JOC Notes

An Unexpected Metal-Promoted Transformation Yields An Anthrylmethyl Spiroanthracene

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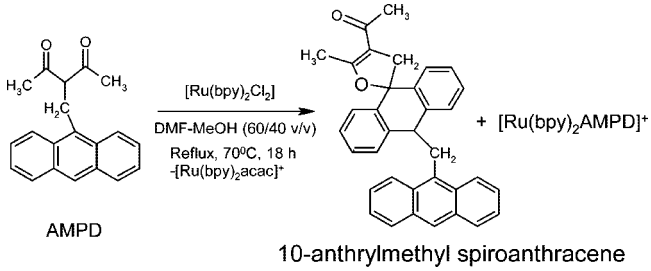
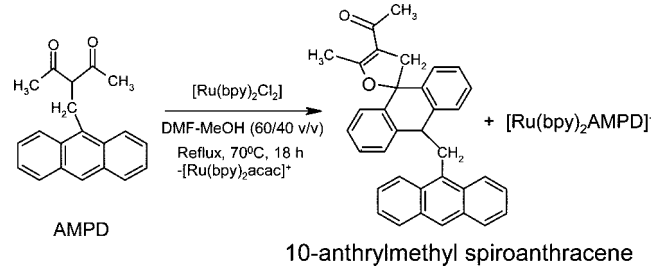


The isolation and characterization of an unusual spiroanthracene, from the reaction of bisdichlororuthenium(II)bipyridine dihydrate with 3-(9-anthrylmethyl)pentane-2,4-dione (AMPD), is reported. This metal-promoted formation of spiroanthracene has been obtained for the first time during the synthesis of metal complexes.

Anthracene derivatives have been investigated for their DNA binding and chemotherapeutic properties. One of the first anthracene derivatives, pseudourea, was tested in clinical trials but was withdrawn due to toxicity.[1,2] Anthracene was shown to be effective against psoriasis,[3] while other anthracene derivatives such as ametantrone, mitoxantrone, and bisantrene were tested for their anticancer activity.[4] These molecules are found to exert their activity by binding to DNA, which may involve groove/electrostatic as well as intercalative binding modes.[5]

SCHEME 1



Our goal is to study how substitution at the C-9 position of the anthryl ring system controls the binding properties of the anthracene derivatives. For example, 9-anthrylmethylammonium chloride (AMAC) binds through intercalation[6] while 9-anthrylpropylammonium chloride (APAC) shows preference for AT-rich regions.[7] The steric, electrostatic, and geometric requirements of the substituents are also expected to influence the DNA binding modes of a given ligand.[8] Kumar et al. have tested the influence of charge and ionic strength on the binding properties of the anthryl ring system, BEDA,[9] which exhibits significant anticancer activity.[10]

During the synthesis of new transition metal heteroleptic complexes in which at least one of the ligands is linked to a fluorophore through a spacer, we have synthesized AMPD,[11] where the anthracene fluorophore is linked to the intercarbonylic carbon atom of 2,4-pentanedione through a spacer at the C-9 position of anthracene. In this note, we report the isolation and characterization of an unusual spiroanthracene from the reaction of bisdichlororuthenium(II)bipyridine dihydrate with 3-(9-anthrylmethyl)pentane-2,4-dione (AMPD) (Scheme 1).

When $[Ru(bpy)_2Cl_2]$ (1 molar equiv) is refluxed for 18 h with AMPD in DMF/methanol (60/40 v/v) at 70 °C, a dark red solution is obtained. The chromatographic separation of this reaction mixture on neutral alumina in acetone solvent yielded a violet compound which gave rectangular crystals on standing at room temperature. The 300 MHz ^{1}H NMR spectrum of the compound in $CDCl_3$ exhibits two sharp singlets at $\delta = 2.29$ and 2.59 ppm due to two methyl groups, a singlet at 3.50 due to the allylic methylene protons, a doublet at 3.92 due to the anthrylmethylene group, and a triplet at $\delta = 3.94$ ppm due to the dibenzylic proton of the spiroanthracene, in addition to the aromatic signal. The emission spectrum (Figure 1) of spiroanthracene in acetonitrile is similar to the spectrum of 9-chloromethylanthracene, indicating that the fluorescence emission is located on the anthrylic group.

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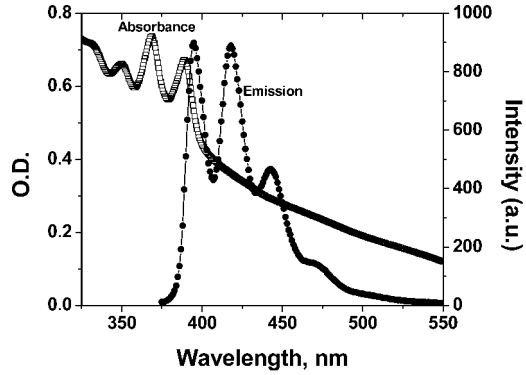


FIGURE 1. Electronic absorption and emission spectrum of 10-anthrylmethyl spiroanthracene in acetonitrile solvent.

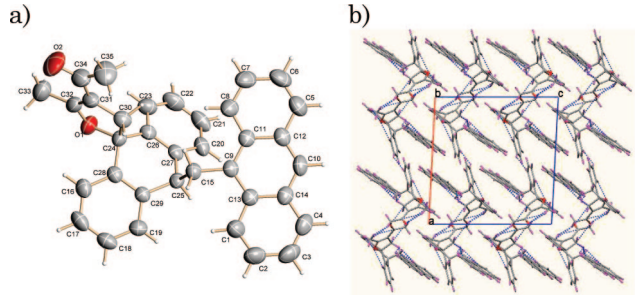


FIGURE 2. (a) ORTEP diagram of the molecule. Ellipsoids are drawn at 50% probability. (b) Crystal packing diagram viewed down the *b* axis.

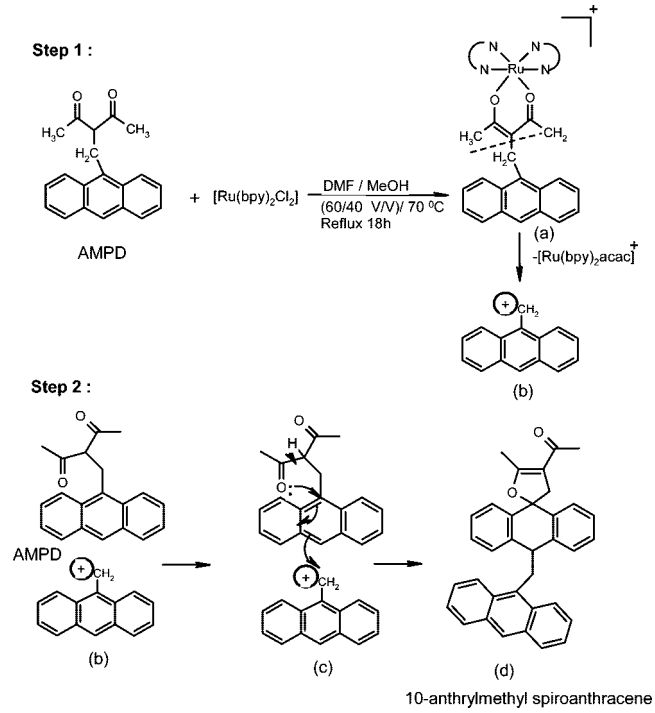
Single crystals of the compound were grown by slow evaporation of the solution in acetone. A violet crystal of approximate size 0.40 × 0.23 × 0.11 mm was used for data collection on a Bruker SMART APEX CCD diffractometer using Mo Kα radiation. All the data were corrected for Lorentzian, polarization, and absorption effects. SHELX-97 (ShelxTL)[12] was used for structure solution and full matrix least-squares refinement on F^2. Hydrogen atoms were included in the refinement as per the riding model. Data collection and refinement parameters are listed in Table S1 (Supporting Information).

X-ray analysis revealed the insertion of oxygen of the pentane 2,4-dione side chain to form a spiroanthracene. The molecules are packed in a zigzag manner when viewed down the *b* axis (Figure 2b).

The molecule has a structure closely related to lepidopterines.[13,14] The presence of the acetylacetone moiety that is cyclized to give rise to the spiroanthracene makes one anthracene ring puckered with a torsion angle C(9)−C(15)−C(25)−C(29) = 159.8(2)°.

When anthracene derivatives with substitution at the C-9 position were reacted in the presence of metal salts/reagents, dimerization of anthracene takes place at the C-9 position, giving rise to different types of dimers, viz. α,α, α,p, or p,p, depending upon the position of attack of either anthrylmethyl radical or anthrylmethyl carbocation. For example, when 9-(halogenomethyl)anthracenes were reacted with Grignard's reagent, the corresponding α,p-dimers were obtained.[15] In the reductive dehalogenation of 9-(iodomethyl)anthracenes in dioxane and in the presence of hydrochloric acid, anhydrous stannous chloride acts as a reducing agent and forms the tetracyclic hydrocarbon, dimethyllepidopterene, by dehalogenative dimerization.[16] Becker et al. have also reported the stannous chloride catalyzed formation of lepidopterenes.[17] During the study of the oxidation of 9-methylanthracene with Cu(II) peroxydisulfate, a dimeric compound identified as lepidopterene was formed.[18]

SCHEME 2. Proposed Reaction Mechanism for the Formation of 10-Anthrylmethyl Spiroanthracene



The isolation of the spiroanthracene promoted by $[Ru(bpy)_2Cl_2]\cdot 2H_2O$ is unprecedented in the literature of anthracene derivatives. Our literature search shows that this type of metal-mediated formation of spiroanthracene derivative as byproduct has been obtained for the first time.

The proposed mechanism (Scheme 2) is based on a mechanism enunciated by Deardurff et al.[18] for the oxidation of 9-methylanthracene with Cu(II) peroxy disulfate, namely, the formation of 9-anthracenylmethyl cation followed by electrophilic attack at the 10 position of a 9-substituted anthracene derivative. In similar way, 9-anthrylmethyl cation is generated during the reaction of AMPD with $[Ru(bpy)_2Cl_2]$. This 9-anthrylmethyl cation formed adds to AMPD, giving rise to 10-anthrylmethyl spiroanthracene. Overall, this is a Friedel–Crafts alkylation-type reaction where, instead of H^+ abstraction, carbocation formation followed by oxygen entrapment results in formation of unprecedented spiroanthracene.

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Experimental Section

AMPD: 3-(9-Anthrylmethyl)pentane-2,4-dione was synthesized according to literature procedure.[11]

10-Anthrylmethyl spiroanthracene (4′-acetyl-10-(9″-anthracenylmethyl)2′,9-spiro-2′3′-dihydrofuranyl-9,10-dihydroanthracene). When $[Ru(bpy)_2Cl_2]$ (0.150 g, 1 molar equiv) is refluxed for 18 h with AMPD (0.085 g) in DMF/methanol (60/40 v/v) at 70 °C, a dark red solution is obtained. The chromatographic separation of this reaction mixture on neutral alumina in acetone solvent yielded a violet compound which gave rectangular crystals on standing at room temperature: yield = 42.85%; mp = 148 °C. Anal. Calcd for $C_{35}H_{28}O_2$: C, 87.4; H, 5.87. Found: C, 87.54; H, 5.82. ^{1}H NMR ($CDCl_3$, room temperature, ppm): δ 2.29 (s, 3H), 2.59 (s, 3H); 3.50 (s, 2H), 3.92 (d, 2H, J = 6.87 Hz), 4.50 (t, 1H, J = 8.2 Hz), 6.70 (d, 2H, J = 7.427 Hz), 6.94 (t, 2H, J = 7.15 Hz), 7.15–7.75 (m, 5H), 7.75–8.20 (m, 5H), 8.20–8.45 (m, 3H). UV–vis (nm, CH_3CN) 332, 350, 369, 389. IR (KBr, cm^{-1}): (υ=CH) 3057, (υCH_3) 2914, (s, υc=o) 1674, (s, υc=c) 1598, (s, υc−o) 1238.

A violet crystal of approximate size 0.40 × 0.23 × 0.11 mm was used for data collection on a Bruker SMART APEX CCD diffractometer using Mo Kα radiation with fine focus tube with 50 kV and 30 mA. Crystal to detector distance = 6.05 cm, 512 × 512 pixels/frame, multiscan data acquisition. Total scans = 4, total frames = 2251, oscillation/frame –0.3°, exposure/frame = 20.0 s/frame, maximum detector swing angle = −30.0°, beam center = (260.2, 252.5), in plane spot width = 1.24, SAINT integration, θ range = 2.31 to 23.50°, completeness to θ of 23.5° is 99.9%. SADABS correction applied, $C_{35}H_{28}O_2$, M = 480.57. Crystals belong to monoclinic, space group $P2_1/c$, a = 15.7130(7), b = 10.6636(5), c = 14.8389(7) Å, β = 92.929(1)°, V = 2483.1(2) Å^3, Z = 4, D_c = 1.286 mg m^{-3}, μ(Mo Kα) = 0.078 mm^{-1}, T = 293(2) K, 19 122 reflections measured, 3681 unique [$I > 2\sigma(I)$], R value 0.0627, $wR2$ = 0.1411.

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Supporting Information Available: Synthesis and characterization, ^{1}H NMR and X-ray crystallographic data (CIF) of 10-anthrylmethyl spiroanthracene. This material is available free of charge via the Internet at http://pubs.acs.org. The crystallographic data have been deposited at the Cambridge Crystallographic Data Centre and allocated the deposition number CCDC 659971.

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