energy collisions with fullerene ions could not be documented previously.[6] For example, collisions of $C_{60}^{\bullet+}$ with D_2 gave rise to no D- or D_2-containing products.[6] We were able, however, to detect both $C_{60}D^+$ and $C_{60}D_2^{\bullet+}$ (see Figure 4). The inability to detect lower mass product ions containing D or D_2 in the experiments reported here and elsewhere[6] may be due to rupture of the D-D bond with subsequent loss of the deuteriums.

The results given here will be elaborated in a comprehensive report of the products and energetics of high-energy collisions of $C_{60}^{\bullet+}$, $C_{70}^{\bullet+}$, and other fullerene radical cations with a number of target gases.[10] Other issues addressed include the kinetic energy of product ions that contain the target gas, the variation of the spectra of product ions as a function of both energy and number of collisions, and the end points in the capture processes. Comparison of the predicted kinetic energies of product ions with the observed values convinces us that the majority of the fullerene product ions produced from high-energy collisions with small target gases result from fragmentation of the intermediate fullerene endohedral complex.[10]

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3,3',5,5'-Tetrapyridylbiphenyl: A Biscyclometalating Bridging Ligand with a High Coupling Ability in Ru^{III},Ru^{II} Mixed Valence Systems

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The search for bridging ligands allowing electronic communication between metal centers is an important target related to long-range electron transfer and photoinduced charge separation.[1] Following the pioneering work of Creutz and Taube on 1,4-pyrazine-bridged Ru^{II},Ru^{III} mixed valence complexes,[2] several bridging ligands of various lengths have been used.[3] Most of them and in particular 4,4'-bipyridine lead to class II complexes (valence-trapped systems).[4,5] Most coupling systems consist of short bridges insuring strong Π-communication like $(CN)_2$, N_2, $NCC^-(t\text{-Bu})CN$, or $\mu\text{-}\eta^2\text{:}\eta^2$ benzene.[3,6,7] We now report that a bis-terdentate ligand containing two NCN coordination sites ("cyclometalating" terpyridine) affords dinuclear species in which the metals are connected by a 4,4'-biphenyl dianion (isoelectronic to the classical bridging ligand 4,4'-bipyridine), the whole edifice being stabilized by the four additional pyridine nuclei. The corresponding mixed-valence state (Ru^{III},Ru^{II}) can easily be generated. It shows exceptionally strong electronic interaction between the two redox centers.

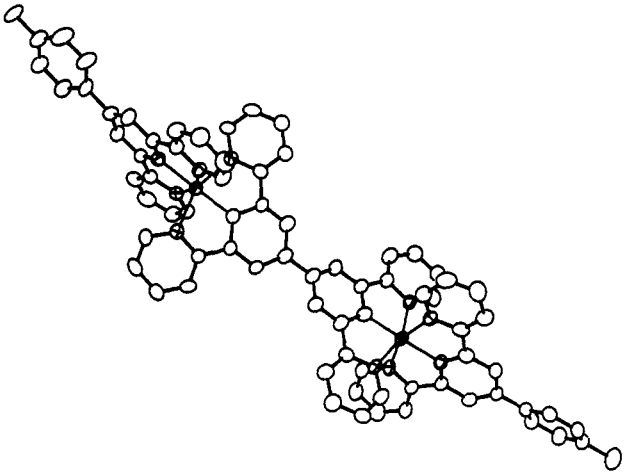
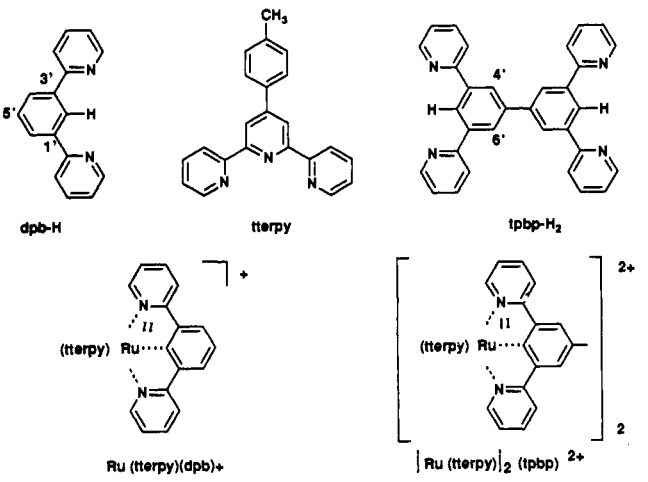


Figure 1. ORTEP drawing of the non-hydrogen atoms of the dinuclear complex cation. Thermal ellipsoids show 40% probability levels (empty ellipses, carbon). Main distances in angstroms: Ru1···Ru2, 11.009 (2); Ru-C, 1.96 (2) and 1.96 (1); Ru-N, 2.042 (8), 2.019 (8), 2.067 (9), 2.080 (8), 2.100 (8), 2.070 (8), 2.007 (7), 2.075 (8), 2.099 (8), and 2.089 (8). Torsion angle around the central C-C bond of the tpbp ligand, 22.2 (7)°.

Chart I



The compound studied and its precursors are represented in Chart I. The terdentate ligand dpb^- (dpb-H: di-(*o*-pyridyl-1,3-benzene) contains a σ-phenyl central coordination site. It was prepared[8] with the aim of using it as a terpy analogue displaying a stronger ligand field than terpy itself. $Ru(tterpy)(dpb)^+PF_6^-$ was prepared from $Ru(tterpy)Cl_3$ (tterpy: 4'-*p*-tolyl-2,2',6',2''-terpyridine) by first replacing the chloride ligands by solvent molecules using $AgBF_4$ in excess as a dechlorinating agent in refluxing acetone, followed by addition of a stoichiometric amount of dpb-H and heating of the mixture under reflux in 1-butanol. Depending upon the experimental conditions, various amounts of an additional dinuclear compound were obtained (up to 60% yield based on $Ru(tterpy)Cl_3$). The same dinuclear complex could be generated from $Ru(tterpy)(dpb)^+PF_6^-$ by reacting the mononuclear species with a large excess of silver(I) salt now used as an oxidant in refluxing butanol. The compound was obtained in 80% yield after chromatographic separation (silica; acetone-

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(8) dpb-H was prepared according to a synthetic method previously described for 2,2'-(1,4-phenylene)dipyridine.[9] 1,3-Dicyanobenzene (4 g; 32.2 mmol) and Co(Cp)COD (0.1 g; COD is 1,5-cyclooctadiene) dissolved in 40 mL of toluene were loaded in an autoclave under 10 atm of acetylene. The autoclave was heated to 130 °C for 3 days. After workup and chromatography (silica; CH_2Cl_2-CH_3OH as eluent), dpb-H was obtained as a colorless oil (6.5 g; 90%). ^1H NMR (200 MHz, CD_2Cl_2):δ 8.7 (m, 3 H), 8.09 (d, 2 H, 2 Hz), 8.06 (dd, 2 H, 2 Hz), 7.85 (m, 4 H), 7.58 (t, 1 H, 8 Hz), 7.27 (ddd, 2 H, 7, 4, 1.5 Hz). MS: m/z = 232; $C_{16}H_{12}N_2$ requires 232.
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H_2O–KNO_3 as eluent). It was assumed to be $[Ru(tterpy)]_2(tpbp)^{2+}$ on the basis of its ^1H NMR spectrum (sharp singlet for the 4'- and 6'-protons) and FAB-MS measurements.[10]

Formation of a C–C coupling product from dpb-H is not obvious from a mechanistic viewpoint, but it is likely to involve radicals located on the 5'-position of the central ring once coordinated to the ruthenium(II) center, this position becoming relatively oxidizable after formation of the $Ru-C_{2'}$ bond.

The chemical nature of $[Ru(tterpy)]_2(tpbp)^{2+}$ was confirmed by a crystallographic study of its PF_6^- salt.[11] The X-ray structure of the complex is shown in Figure 1. The electrochemical data for both mono- and dinuclear complexes are as follows:

$Ru^{III/II}(tterpy)(dpb)^{2+/+}$: $E_{1/2}$ = +0.485 V (vs SCE in CH_3CN)

$[Ru_2^{III,III/III,II}(tterpy)_2](tpbp)^{4+/3+}$: $E_{1/2}$ = +0.50 V

$[Ru_2^{III,II/II,II}(tterpy)_2](tpbp)^{3+/2+}$: $E_{1/2}$ = +0.34 V

Each electrochemical process is reversible. The calculated comproportionation constant K_c for the reaction $Ru_2^{III,III} + Ru_2^{II,II} \rightleftharpoons 2Ru_2^{III,II}$ is ~600, i.e., comparable to that in $ClRu(bipy)_2(pz)Ru(Cl)(bipy)_2^{3+}$ [12] (pz is 1,4-pyrazine) in spite of a much larger distance between the metals, 11.009 (2) Å.

The UV-visible spectrum of the $Ru_2^{II,II}$ complex was as expected. It shows very intense metal-to-ligand charge transfer (MLCT) bands in the visible region (λ_{max} = 516 and 543 nm; ϵ = 30 700 M^{-1} cm^{-1} for both maxima). Neither the $Ru_2^{II,II}$ species nor the oxidized form $Ru_2^{III,III}$ (excess Br_2 in CH_3CN) displayed any absorption in the near-infrared (near-IR) domain.

The most striking property of the mixed-valence state $[Ru_2(tterpy)_2](tpbp)]^{3+}$ is related to its intervalence transfer (IT) transition. The mixed-valence complex was generated by addition of gradual amounts of Br_2 in CH_3CN. As expected, an intense MLCT band was also present in the visible (λ_{max} = 523 nm; ϵ = 31 700 M^{-1} cm^{-1}). The near-IR spectrum shows a huge IT band centered at λ_{max} ~ 1820 nm, with an extraordinary extinction coefficient (ϵ ~ 27 000 M^{-1} cm^{-1}). The band is much narrower ($\Delta\nu_{1/2} = 2.82 \times 10^3$ cm^{-1}) than expected from calculations following Hush's theory,[13] also supporting significant delocalization for the $Ru_2^{III,II}$ state. The α value[13] found in the present case amounts to α = 0.23.

The very special coupling properties of the $tpbp^{2-}$ ligand in the present dinuclear ruthenium complex open the route to long-distance electron transfer across related anionic aromatic bridges.

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(10) Ru(tterpy)(dpb)$^+$(PF_6^-): ^1H NMR (200 MHz, CD_3CN) δ 8.98 (s, 2 H), 8.55 (d, 2 H, 8 Hz), 8.25 (d, 2 H, 8 Hz), 8.16 (m, 4 H), 7.70 (td, 2 H, 8, 2 Hz), 7.56 (m, 4 H), 7.45 (t, 1 H, 8 Hz), 7.09 (m, 4 H), 6.94 (m, 2 H), 6.65 (m, 2 H), 2.51 (s, 3 H); FAB-MS (nitrobenzyl alcohol matrix) m/z = 656.1, Ru(tterpy)(dpb)$^+$ requires 656. $[Ru(tterpy)]_2(tpbp)^{2+}(PF_6^-)_2$: ^1H NMR (200 MHz, CD_3CN) δ 9.05 (s, 4 H), 8.97 (s, 4 H), 8.62 (d, 4 H, 8 Hz), 8.48 (d, 4 H, 8 Hz), 8.14 (d, 4 H, 8 Hz), 7.78 (d, 4 H, 8 Hz), 7.70 (d, 4 H, 8 Hz), 7.57 (d, 4 H, 8 Hz), 7.30 (d, 4 H, 6 Hz), 7.18 (d, 4 H, 6 Hz), 7.04 (t, 4 H, 6 Hz), 6.73 (t, 4 H, 6 Hz), 2.53 (s, 6 H); FAB-MS (nitrobenzyl alcohol matrix) m/z = 1455.2, $[Ru_2(tterpy)_2(tpbp)(PF_6)]^+$ requires 1455.

(11) The compound $[Ru_2(tterpy)_2(tpbp)](PF_6)_2 \cdot (CH_3)_2CO$ crystallized in the monoclinic space group $P2_1/n$, a = 22.464 (3) Å, b = 17.834 (2) Å, c = 20.107 (2) Å, β = 98.72 (1)°, V = 7962 (3) Å^3, μ(Cu Kα) = 41.86 cm^{-1} and D_{calcd} = 1.38 $g \cdot cm^{-3}$ for Z = 4, $Ru_2P_2F_{12}ON_{10}C_{79}H_{60}$ MW = 1657.5. Reflections were measured on an Enraf-Nonius CAD 4 diffractometer using Cu Kα graphite-monochromated radiation ($\omega/2\theta$ scan mode, scan width (ω) 0.55 + 0.14 tan θ, 4° < θ < 59°). The compound is unstable at room temperature, due to a loss of acetone; 11 264 unique data, 7458 with $I > 3\sigma(I)$. A decay correction and an empirical absorption correction (ψ scan) were applied. The non-hydrogen atoms were located by direct methods and refined anisotropically. The hydrogen atoms except those of the acetone molecule were included as idealized contributions. Actual R = 0.067 and R_w = 0.121. All calculations were done with SDP (Structure Determination Package; B. A. Frenz and Associates Inc., College Station, TX, and Enraf-Nonius, Delft, 1983). Diffraction and calculation work was performed at Laboratoire de Cristallographie Biologique, IBMC, Strasbourg.

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Supplementary Material Available: An atom-labeling scheme of $[Ru(tterpy)]_2(tpbp)^{2+}$ and tables of positional and isotropic equivalent thermal parameters, anisotropic thermal parameters, bond distances and bond angles, and least-squares planes (13 pages); listing of observed and calculated structure factors (30 pages). Ordering information is given on any current masthead page.

The First Potent Inhibitor of Squalene Synthase: A Profound Contribution of an Ether Oxygen to Inhibitor–Enzyme Interaction†

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An accounting of the noncovalent forces between host and guest is key to understanding the interactions involved in molecular recognition. Such knowledge could provide predictive input for the design of new inhibitors of physiologically important enzymes. In this communication, we report the discovery of ether **6**, the first potent inhibitor of squalene synthase. This agent was designed on the basis of a proposed mechanism for the enzymatic reaction. We demonstrate herein that the ether oxygen of **6** makes a substantial contribution to the overall binding energy between enzyme and inhibitor.

Squalene synthase,[1] a key enzyme of the cholesterol biosynthetic pathway, catalyzes the reductive dimerization of farnesyl diphosphate (FPP, **1**) to squalene (**3**) via the intermediate cyclopropane, presqualene diphosphate (**2**) (Scheme I). Studies on the related prenyl transferase reaction[2] and the second step of the squalene synthase reaction[1a,2a,3] suggest that both transformations in Scheme I proceed through an initial carbocation–diphosphate ion pair. As illustrated for step 1 in Figure 1A, we envision that the donor[1] FPP is bound in the enzyme's active site via hydrophobic interactions with the isoprene portion and ionic interactions with the highly charged diphosphate moiety. We expect that the enzyme catalyzes the heterolytic cleavage of A to B by binding the two fragments more tightly as the transition-state separation is approached. Furthermore, we propose that squalene synthase utilizes an active-site acid catalyst to promote ion-pair formation.

We previously reported that **4** (Table I), a stable analogue of FPP where the reactive allylic and anhydride oxygen atoms were each replaced with CH_2, was a competitive inhibitor of rat liver microsomal squalene synthase (I_{50} = 31.5 μM, K_i = 10 μM; apparent K_m(FPP) = 12.7 μM).[4,5] Linker homologue **5**, an

† This paper is dedicated to Professor Gilbert Stork on the occasion of his 70th birthday.

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