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Indication of Pd-C or Cu-C Intermediate in Respective Bimetallic Nanoclusters Pd/Au-PVP or Cu/Au-PVP Catalyzed Oxidations of *endo*-4-Oxatricyclo[5.2.1.0^{2,6}]-8-decene and Tetrahydro-γ-carbolines

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Abstract

Catalytic oxidations of tricyclic *endo*-norbornene-fused tetrahydrofuran with bimetallic nanoclusters Cu/Au-PVP and H_2O_2 or *t*-BuOOH as an oxidant provided C-H bond oxidation adjacent to the ether function and 4-oxa-tricyclo[5.2.1.0]-8,9-*exo*-epoxydecane (**4**), however, oxidation with Pd/Au-PVP took place at the C=C function giving epoxide **4** and oxidative three-bond forming dimeric product, dodecahydro-1,4:6,9-dimethanodibenzofurano[2,3-b:7,8-b']bisoxolane (**5**). Formation of the latter suggests the involvement of a reactive Pd-C intermediate. Similarly, oxidative C-C bond forming reactions were found in cycloaddition reactions of *N*2-Boc-1,2,3,4-tetrahydro-γ-carbolines and 2,3-dihydroxybenzoic acid with 2 – 5 mol% Cu/Au-PVP and H_2O_2 at 25 °C, providing two-bond-forming [4+2] cycloadducts. Under similar reaction conditions, Pd/Au-PVP did not produce the cycloadduct, indicating a need of complexation between Cu with the carboxylic acid group of 2,3-dihydroxybenzoic acid and allylic amine function of γ-carbolines in the cyclization reaction. The reported intermolecular coupling reactions using Pd/Au-PVP or Cu/Au-PVP nanocluster catalysts under oxidative conditions at 25 °C are unprecedented.

Graphical Abstract

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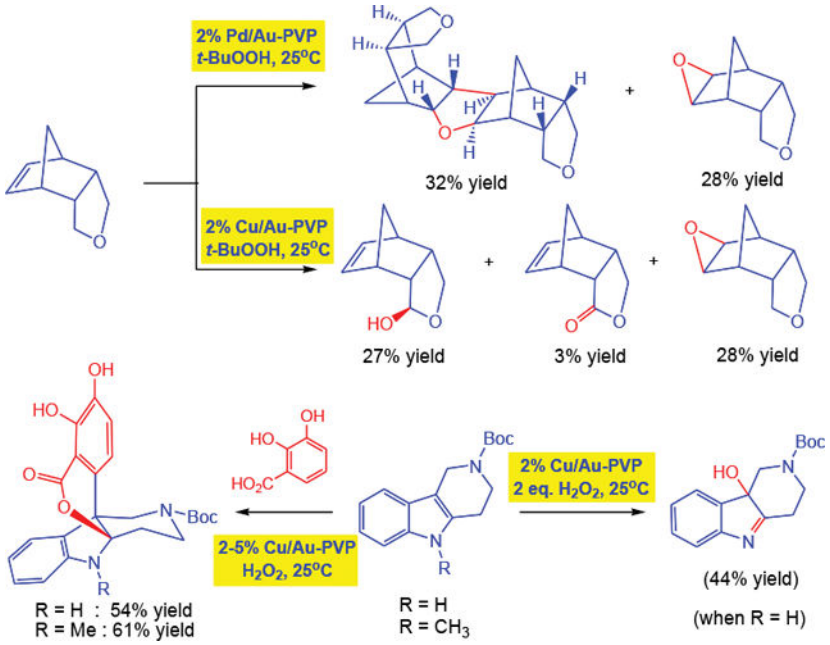

Keywords

Bimetallic Cu/Au-PVP and Pd/Au-PVP nanoclusters; catalytic C-H oxidation; oxidative C-C bond formation

The development of catalytic C-H functionalization for the formation of C-C and C-heteroatom bond has exceled rapidly in the last few decades.[1] Oxidations of C-H and C=C bonds to form C-O and C-C bonds using polymer stabilized bimetallic nanoclusters are limited.[2] Notably, indication of the formation of Pd-C or Cu-C intermediate in the bimetallic nanoclusters catalyzed oxidative functionalization of unactivated C-H bond may shed light onto the mechanism and synthetic applications.

Norbornene has been shown to form Pd-O bond[3] and Pd-C bond,[4] while C-H bond adjacent to heteroatoms, such as oxygen, have lower bond-dissociation energy, ~95 kcal/mol, and thereby is prone to oxidation.[5] We examined initially the oxidation of tricyclic norbornene-fused tetrahydrofuran **1** and its saturated norbornane analog **6** (Scheme 1) and compared the catalytic reactivity of bimetallic nanoclusters Cu/Au-PVP and Pd/Au-PVP using hydrogen peroxide or *t*-butyl hydroperoxide as an oxidant. Due to our unusual discovery of C-C and C-O bond formation in these catalytic reactions, oxidative bimolecular couplings of 1,2,3,4-tetrahydro-γ-carbolines and 2,3-dihydroxybenzoic acid in the presence of aforementioned catalysts and oxidant were pursued.

Polyvinylpyrrolidone (PVP), used as a stabilizer for nanoclusters,[6] is made from the polymerization of *N*-vinylpyrrolidinone and used in food, pharmaceutical and material industries. It is low cost and available in different molecular weights. After testing different lengths, PVP having molecular weight of ~40,000 is suitable for the stabilization of bimetallic nanoclusters Cu/Au or Pd/Au.[2a] Consequently, it was selected for our studies

in search of bimolecular coupling reactions. Bimetallic nanoclusters Cu/Au (3:1)-PVP were prepared by the treatment of a mixture of 3 equiv. of CuCl, 1 equiv. of $HAuCl_4•3H_2O$, and 0.11 equiv. of PVP (MW 40,000) in H_2O with 7 equiv. of $NaBH_4$ in 25 °C for 2 h.[2a] Similarly, Pd/Au (3:1)-PVP was prepared from the reaction of 3 equiv. of Na_2PdCl_4, 1 equiv. of $HAuCl_4•3H_2O$, 0.11 equiv. of PVP (MW 40,000) and 10 equiv. of $NaBH_4$ in H_2O at 25 °C.[2c] Different concentrations can be used in the preparations, and a final concentration of either 10 mM or 25 mM was prepared. *N,N*-Dimethylformamide (DMF) is also suitable to be used as a solvent in place of H_2O, and a 25-mM concentration of bimetallic nanoclusters in DMF was prepared. The ratio of 3:1 for Cu/Au and Pd/Au provided higher reactivity than other ratios such as 2:1 and 1:1. It was found that higher concentration of the reaction solution, greater the reaction rate. Monometallic nanoclusters Cu, Pd, or Au alone did not provide the same reactivity as those derived from bimetallic nanoclusters.[2a]

Tricylic norbornene-fused tetrahydrofuran **1** possesses ring strain,[7] angle strain, and a cyclic ether. Its lactone derivative, **3**, has been used in the synthesis of vasoactive lipid prostanoids,[8] whose biosynthesis originates from cyclooxygenases 1 and 2.[9] The catalytic oxidation of **1** using bimetallic nanoclusters may reveal the chemo-, regio-, and stereo-selectivity and future utilization of the catalysts.

Compound **1** was prepared by modification of a reported procedure[10] starting from carbic anhydride *via* a reduction with lithium aluminum hydride in THF followed by ring closure with *p*-toluenesulfonyl chloride and pyridine. Hydrogenation of **1** with a catalytic amount of 5% Pd/C under 30 psi. of hydrogen in methanol gave compound **6**, which was used as a substrate for comparison of results from the oxidation of **1**. When norbornene **1** was treated with 2 mol% of Cu/Au-PVP and 2 equiv. of 30% H_2O_2 in water and acetonitrile at 25 °C for 3 days, *exo*-lactol **2** (4% yield) and lactone **3** (2% yield) were isolated along with unreacted **1** (88% recovery) (Scheme 1). The reaction has a low reaction rate and apparently C-H oxidation took place at the α-carbon adjacent to the ether function, due to its low C-H bond dissociation energy, ~93 kcal/mol. Results reveal that the double bond of norbornene **1** is unreactive under the reaction conditions and this is unusual in light of high reactivity of the alkene function of norbornene under copper-metal-organic frameworks (Cu-MOFs) catalyzed oxidation conditions,[11] in which the epoxide was the major product. When a more reactive oxidant, *t*-butyl hydroperoxide, 1.2 equiv., was used in place of hydrogen peroxide in the aforementioned 2 mol% Cu/Au-PVP catalytic oxidation reaction, yields of *exo*-lactol **2** and lactone **3** increased to 18% and 9%, respectively. In addition, epoxide **4** was isolated in a 32% yield along with a 14% recovery of **1**. An increase amount of *t*-BuOOH to 2.5 equiv. under similar reaction conditions gave a 27% yield of lactol **2**, 3% yield of lactone **3**, and 28% yield of epoxide **4** along with 25% recovery of **1**. The ^1H and ^{13}C NMR spectral data of compounds **2**,[8] **3**[12] and **4**[13] are in agreement with those reported.

Possibly, in the presence of *t*-BuOOH, epoxide **4** formed by a fragmentation pathway (*vide infra*) differing from that in the Cu-Au-PVP and H_2O_2 system, where only C-H oxidation was found. The stereochemistry at C3 of *exo*-lactol **2** was characterized by comparison of its NMR data with that reported.[8] The oxidation of *exo*-lactol **2** to lactone **3** under the Cu/Au-PVP reaction conditions was sluggish likely due to shielding of the *endo*-oriented lactol C-H by π-electrons of the alkene moiety of norbornene ring. The *endo* C-H is required to be

removed by a base or Lewis base for the oxidation. The pH value of the Cu/Au-PVP in H_2O is ~5.6, weakly acidic.

We were intrigued whether different catalyst systems, such as Pd/Au-PVP and H_2O_2 or *t*-BuOOH would give different product(s) based on the complexation of norbornene with Pd.[3] Surprisingly, oxidation of **1** with 2 mol% Pd/Au-PVP and 4 equiv. of 30% H_2O_2 in acetonitrile-water at 25 °C for 6 days gave epoxide **4** (28% yield) and a dimeric product, norbornane-tetrahydrofuran **5** in a 32% yield along with 5% recovery of **1** (Scheme 1). The structure of **5** was characterized by a single-crystal X-ray analysis and depicted in Figure 1, showing two units of norbornane join together to form a tetrahydrofuran ring by one C-C bond and two C-O bonds, i.e., **5** derived from a three-bond forming reaction. Two methylene bridges of the two norbornane units of **5** are opposite to each other and the C-C bond and two C-O bonds orient at the *exo* face in each of the two norbornane units. The use of 1.2 equiv. of *t*-BuOOH as an oxidant under similar reaction conditions gave similar amounts of epoxide **4** (22% yield) and **5** (31% yield) along with 21% recovery of **1**. Lactol **2** and lactone **3** were not found, revealing that the relative reaction rate of C-H oxidation is slow comparing with the oxidation of C=C, that is, a different reaction pathway occurs with Pd/Au-PVP system. Moreover, treatment of one equiv. each of **1** and **4** along with 5 mol% of Pd/Au-PVP at 25 °C for 2 days and 50 °C for 1 day in the absence of an oxidant gave only recovered starting materials and no dimer **5** was found. Results suggest **5** does not form from the reaction of norbornene **1** and epoxide **4**.

Norbornane-fused tetrahydrofuran **6**, an analog of **1** without a double bond, was used for comparison. As expected, C-H bond oxidation of **6** with 5 mol% Pd/Au-PVP and 5 equiv. of 30% H_2O_2 was sluggish at 25 °C. Upon stirring for three days, reactions proceeded gradually and gave **7** and **8** in 2% and 1% yield, respectively, along with 91% recovery of **6**. Similar results were found when or 3 equiv. of *t*-BuOOH was used instead of H_2O_2, yielding **7** and **8** in 9% and 3%, respectively, as well as 78% recovery of **6**. On the other hand, oxidation of norbornane **6** with 5 mol% of Cu/Au (3:1)-PVP and 15 equiv. of 30% H_2O_2 in acetonitrile-H_2O (1:1) at 25 °C for 20 h gave a 4% yield of *exo*-lactol **7** and 50% yield of lactone **8** along with a 17% recovery of **6** (Scheme 1). The spectral data of molecules **7**[8] and **8**[14] are in agreement with those reported. A greater conversion was found when *t*-BuOOH was used as an oxidant in the Cu/Au-PVP (2.5 mol%) catalyzed oxidation reaction of **6** at 50 °C for 12 h. Respective *Exo*-lactol **7** and lactone **8** were isolated in 53% and 16% yield along with a 13% recovery of **6**. At room temperature, only ~15% of **6** was reacted after 24 h based on analysis of ^{1}H NMR spectrum of an aliquot from the reaction mixture. The stereochemistry at C3 of lactol **7** was supported by a 2D NOESY (nuclear Overhauser effect spectroscopy), where C3-H at δ 5.37 ppm did not correlate with C2 and C6-H's at ~ δ 2.44 – 2.65 ppm, but correlated with C8 and C9-H's at ~ δ 1.25 – 1.50 ppm, and C1-H at δ 2.34 – 2.37 ppm. Results of C-H oxidation are similar to that from the oxidation of **1** (*vide supra*). Hence, Cu/Au-PVP-H_2O_2 provided greater yields in C-H oxidation reactions, while Pd/Au-PVP-H_2O_2 or -*t*-BuOOH prefers to react with the olefin function.

Information of the single-crystal X-ray structural analysis of molecule **5** is summarized in Table 1, including its formulas, crystal data, method of collection, and method of

structure solution and refinement. The X-ray structure has been deposited at The Cambridge Crystallographic Data Centre and details of the data collection and structural solution and refinement are described in the Supporting Information (SI).

Next, we examined whether the dimeric species could be formed from the oxidation of an amide analog of norborene tetrahydrofuran **1**. Hence, *N*-acetyl tricyclic pyrrolidine **9**, was treated under similar reaction conditions with 2 mol% of Cu/Au-PVP and 8 equiv. of *t*-BuOOH at room temperature for 24 h, α-C-H oxidation of pyrrolidine ring product **10** (27% yield), epoxide **11** (9% yield), and α-*t*-butoxy epoxide **12** (18% yield) were isolated along with a 14% recovery of **9** (Scheme 2). No dimeric species was detected. Several oxidants have been reported for the oxidation of amide α-carbon,[15] but catalytic oxidation of amides with bimetallic nanoclusters has not appeared previously. Under the reaction conditions, the relative rates of formation of α-C-H oxidation and alkene epoxidation are similar. Product **12** is likely derived from the oxidation of **10** or/and **11**. Similar to the oxidation of **1**, the use of catalyst Cu/Au-PVP and 30% H_2O_2 in the oxidation of **9** was sluggish and gave no identifiable oxidized products. Astonishingly, oxidation of **9** with 5 mol% Pd/Au-PVP and *t*-BuOOH at room temperature gave α-*t*-butoxy pyrrolidine **10** (13% yield), epoxide **11** (18% yield), **12** (5% yield) and 2-*endo*-carboxylic lactone **13** (2% yield) along with 13% recovery of **9**. No dimeric furan was found. Similar to the finding in oxidation of **1**, Cu/Au-PVP is more reactive than Pd/Au-PVP in C-H oxidation reactions. ^{1}H NMR spectra of compounds **10** and **12** indicate an inseparable mixture of C2-*exo* (or β; S* configuration) and C2-*endo* (or α; R* configuration) isomers in a ratio of ~9:1. The stereochemistry of major isomer, C2-*exo*, of **10** was supported by 2D NOESY NMR spectroscopy, in which C2-*endo* hydrogen at δ 5.14 ppm showed correlations with C4 hydrogen at δ 3.09 ppm and with C3 hydrogen at δ 2.90 ppm (see SI for 2D NOESY spectrum). No correlations were found between C2-*endo* hydrogen with C8-*exo* hydrogen at δ 2.85 – 2.82 ppm. The structures of epoxide **11** and lactone **13** were firmly characterized by single-crystal X-ray analyses. The molecular structures and their selective bond lengths and angles are listed in Figures 2 and 3, and characterization data are summarized in Table 1. The formation of lactone **13** may derive from α-hydroxylation of **11** followed by opening of the lactol ring and oxidation of the resulting aldehyde to carboxylic acid. The acid subsequently attacks C6,C7-epoxide moiety, resulting in β-hydroxy-lactone **13**. The absence of the corresponding dimeric furan product in *N*-acetyl tricyclic pyrrolidine **9** suggests the rate of formation of epoxide is faster than that of the bimolecular reaction involving the addition of Pd-C species to an alkene as described in the proposed mechanism (*vide infra*).

The reactive alkene function of indole core of tetrahydro-γ-carbolines[16] and their potent histone deacetylase 6 inhibition[17] led us to investigate the oxidation of *N*2-Boc-1,2,3,4-tetrahydro-γ-carboline (**14**), searching for the possible existence of Pd-C or Cu-C intermediate. Oxidation of **14** with 2 mol% of Cu/Au-PVP and 2 equiv. of 30% H_2O_2 in acetonitrile and water at 25 °C for 16 h gave the 4a-hydroxyl product **15** (44% yield; Scheme 3), as a mixture of two rotamers, deriving from the relative stereochemistry between the C4a-hydroxyl and *N*3-Boc groups. No corresponding dimeric furan was found. The structure of **15** was characterized by its HRMS, ^{1}H and ^{13}C NMR, 2D COSY, 2D NOESY, and 2D HSQC. Furthermore, removal of the Boc group with trifluoroacetic acid (TFA) in

CH_2Cl_2 at 25 °C gave a single stereoisomer **16** in an 87% yield. The ^{13}C NMR signals at δ 200.3 and 204.1 ppm are assigned for the C=N group of **15** and **16**, respectively, and the chemical shifts are in agreement with that reported.[18] The formation of **15** may derive from a β-elimination of an adduct intermediate, resulting from the addition of HO group onto C4a and Cu onto C9a. The β-elimination consists of the exclusion of C9a-Cu and *N*9-H.

Based on the aforementioned observation, we investigated the bimolecular coupling reaction of **14** and 2,3-dihydroxybenzoic acid (**18**). To our delight, treatment of **14** with an equimolar **18**, 5 mol% of Cu/Au-PVP, and 1.2 equiv. of 30% hydrogen peroxide at 25 °C for 24 h, afforded a 54% yield of a [4+2] cycloadduct, **19**,[16a] along with a 26% recovery of **14** (Scheme 3). Besides 1D and 2D NMR and HRMS analyses, the structure of **19** was also confirmed by a single-crystal X-ray analysis (Figure 4). X-ray structural analysis information of molecule **19** is summarized in Table 2. A decrease amount of Cu/Au-PVP catalyst to 0.5 mol% and increase 30% H_2O_2 to 2 equiv. gave 48% yield of **19** and 22% yield of alcohol **16** along with 20% recovery of **14**. Hence, a lesser amount of catalyst and greater amount of oxidant appear to diminish the formation of bimolecular product and increase the oxidation of the indole ring. When the methyl ester of **18** was used in the oxidation reaction, under similar reaction conditions, no cycloadduct **19** was found, and only starting materials **14** and methyl 2,3-dihydroxybenzoate along with a small amount of compound **15** were isolated. Significantly, when *N*9-methyl-*N*2-Boc-1,2,3,4-tetrahydro-γ-carboline (**17**) and **18** were subjected to 2 mol% of Cu/Au-PVP and 3 equiv. of 30% H_2O_2 in DMF at 25 °C for 24 h, the corresponding [4+2] cycloadduct **20** was isolated in a 61% yield along with 6% of **17** recovered. Cycloaddition of *N*-alkyl β-carbolines such as **17** has not been reported previously, which may provide synthetic routes leading to complex multi-ring alkaloids, such as voacalgines.[16b] Results suggest that formations of **19** or **20**, derived from a two-bond forming reaction, under the catalytic oxidation with H_2O_2 likely does not involve free-radical species as reported in iron(II) phthalocyanine catalyst and *t*-BuOOH, requiring a NH moiety in the indole ring.[16a] Since Cu possesses a high affinity to the carboxylic acid group, our finding implies that Cu/Au-PVP nanoparticles complex with the pair of electrons on nitrogen-9 of **14** or **17** and the carboxylic acid moiety of **18** followed by oxidation of the two hydroxyl groups of the catechol ring to form *ortho* quinone group by Cu/Au-PVP-H_2O_2,[19] and subsequent formation of C11b-C4b bond, through a nucleophilic addition reaction, as suggested in structure **21** (Scheme 3). An attack from the carboxylate oxygen onto C6a-N7 imino-double bond and aromatization *via* C4b-hydrogen shift and protonation leads to **19** or **20**. The catalytic reactions are efficient and the one-to-one cycloadduct **19** or **20** was the predominant product. The reaction hints a possible formation of Cu-C11b bond, from a resonance structure of **21**, in the joining of C11b and C4b bond. Noteworthy, catalytic oxidation of **14** and **18** with 4 mol% Pd/Au-PVP in DMF at 25 °C over 2 days gave only recovered starting material **14** and no [4+2] cycloadduct **19**, suggesting the absence of or a weak complexation of Pd-Au and the carboxylic acid group of **18**, diminishes the cycloadduct formation. γ-Carboline **14** was made from a Fischer indole synthesis via the coupling of phenylhydrazine and *N*-Boc-4-piperidone, and **17** was made from alkylation of **14** with NaH and methyl iodide in THF (see Experimental Section).

A mechanism for the formation of **2** is proposed in Scheme 4, left panel.[20] Oxidation of Cu/Au-PVP by H_2O_2 or *t*-BuOOH gives (PVP)-Au/Cu^{II}=O (**I**) and H_2O or *t*-BuOH. Complex **I** abstracts an *exo*-hydrogen from α-carbon of the ether moiety of **1**, resulting in HO-Cu^{I} intermediate **II**, complexing with the carbon radical, or C-Cu^{II}-(OH) complex **III**. The complex undergoes hydroxyl group migration from Cu to C afforded **2**. Alternatively, reductive elimination in complex **III** provides **2** and Cu/Au-PVP. The formation of **II** or **III** may also involve (HO)Cu^{II}(OH)/Au-(PVP) reactive species,[2a] which undergoes hydrogen atom abstraction from C-H adjacent to the ether group. The resulting carbon intermediate extracts a hydroxyl group from H_2O_2 or •Cu^{I}(OH)/Au-(PVP). Mechanisms for the formations of **4** and **5** are suggested in Scheme 4, right panel.[3] Oxidation of 2 equiv. of Pd/Au-PVP by H_2O_2 or *t*-BuOOH gives 2 equiv. of (PVP)-(Au)-Pd^{I}-OH **IV** and H_2O or *t*-BuOH. Complex **IV** coordinates to the alkene function of **1** and proceeds *exo*-addition, affording in 8-hydroxy-9-palladium intermediate **V**.[3a,b] It can proceed by either fragmentation[3c] to give epoxide **4** or by a *cis-exo* addition onto the alkene function of another molecule **1** to give oxopalladacyclohexane **VI**. Complex **VI** undergoes reductive elimination[3a] to furnish furan dimer **5** and regenerates Pd/Au-PVP. The formation of **5** is concentration dependence, in that at lower reaction concentrations, lesser amounts of **5** formed. Noteworthy, the oxidation reactions took place at room temperature implying the reactions require relatively low activation energies and may be applicable to the synthesis of other heterocyclic systems.

In summary, catalytic oxidation reactions of *endo*-norbornene-fused tetrahydrofuran **1** and *endo*-norbornane-fused tetrahydrofuran **6** separately with Cu/Au-PVP or Pd/Au-PVP using either H_2O_2 or *t*-BuOOH as an oxidant were carried out. Only C-H bond adjacent to the ether group was oxidized by Cu/Au-PVP and H_2O_2, while the use of *t*-BuOOH gave both C-H bond oxidation α to the ether function and epoxidation of the alkene function. In contrary, Pd/Au-PVP and H_2O_2 or *t*-BuOOH produced the epoxide and dimeric norbornane-tetrahydrofuran **5** as the major products. These contrasting results suggest that Cu/Au system prefers C-H bond oxidation and Pd/Au system favors oxidation of the alkene function. Notably, the formation of coupling product **5** suggests the presence of a reactive intermediate containing a Pd-C bond. Oxidation of norbornane-fused tetrahydrofuran **6** with Cu/Au-PVP and H_2O_2 or *t*-BuOOH gave higher yields of the corresponding lactol and lactone than those with Pd/Au-PVP and H_2O_2 or *t*-BuOOH, supporting the aforementioned finding that Cu/Au-PVP favors C-H oxidation reactions. Hydrogen peroxide, a weak oxidant, was ineffective in the oxidation of *N*-acetyl tricyclic norbornenyl pyrrolidine **9** with either Cu/Au-PVP or Pd/Au-PVP, while the use of *t*-BuOOH produced oxidation of α-CH bond of the amide function along with the epoxidation of the alkene function. The presence of metal-C bond was further revealed in the oxidations of tetrahydro-γ-carbolines **14** and **17**. In the absence of 2,3-dihydroxybenzoic acid (**18**), reaction of **14** with Cu/Au-PVP catalyst and H_2O_2 at 25 °C led to the oxidation on the alkene function of the indole ring, resulting C4a-hydroxy-carboline **15**. On the other hand, in the presence of **18**, one-to-one cycloadducts, **19** and **20**, were produced, suggesting the presence of a Cu-C reactive intermediate. The discovered bimolecular coupling reactions may provide mild and simple methods for the synthesis of bioactive and structurally complex heterocycles.

Chemicals Na_2PdCl_4, CuCl, carbic anhydride, and 4-piperidone hydrochloride were purchased from Fisher Scientifics and tetrachloroauric (III) acid•trihydrate ($HAuCl_4•3H_2O$) purchased from VWR Int. ^1H NMR (400 and 600 MHz) and ^{13}C NMR (100 and 150 MHz) spectra were obtained from a Bruker Avance Neo 400-MHz NMR and a 600-Mz Bruker NMR spectrometers, and were measured from a solution in $CDCl_3$ unless otherwise mentioned. The chemical shift data reported in ^1H NMR are given in units of δ relative to TMS (δ = 0) or $CHCl_3$ (δ = 7.26 ppm). For ^{13}C NMR spectra, the chemical shifts are recorded relative to $CDCl_3$ (δ = 77.0 ppm). Low-resolution mass spectra were taken from a Waters Acquity TQD Ultra Performance LC/MS/MS system. High-resolution mass spectra were obtained using a LCT Premier time of flight mass spectrometer (Waters Inc.). All solvents distilled over appropriated drying agent such as CaH_2 for DMF, dichloromethane and acetonitrile, or Na/benzophenone for THF and diethyl ether. Flash column chromatography was carried out on silica gel (400 mesh) for purification of organic products. Single-crystal X-ray structures were obtained from a Siemens SMART 1000 low-temperature (LT-2A) and a Rigaku XtaLAB Synergy-S single-crystal X-ray diffractometers.

Preparation of bimetallic nanoclusters Cu/Au (3:1)-PVP and Pd/Au (3:1)-PVP in H_2O or DMF.

A solution of 29.5 mg (0.075 mmol) of $HAuCl_4.3H_2O$, 22.2 mg (0.225 mmol) of CuCl and 0.33 g (8.25 μmol) of PVP (MW 40,000) in 12 mL of deionized water was treated with 20 mg (0.525 mmol) of sodium borohydride. The solution was stirred at room temperature for 2 h resulting a 25 mM Cu/Au (3:1)-PVP in water. By replacing deionized water with 12 mL of distilled DMF, a 25 mM Cu/Au-PVP in DMF was obtained.

Following a similar procedure, reduction of a solution of 29.5 mg (0.075 mmol) of $HAuCl_4.3H_2O$, 66 mg (0.225 mmol) of Na_2PdCl_4 and 0.33 g (8.25 μmol) of PVP (MW 40,000) in 12 mL of deionized water with 28.5 mg (0.75 mmol) of $NaBH_4$ stirring at 25 °C for 2 h gave a 25 mM Pd/Au (3:1)-PVP in water. Replacing H_2O with 12 mL of DMF in the aforementioned reaction gave a 25 mM Pd/Au-PVP in DMF solution. Solutions of Cu/Au-PVP and Pd/Au-PVP catalysts can be stored for several weeks in a refrigerator without observable decrease of reactivity.

endo-4-Oxatricyclo[5.2.1.$0^{2,6}$]-8-decene (1).

To a mixture of 2.46 g (15 mmol) of carbic anhydride in 30 mL of THF under argon was added 1.2 g (31.9 mmol) of $LiAlH_4$ at 0 °C in three portions. The mixture was stirred at 25 °C for 8 h, diluted with aqueous 1N NaOH slowly, then 50 mL of ethyl acetate, filtered through a layer of Celite, and washed several times with ethyl acetate. The filtrate was washed with water and brine, dried ($MgSO_4$), concentrated to give 1.72 g (74% yield) of *endo*-(5,6-dihydroxymethyl)bicyclo[2.2.1]-2-decene, which was used in the subsequent reaction without purification. To a solution of 6.0 g (44 mmol) of *endo*-(5,6-dihydroxymethyl)bicyclo[2.2.1]-2-decene, 12 mL of pyiridine in 30 mL of dichloromethane under argon was added 7.56 g (39.7 mmol) of *p*-toluenesulfonyl chloride. The mixture was stirred at 25 °C for 24 h, diluted with 50 mL of water, and extracted three times with diethyl ether. The combined extract was washed with water and brine, dried ($MgSO_4$),

distilled under normal pressure to remove solvents, and column chromatographed on silica gel using a gradient mixture of pentane and diethyl ether as eluent to give compound **1**. Note: compound **1** vaporizes under reduced pressure and should be stored in a refrigerator.

Yield: 3.76 g (63% yield); white solid; mp 80 – 81 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.23 (s, 2H, =CH), 3.63 – 3.57 (m, 2H, CH_2O), 3.46 (dd, *J* = 8.8, 2 Hz, 2H, CH_2O), 2.94 – 2.85 (m, 4H, CH-C= and C10-Hs), 1.55 (d, *J* = 8 Hz, 1H, C10-H), 1.46 (d, *J* = 8 Hz, 1H, C10-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 135.0 (2C), 70.0 (2C), 52.6 (1C), 47.9 (2C), 45.8 (2C). The spectral data is in agreement with that reported.[21]

MS (ESI, MeOH): m/z (%)= 137.19 ($M + H^+$, 100).

endo-4-Oxatricyclo[5.2.1.0^{2,6}]-decane (6).

A mixture of 2.04 g (15 mmol) of compound **1** and 100 mg of 5% Pd/C in 50 mL of methanol was shaken in a hydrogenator under 30 psi of H_2 at 25 °C for 20 h. It was removed from the hydrogenator, filtered through a pad of Celite, and the solids were washed several times with diethyl ether. The filtrate was distilled under normal pressure to remove the solvents and dried under reduced pressure for few minutes to give compound **6**, which was used in the subsequent oxidation reactions without purification.

Yield: 1.80 g (87% yield); white solid; 113 – 114 °C (Lit.[22] 109 – 110 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.88 (d, *J* = 9.6 Hz, 2H, CH_2O), 3.40 – 3.35 (m, 2H, CH_2O), 2.55 – 2.49 (m, 2H), 2.21 – 2.18 (m, 2H), 1.60 – 1.43 (m, 4H), 1.32 – 1.26 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 68.9, 45.9, 42.5, 40.6, 23.1.

MS (ESI, MeOH): m/z (%) = 139.22 ($M + H^+$, 100).

Oxidation of *endo*-4-oxatricyclo[5.2.1.0^{2,6}]-8-decene (1) with Cu/Au-PVP and H_2O_2. Formation of 3-*exo*-hydroxy-*endo*-4-oxatricyclo[5.2.1.0^{2,6}]-8-decene (2) and 3-oxo-*endo*-4-oxatricyclo[5.2.1.0^{2,6}]-8-decene (3).

To a solution of 100 mg (0.73 mmol) of **1** in 0.75 mL of acetonitrile, were added an aqueous solution of 0.6 mL (0.015 mmol; 2 mol%) of Cu/Au (3:1)-PVP (25 mM in water) and 0.15 mL (1.47 mmol; 2 equiv.) of 30% H_2O_2. The solution was stirred at 25 °C for 3 days, diluted with aqueous $Na_2S_2O_5$, and extracted with diethyl ether three times. The combined extracts were washed with water and brine, dried (anh. Na_2SO_4), concentrated by normal distillation, and column chromatographed on silica gel to give lactol **2** and lactone **3** along with recovered **1**.

Yields: **2**: 4.4 mg (4% yield); **3**: 2.2 mg (2% yield); recovery of **1**: 88 mg (88%).

Compound **2**:

White crystal, mp 103–104 °C

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.20 (dd, *J* = 5.6, 2.8 Hz, 1H, =CH), 6.09 (dd, *J* = 5.6, 2.8 Hz, 1H, =CH), 4.99 (d, *J* = 2.4 Hz, 1H, OCHO), 3.97 (dd, *J* = 9, 7.6 Hz, 1H, CHO), 3.46 (dd, *J* = 9, 2 Hz, 1H, CHO), 3.05 – 2.82 (m, 4H), 2.16 (s, 1H, OH), 1.45 (d, *J* = 8 Hz, 1H, C10-H), 1.36 (d, *J* = 8 Hz, 1H, C10-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 134.7 (=C), 134.4 (C=), 100.4 (O-C-O), 69.3 (C-O), 55.5, 51.9, 46.0, 45.8, 44.9.

MS (ESI, MeOH): m/z (%) = 153.10 ($M + H^+$, 100).

The spectral data of **2** are in agreement with that reported.[8]Compound **3**:

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.35 – 6.26 (m, 2H, CH=CH), 4.31 (dd, *J* = 10, 8.8 Hz, 1H, CHO), 3.82 (dd, *J* = 10, 3.2 Hz, 1H, CHO), 3.38 – 3.34 (m, 1H), 3.28 (dd, *J* = 9.2, 4.4 Hz, 1H), 3.16 – 3.08 (m, 2H), 1.67 (d, *J* = 8.4 Hz, 1H, C10-H), 1.49 (d, *J* = 8.4 Hz, 1H, C10-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.1 (C=O), 137.0 (C=), 134.4 (C=), 70.3 (C-O), 51.9, 47.6, 46.2, 45.8, 40.3.

MS (ESI, MeOH): m/z (%) = 151.18 ($M + H^+$, 80).

The spectral data of **3** are in agreement with that reported.[12]

(1) Under similar reaction conditions, oxidation of 100 mg (0.73 mmol) of **1** in 0.7 mL of acetonitrile with 0.6 mL (0.015 mmol; 2 mol%) of Cu/Au-PVP (25 mM in H_2O) and 0.12 mL (0.88 mmol; 1.2 equiv.) of *t*-BuOOH (70% in water) at 25 °C for 3 days gave 20 mg (18% yield) of lactol **2**, 9.8 mg (9% yield) of lactone **3**, and 35.5 mg (32% yield) of epoxide **4** along with 14 mg (14% recovery) of **1**. (2) Oxidation of 100 mg (0.73 mmol) of **1** in 0.7 mL of acetonitrile with 0.6 mL (0.015 mmol; 2 mol%) of Cu/Au-PVP (25 mM in H_2O) and 0.25 mL (1.83 mmol; 2.5 equiv.) of *t*-BuOOH (70% in water) at 25 °C for 1.5 days gave 30 mg (27% yield) of lactol **2**, 3.3 mg (3% yield) of lactone **3**, and 31 mg (28% yield) of epoxide **4** along with 25 mg (25% recovery) of **1**.

Oxidation of *endo*-4-oxatricyclo[5.2.1.0^{2,6}]-8-decene (1) with Pd/Au-PVP and H_2O_2. Formation of 4-oxa-tricyclo[5.2.1.0]-8,9-*exo*-epoxydecane (4) and dodecahydro-1,4:6,9-dimethanodibenzofurano[2,3-b:7,8-b']bisoxolane (5).

To a solution of 100 mg (0.73 mmol) of **1** in 0.75 mL of acetonitrile, were added 0.6 mL (0.015 mmol; 2 mol%) of an aqueous solution of Pd/Au (3:1)-PVP (25 mM in H_2O) and 0.33 mL (2.92 mmol; 4 equiv.) of 30% H_2O_2. The solution was stirred at 25 °C for 6 days, and diluted with 1 mL of aqueous $Na_2S_2O_5$. The mixture was extracted with ethyl acetate three times and the combined extract was washed with water and brine, dried (anhydrous Na_2SO_4), concentrated and column chromatography on silica gel using a gradient mixture

of pentane and diethyl ether to give epoxide **4** and dimeric tetrahydrofuran **5**, as well as recovered **1** (5 mg; 5% recovery).

Compound **4**:

Yield: 31 mg (28% yield); an oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.95 (d, *J* = 10.4 Hz, 2H, CH_2O), 3.44 (dd, *J* = 10.4, 6.8 Hz, 2H, CH_2O), 3.27 (s, 2H, 2 x CH-O), 2.73 – 2.65 (m, 2H), 2.58 – 2.51 (m, 2H), 1.46 (d, *J* = 10 Hz, 1H), 0.84 (d, *J* = 10 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 68.2 (2C, C-O), 49.5 (2C, C-O epoxide), 46.2 (2C), 39.8 (2C), 29.6 (1C).

MS (ESI, MeOH): m/z (%) = 152.899 ($M + H^+$; 50).

Spectral data of **4** is in agreement with that reported.[13]

Compound **5**: mp 180–182 °C.

Yield: 34 mg (32% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.25 (d, *J* = 6.4 Hz, 2H, CHO), 3.90 (dd, *J* = 17.2, 9.6 Hz, 4H, CH_2O), 3.32 (ddd, *J* = 17.2, 10, 6.8 Hz, 4H, CH_2O), 2.55 – 2.41 (m, 4H), 2.25 (d, *J* = 4.8 Hz, 2H), 2.16 – 2.06 (m, 4H), 1.60 (d, *J* = 12.4 Hz, 2H), 1.26 (dt, *J* = 12.4, 2 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 84.8 (2C, CHO), 68.8 (2C, CH_2O), 68.2 (2C, CH_2O), 49.0 (2C), 47.1 (2C), 46.2 (2C), 44.6 (2C), 43.7 (2C), 37.3 (2C).

MS (ESI, MeOH): m/z (%) = 289.117 ($M + H^+$, 30), 311.177 ($M+Na^+$, 100).

HRMS-ESI: m/z $[M + H]^+$ calcd for $C_{18}H_{25}O_3^+$: 289.1798, found: 289.1801.

The compound crystallized from diethyl ether to give single crystals, whose structure was solved by X-ray analysis.

Under similar reaction conditions, oxidation of 100 mg (0.73 mmol) of **1** in 0.7 mL of acetonitrile with 0.6 mL (0.015 mmol; 2 mol%) of Pd/Au-PVP (25 mM in H_2O) and 0.12 mL (0.88 mmol; 1.2 equiv.) of *t*-BuOOH (70% in water) at 25 °C for 7 days gave 24.4 mg (22% yield) of epoxide **4** and 32.5 mg (31% yield) of dimer **5** along with 21 mg (21% recovery) of **1**.

Treatment of norbornene 1 and epoxide 4 with Pd/Au-PVP. No formation of dimer 5.

To a solution of 38 mg (0.28 mmol) of compound **1** and 43 mg (0.28 mmol) of compound **4** in 0.2 mL of acetonitrile was added 0.22 mL (5.5 μmol; 2 mol%) of Pd/Au-PVP (25 mM in H_2O). The solution was stirred at 25 °C for 2 days and 50 °C for 1 day, cooled to 25 °C, diluted with water (10 mL) and extracted twice with dichloromethane (20 mL each). The

combined extracts were washed with water and brine, dried (anh. Na_2SO_4), concentrated, and column chromatographed on silica gel using a gradient mixture of hexane and diethyl ether as eluents to give compound **1** and compound **4**.

Yields: compound **1**: 36 mg (95% recovery); compound **4**: 40 mg (93% recovery).

The spectral data of compounds **1** and **4** are identical to those of the aforementioned authentic samples.

Oxidation of *endo*-4-oxatricyclo[5.2.1.$0^{2,6}$]-decane (6) with Cu/Au-PVP and H_2O_2. Formation of 3-exo-hydroxy-*endo*-4-oxatricyclo[5.2.1.$0^{2,6}$]-decane (7) and 3-oxo-*endo*-4-oxatricyclo[5.2.1.$0^{2,6}$]-decane (8).

To a solution of 50 mg (0.36 mmol) of *endo*-4-oxatricyclo[5.2.1.$0^{2,6}$]-decane (**6**) in 1.5 mL of acetonitrile, were added an aqueous solution of 2.9 mL (0.018 mmol; 5 mol%) of Cu/Au (3:1)-PVP (6.3 mM in water) and 0.62 mL (5.4 mmol; 15 equiv.) of 30% H_2O_2 (30% in water). The solution was stirred at 25 °C for 20 h, diluted with 20 mL of aqueous NH_4OH, and extracted with diethyl ether three times. The combined extracts were washed with water and brine, dried (anhydrous Na_2SO_4), concentrated, and column chromatographed on silica gel to give **7** and **8** along with recovered **6**.

Yields: Compound **7**: 2.8 mg (4% yield), compound **8**: 27 mg (50% yield), recovery of **6**: 8.5 mg (17% recovery).

Compound **7**: an oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.37 (s, 1H, OCHO), 3.96 (dd, *J* = 9.6, 2.0 Hz, 1H, CH_2O), 3.87 (dd, *J* = 9.6, 7.2 Hz, 1H, CH_2O), 3.65 – 3.40 (bs, 1H, OH), 2.65 – 2.59 (m, 1H), 2.48 – 2.44 (m, 1H), 2.37 – 2.34 (m, 1H), 2.20 – 2.17 (m, 1H), 1.50 – 1.25 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 99.2 (O-C-O), 66.8 (C-O), 53.1, 44.2, 42.0, 40.3, 39.1, 23.6, 22.5.

MS (ESI, MeOH): m/z (%) = 155.20 ($M + H^+$; 40).

The spectral data is in agreement with that reported.[8]Compound **8**: an oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.30 (dd, J = 10, 8.4 Hz, 1H, CH_2O), 4.25 (dd, *J* = 10, 3.2 Hz, 1H, CH_2O), 2.99 (dd, *J* = 11.6, 5.6 Hz, 1H, CHC=O)), 2.92 – 2.84 (m, 1H), 2.69 – 2.64 (m, 1H), 2.38 – 2.34 (m, 1H), 1.60 – 1.46 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.8 (C=O), 68.4 (C-O), 46.8, 42.0, 41.9, 40.4, 39.9, 25.5, 21.6.

MS (ESI, MeOH): m/z (%) = 153.17 ($M + H^+$; 70).

The spectral data is in agreement with that reported.[14]

(1) Under similar reaction conditions, oxidation of 100 mg (0.73 mmol) of **6** in 0.7 mL of acetonitrile with 0.8 mL (0.02 mmol; 2.5 mol%) of Cu/Au-PVP (25 mM in H_2O) and 0.15 mL (1.10 mmol; 1.5 equiv.) of *t*-BuOOH (70% in water) at 50 °C for 12 h gave 59 mg (53% yield) of lactol **7** and 18 mg (16% yield) of lactone **8** along with 13 mg (13% recovery) of **6**. (2) Oxidation of 100 mg (0.73 mmol) of **6** in 0.7 mL of acetonitrile with 1.46 mL (36.5 μmol; 5 mol%) of Pd/Au-PVP (25 mM in H_2O) and 0.41 mL (3.65 mmol; 5 equiv.) of H_2O_2 (30% in water) at 25 °C for 3 days gave 2.5 mg (2% yield) of lactol **7** and 1.2 mg (1% yield) of lactone **8** along with 91 mg (91% recovery) of **6**. (3) Oxidation of 100 mg (0.73 mmol) of **6** in 0.7 mL of acetonitrile with 1.46 mL (36.5 μmol; 5 mol%) of Pd/Au-PVP (25 mM in H_2O) and 0.30 mL (2.20 mmol; 3 equiv.) of *t*-BuOOH (70% in water) at 25 °C for 3 days gave 10 mg (9% yield) of lactol **7** and 3.3 mg (3% yield) of lactone **8** along with 78 mg (78% recovery) of **6**.

4-Acetyl-*endo*-4-azatricyclo[5.2.1.$0^{2,6}$]dec-8-ene (9).[23]

A mixture of 8.21 g (50 mmol) of carbic anhydride and 15 mL (0.124 mol) of NH_4OH in 30 mL of p-xylene in a round-bottom flask equipped with a Dean-Stark apparatus was heated under reflux for 6 h. During that time, water was collected from the Dean-Stark apparatus. The solution was cooled to 25 °C, filtered to collect the solid, and the solid was washed with diethyl ether (20 mL) and dried under vacuum to give 4.99 g of 3,5-dioxo-*endo*-4-azatricyclo[5.2.1.$0^{2,6}$]dec-8-ene. The above filtrate was concentrated and separated on a silica gel column using a mixture of hexane and ethyl acetate (1:1) as an eluent to obtain additional 0.87 g of aforementioned azatricyclic intermediate.

3,5-Dioxo-*endo*-4-azatricyclo[5.2.1.$0^{2,6}$]dec-8-ene:

Yield: 5.86 g (72% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.20 – 7.80 (bs, 1H, NH), 6.22 (s, 2H, CH=CH), 3.40 (d, *J* = 1.2 Hz, 2H, CHC=O), 3.30 (dd, *J* = 2.8, 1.6 Hz, 2H, CH-C=), 1.77 (d, *J* = 8.8 Hz, 1H, C10H), 1.54 (d, *J* = 8.8 Hz, 1H, C10H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.9 (2C, C=O), 134.6 (2C, CH=), 52.3 (CH_2), 47.3 (2C, CH), 45.0 (2C, CH).

MS (ESI, MeOH): m/z (%) = 164.0 ($M + H^+$, 70).

Spectral data is in agreement with that reported.[23]

To a mixture of 1.14 g (30 mmol) of lithium aluminum hydride in 100 mL of dried THF under argon at 0 °C, was added 1.63 g (10 mmol) of 3,5-dioxo-*endo*-4-azatricyclo[5.2.1.$0^{2,6}$]dec-8-ene over 10 min. The mixture was heated to reflux over an oil bath for 24 h, cooled to 25 °C, quenched with 10 mL of H_2O, filtered through a layer of Celite, and washed several times with diethyl ether. The combined filtrates were concentrated on a rotary evaporator to give 4.47 g of crude amine intermediate. To it, were added 50 mL of dichloromethane, 1.21 mL (15 mmol) of pyridine and 0.86 mL (12.1 mmol) of acetyl chloride sequentially under argon at 25 °C. The mixture was stirred for 4

h, diluted with 20 mL of aqueous NH_4OH, and extracted three times with dichloromethane (50 mL each). The combined extract was washed with water and brine (20 mL each), dried (anhydrous Na_2SO_4), concentrated, and column chromatographed on silica gel using ethyl acetate and then a mixture of dichloromethane and methanol (10:1) as eluents to yield compound **9**.

Compound **9**:

Yield: 1.062 g (60% overall yield); an oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.24 (dd, *J* = 6, 2.8 Hz, 1H, =CH), 6.18 (dd, *J* = 6, 2.8 Hz, 1H, CH=), 3.42 (dd, *J* = 11.2, 8.8 Hz, 1H, CHN), 3.32 (dd, *J* = 13.2, 8.8 Hz, 1H, CHN), 3.25 (dd, *J* = 12.8, 3.6 Hz, 1H, CHN), 3.06 (dd, *J* = 10.8, 3.2 Hz, 1H, CHN), 3.03 – 2.87 (m, 4H, 4 CH), 1.94 (s, 3H, CH_3CO), 1.58 (dt, *J* = 8.4, 1.6 Hz, 1H, C10-H), 1.45 (dt, *J* = 8.4, 1.6 Hz, 1H, C10-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.4 (CO), 136.1 (C=), 134.6 (=CH), 51.9 (CH_2N), 50.0 (CH_2N), 47.8 (CH), 46.7 (2C, CH), 45.8 (CH), 44.3 (CH_2), 22.6 (CH_3).

MS (ESI, MeOH): m/z (%) = 178.2 ($M + H^+$, 65).

HRMS-ESI: m/z $[M + H]^+$ calcd for $C_{11}H_{16}NO^+$: 178.1232, found: 178.1241.

The spectral data is in agreement with that reported.[24]

Oxidation of 9 with Cu/Au-PVP and *t*-BuOOH. Formation of 2β-(*t*-butoxy)-4-acetyl-*endo*-4-azatricyclo[5.2.1.0^{2,6}]dec-8-ene (10), *N*-acetyl-4-aza-tricyclo[5.2.1.0]-8,9-*exo*-epoxydecane (11), and 2β-(*t*-butoxy)-*N*-acetyl-4-aza-tricyclo[5.2.1.0]-8,9-*exo*-epoxydecane (12).

To a solution of 200 mg (1.13 mmol) of **9** in 2 mL of acetonitrile, were added an aqueous solution of 0.9 mL (0.023 mmol; 2 mol%) of Cu/Au (3:1)-PVP (25 mM in water) and 1.2 mL (8.8 mmol; 8 equiv.) of *t*-BuOOH (70% in water). The solution was stirred at 25 °C for 24 h, diluted with aqueous $Na_2S_2O_5$, and extracted with ethyl acetate three times. The combined extracts were washed with water and brine, dried (anhydrous Na_2SO_4), concentrated, and column chromatographed on silica gel to give **10** (as an inseparable mixture of 2β and 2α isomers in a ration of 9:1), **11**, and **12** along with recovered **9**.

Yields: Compound **10**: 76 mg (27% yield), compound **11**: 20 mg (9% yield), **12**: 54 mg (18% yield), recovery of **9**: 28 mg (14% recovery).

Compound **10**:

White solids, mp 41.0–42.0 °C

^{1}H NMR (600 MHz, $CDCl_3$), major 2β-isomer: δ 6.17 (dd, *J* = 5.4, 3.0 Hz, 1H, =CH), 6.03 (dd, *J* = 5.4, 3.0 Hz, 1H, =CH), 5.14 (s, 1H, C2-H), 3.55 (dd, *J* = 12.0, 1.8 Hz, 1H, C9-H),

3.27 (dd, *J* = 12.0, 9.0 Hz, 1H, C9-H), 3.11–3.07 (bs, 1H, C4-H), 2.95–2.92 (bs, 1H, C7-H), 2.89 (dd, *J* = 9.0, 4.2 Hz, 1H, C3-H), 2.85–2.82 (m, 1H, C8-H), 2.11 (s, 3H, CH_3CO), 1.49 (d, *J* = 8.4 Hz, 1H, C10-H), 1.36 (d, *J* = 8.4 Hz, 1H, C10-H), 1.21 (s, 9H, Me_3C).

^{13}C NMR (150 MHz, $CDCl_3$): δ 168.8 (C=O), 134.2 (=C), 132.5 (C=), 92.5 (C2), 79.3 (O-$\underline{C}Me_3$), 50.4 (C-N), 49.5, 46.2, 45.8, 44.7, 40.9, 25.4 (3C, $\underline{Me}_3C$), 21.3 ($\underline{C}H_3CO$).

HRMS-ESI: m/z $[M + H]^+$ calcd for $C_{15}H_{24}NO_2^+$: 250.1807, found: 250.1821.

Compound **11**:

White solids, mp 119–120 °C

^1H NMR (400 MHz, $CDCl_3$): δ 3.90 (dd, *J* = 13.4, 2.6 Hz, 1H, C5-H), 3.58 (dd, *J* = 12.0, 2.6 Hz, 1H, C6-H), 3.39 (dd, *J* = 12.0, 9.0 Hz, 1H, C2-H), 3.27 (d, *J* = 4.0 Hz, 1H, C9-H), 3.22–3.19 (m, 1H, C2-H), 3.17 (d, *J* = 4.0 Hz, 1H, C9-H), 2.85–2.71 (m, 2H, C3 & C8-Hs), 2.66–2.63 (m, 2H, C4 & C7-Hs), 2.04 (s, 3H, CH_3CO), 1.49 (d, *J* = 10.0 Hz, 1H, C10-H), 0.88 (d, *J* = 10.0 Hz, 1H, C10-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 168.3 (C=O), 48.6 (C-O), 48.5 (C-O), 47.0 (C-N), 44.6, 44.5, 42.8, 40.5, 40.4, 29.4, 22.6 ($\underline{C}H_3CO$).

HRMS-ESI: m/z $[M + Na]^+$ calcd for $C_{11}H_{15}NO_2Na^+$: 216.1000, found: 216.0977; $[M + H]^+$ calcd for $C_{11}H_{16}NO_2^+$: 194.1181, found: 194.1199.

Compound **12**:

Colorless oil.

^1H NMR (400 MHz, $CDCl_3$), major 2β-isomer: δ5.55 (s, 1H, C2-H), 4.04 (d, *J* = 12.8 Hz, 1H, C9-H), 3.28 (dd, *J* = 12.8, 7.6 Hz, 1H, C9-H), 3.19 (s, 1H, C5-H), 2.98 (d, *J* = 2.4 Hz, 1H, C6-H), 2.81–2.78 (bs, 1H, C4-H), 2.69 (s, 1H, C3 & C8-Hs), 2.62 (s, 1H, C7-H), 2.20 (s, 3H, CH_3CO), 1.47 (d, *J* = 10.0 Hz, 1H, C10-H), 0.83 (d, *J* = 10.0 Hz, 1H, C10-H).

^{13}C NMR (150 MHz, $CDCl_3$): δ 168.5 (C=O), 89.7 (C2), 79.6 (O$\underline{C}Me_3$), 48.4, 47.5, 47.1, 43.2, 40.1, 39.6, 38.7, 27.7, 25.4 (3C, $(\underline{C}H_3)_3C$), 21.3 ($\underline{C}H_3CO$).

HRMS-ESI: m/z $[M + Na]^+$ calcd for $C_{15}H_{23}NNaO_3^+$: 288.1576, found: 288.1608.

Oxidation of 9 with Pd/Au-PVP and *t*-BuOOH. Formation of 10, 11, 12, and (3S*,3aS*,5S*,6aS*,7S*)-hexahydro-6-hydroxy-8-[(*N*-acetylamino)methyl]-3,5-methano-2*H*-cyclopenta[b]furan-2-one (13).

To a solution of 100 mg (0.56 mmol) of **9** in 1 mL of acetonitrile, were added an aqueous solution of 1.1 mL (0.028 mmol; 5 mol%) of Pd/Au (3:1)-PVP (25 mM in water) and 0.62 mL (4.5 mmol; 8 equiv.) of *t*-BuOOH (70% in water). The solution was stirred at 25 °C for 5 days, diluted with aqueous $Na_2S_2O_5$, and extracted thee times with ethyl acetate. The combined extracts were washed with water and brine, dried (anhydrous Na_2SO_4),

concentrated, and column chromatographed on silica gel using a gradient mixture of hexane and ethyl acetate followed by dichloromethane and methanol as eluents to give **10** (as an inseparable mixture of 2β and 2α isomers in a ration of 9:1), **11**, **12**, and **13** along with recovered **9**. Crystallization of **13** in diethyl ether gave single crystals, whose structure was determined by single-crystal X-ray analysis.

Yields: Compound **10**: 18 mg (13% yield), compound **11**: 19 mg (18% yield), **12**: 7.5 mg (5% yield), **13**: 2.5 mg (2% yield) recovery of **9**: 13 mg (13% recovery).

Compound **13**:

White solids, mp 69 – 70 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.05–6.03 (bs, 1H, NH), 4.54 (d, *J* = 5.2 Hz, 1H, C7-H), 4.02–4.01 (bs, 1H,C6-H), 3.96 (ddd, *J* = 11, 8.4, 6 Hz, 1H, C9-H), 3.30–3.25 (m, 1H, C9-H), 2.82 (ddd, *J* = 15, 11, 4.4 Hz, 1H, C8-H), 2.69 (dd, *J* = 10.4, 4.8 Hz, 1H, C3-H), 2.56–2.48 (m, 1H, C3a-H), 2.43–2.40 (bs, 1H, C5-H), 2.17 (d, *J* = 11.6 Hz, 1H, C4-H), 2.07 – 2.02 (bs, 1H, OH), 2.01 (s, 3H, CH_3), 1.61 (d, *J* = 11.6 Hz, 1H, C4-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 179.7 (OC=O), 171.2 (NHC=O), 87.6 (C7), 73.2 (C6), 46.7 (C9), 46.2 (C5), 43.6 (C-8), 41.6 (C3), 37.9 (C3a), 33.8 (C4), 21.1 (CH_3).

HRMS-ESI: m/z $[M + Na]^+$ calcd for $C_{11}H_{15}NNaO_4^+$: 248.0893, found: 248.0887.

2-(*t*-Butoxycarbonyl)-1,2,3,4-tetrahydro-γ-carboline (14).[16a]

To a mixture of 4.7 g (30 mmol) of 4-piperidone hydrochloride and 9.3 g (67 mmol) of potassium carbonate in 60 mL of chloromethane, was added 13.2 g (60 mmol) of di-*t*-butyl dicarbonate, and the mixture was stirred at 25 °C for 3 days. The reaction mixture was filtered and the filtrate was concentrated to dryness, column chromatographed on silica gel using a gradient mixture of hexane and diethyl ether as eluent to give 5.9 g (98% yield) of *N*-Boc-4-piperidinone as an oily material. ^{1}H and ^{13}C NMR spectra are in agreement with those reported.[16a]

A solution of 1.17 g (5.87 mmol) of *N*-Boc-4-piperidinone and 0.64 mL (6.51 mmol) of phenyl hydrazine in 10 mL of acetic acid was heated at 65 °C for 16 h, cooled to 25 °C, basified with 20 mL of aqueous NH_4OH and 12 mL of 15% aqueous NaOH to pH = 10, and extracted three times with ethyl acetate (100 mL each). The combined extracts were washed with water and brine, dried (anh. Na_2SO_4), concentrated, and column chromatographed on silica gel using a gradient of hexane and diethyl ether as eluents to give compound **14** and recovered *N*-Boc-4-piperidinone (0.458 g, 39%).

Yield: 0.587 g (37% yield); brown solids, mp 139 – 140 °C (lit.[16a] 139.8 – 140.7 °C)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95–7.83 (bs, 1H, NH), 7.45 (d, *J* = 7.6 Hz, 1H, C5-H), 7.31 (d, *J* = 7.6 Hz, 1H, C8-H), 7.15 (t, *J* = 8.4 Hz, 1H, C7-H), 7.10 (t, *J* = 7.6 Hz, 1H, C6-H), 4.65 (s, 2H, C4-H), 3.87–3.77 (bs, 2H, C2-H), 2.85–2.78 (bs, 2H, C1H), 1.51 (s, 9H, *t*-Bu).

^{13}C NMR (100 MHz, $CDCl_3$): δ 155.3 (C=O), 135.9, 132.3 (C5a), 125.6, 121.6, 119.6, 117.6, 110.8, 107.4, 79.9 (C-O), 41.5 (C4), 40.7 (C2), 28.6 (3C, *t*-Bu), 23.6 (C1).

^{1}H and ^{13}C NMR spectra are in agreement with those reported.[16a]

HRMS-ESI: m/z $[M + H]^+$ calcd for $C_{16}H_{20}N_2O_2^+$: 273.1598, found: 273.1601.

Oxidation of 14 with Cu/Au-PVP and H_2O_2. Formation of *N*3-*t*-butoxycarbonyl 2,3,4,9b-tetrahydro-1*H*-pyrido[4,3-b]indol-4a-ol (15).

To a solution of 60 mg (0.22 mmol) of **14** in 0.5 mL of acetonitrile, were added 0.15 mL (3.6 μmol; 2 mol%) of Cu/Au (3:1)-PVP (25 mM in water) and 49 03BCL (0.44 mmol) of 30% H_2O_2. The solution was stirred at 25 °C for 6 h, dilute with 10 mL of aqueous sodium thiosulfate, and extracted three times with ethyl acetate. The combined extract was washed with water and brine, concentrated and column chromatographed using a gradient mixture of hexane, diethyl ether and isopropanol as eluents to give 28 mg (44% yield) of **15** as an oil. In a separate experiment, the crude reaction mixture was concentrated to dryness, without the treatment of aqueous $Na_2S_2O_5$ and extraction, and directly subjected to silica gel column chromatography. The same product **15** was isolated, suggesting the corresponding hydrogen peroxide product of **15** was not formed.

Compound **15**: 28 mg (44% yield); an oil.

^{1}H NMR (400 MHz, acetone-d_6), a mixture of *cis*- and *trans*-isomers (between hydroxyl and Boc group): δ 7.51 (d, *J* = 7.6 Hz, 1H, C5-H), 7.50 (t, *J* = 7.6 Hz, 1H, C7-H), 6.95 (d, *J* = 8.0 Hz, 1H, C8-H), 6.82 (t, *J* = 7.6 Hz, 1H, C6-H), 3.75–3.69 (m, 1H, C2-H), 3.64–3.51 (m, 1H, C2-H), 3.51 (d, *J* = 11.6 Hz, 1H, C4H), 3.44 (d, *J* = 11.6 Hz, 1H, C4-H), 2.20–2.05 (m, 1H, C1-H), 1.90–1.80 (m, 1H, C1-H), 1.32 & 1.30 (2s, 9H, *t*-Bu).

^{13}C NMR (100 MHz, $CDCl_3$), a mixture of *cis*- and *trans*-isomers: δ 200.4, 200.2 (C9a=N), 160.2 (C8a-N), 154.4 (C=O of Boc), 137.6 (C7), 124.8 (C5), 120.4 (C4b), 119.3 (C6), 112.6 (C8), 79.9 & 77.3 (C-O of Boc), 72.2 & 71.2 (C-OH), 55.8 & 55.0 (C4), 45.1 (C2), 36.1 & 35.6 (C1), 28.5 (3C, *t*-Bu).

HRMS-ESI: m/z $[M + Na]^+$ calcd for $C_{16}H_{20}N_2O_3Na^+$: 311.1366, found: 311.1335 (100%).

2,3,4,9b-Tetrahydro-1*H*-pyrido[4,3-b]indol-9b-ol (16).

To a solution of 19 mg (65 μmol) of **15** in 1 mL of CH_2Cl_2 was added 38 μL (0.5 mmol) of TFA, and the solution was stirred at 25 °C for 4 h. It was diluted with 1.5 mL of aqueous $NaHCO_3$ solution until pH 7 followed by the addition of 75 μL of 15% aqueous NaOH solution, and extracted three times with dichloromethane. The combined extract was washed with brine (3 mL), dried (anh. Na_2SO_4), and concentrated under vacuo to give compound **16**.

Yield: 10.4 mg (87% yield).

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.63 (d, *J* = 7.6 Hz, 1H, C5-H), 7.47 (t, *J* = 7.6 Hz, 1H, C7-H), 6.91–6.84 (m, 2H, C8-H & C6-H), 5.02–4.92 (bs, 1H, NH), 4.75–4.52 (bs, 1H, OH),

3.35–3.28 (m, 1H, C2-H), 3.25 (d, *J* = 11.6 Hz, 1H, C4H), 3.22–3.12 (m, 1H, C2-H), 2.94 (d, *J* = 11.6 Hz, 1H, C4-H), 2.32–2.24 (m, 1H, C1-H), 2.23–1.94 (m, 1H, C1-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 204.2 (C9a=N), 160.3 (C8a-N), 137.2 (C7), 124.6 (C5), 120.1 (C4b), 119.1 (C6), 112.3 (C8), 73.7 (C-OH), 58.4 (C4), 47.5 (C2), 38.2 (C1).

HRMS-ESI: m/z $[M + H]^+$ calcd for $C_{11}H_{13}N_2O^+$: 189.1028, found: 189.1048 (100%).

Catalytic oxidative coupling of 14 and 2,3-dihydroxybenzoic acid (18). Formation of [4+2] adduct, *tert*-butyl (6aR*,11bR*)-3,4-dihydroxy-5-oxo-5*H*,7*H*-6a,11b-(ethanoiminomethano)isochromeno[3,4-b]indole-13-carboxylate (19).

To a solution of 0.10 g (0.37 mmol) of **14** and 68 mg (0.44 mmol) of **18** in 1 mL of acetonitrile, were added 0.75 mL (17.5 μmol; 5 mol%) of Cu/Au (3:1)-PVP (25 mM in water) and 45 μL (0.44 mmol; 1.2 equiv.) of 30% H_2O_2. After stirring at 25 °C for 24 h, the reaction solution was diluted with aqueous $Na_2S_2O_5$ and few drops of NH_4OH, and extracted five times with ethyl acetate (20 mL each). The combined extract was washed with water and brine, dried (anhydrous Na_2SO_4), concentrated and column chromatographed on silica gel using a gradient mixture of hexane and diethyl ether to give 26 mg (26% recovery) of starting material **14** and compound **19**. Crystallization of compound **19** in diethyl ether gave single crystals, which were subjected for X-ray analysis.

Yield: 85 mg (54% yield); light yellow solids, mp 224 – 226 °C

^{1}H NMR (600 MHz, $CDCl_3$), two rotamers are present; assignment was based of 2D COSY spectrum: δ 11.60–11.40 (bs, 1H, OH), 7.33–7.27 (m, 2H, Ar-H), 7.20–7.14 (m, 1H, Ar-H), 6.87–6.82 (m, 3H, Ar-H), 5.80–5.66 (bs, 1H, NH), 4.87–4.83 (s, 1H, OH), 4.74 (d, *J* = 14 Hz, 1H, C12-H), 4.25–4.19 (m, 1H, C14-H), 3.10–3.01 (m, 1H, C14-H), 2.75 (d, *J* = 14 Hz, 1H, C12-H), 2.35–2.24 (m, 1H, C15-H), 2.09–2.00 (m, 1H, C15-H), 1.46 & 1.35 (2s, 9H, *t*-Bu).

^{13}C NMR (100 MHz, $CDCl_3$), two rotamers: δ 168.5 (C=O lactone), 153.8 & 153.5 (C=O Boc), 150.2 & 150.0 (Ar, C-O), 145.8 (Ar, C7a), 144.8 (Ar, C-O), 131.7 & 131.4 (Ar), 129.1 (Ar), 127.2 (Ar), 123.4 (Ar), 121.0 & 120.7 (Ar), 120.2 (Ar), 118.3 & 117.8 (Ar), 111.1 (Ar), 107.1 & 106.8 (C6a), 106.3 (Ar), 80.6 & 80.4 (O-$\underline{C}Me_3$), 50.7 & 49.7 (C12), 48.6 (C11b), 41.6 & 40.7 (C14), 31.7 (C15), 28.4 (3C, Me_3).

HRMS-ESI: m/z $[M + H]^+$ calcd for $C_{23}H_{25}N_2O_6^+$: 425.1713, found: 425.1725 (100%).

The spectral data are similar to those reported.[16a]

The use of 0.5 mol% of Cu/Au-PVP in acetonitrile-water and 2 equiv. of 30% H_2O_2 at 25 °C for 4 days gave 48% yield of **19**, 22% yield of **16**, and 20% recovery of **14**.

2-(*t*-Butoxycarbonyl)-9-methyl-1,2,3,4-tetrahydro-γ-carboline (17).

To a dried flask containing 45 mg (1.13 mmol) of NaH (60% in mineral oil) under argon, 1 mL of distilled diethyl ether was added, stirred, and the ether was removed via a syringe and discarded. The washing process was repeated, then dried under vacuum and maintained under argon, added 1 mL of THF, and cooled over an ice-water bath. To it, a solution of 0.12 g (0.45 mmol) of carboline **14** in 1 mL of THF was added, stirred at 25 °C for 30 min., added 42 μL (0.67 mmol) of methyl iodide, and stirred for 15 h. The solution was diluted with 5.0 mL of aqueous NH_4Cl, extracted three times with 20-mL each of dichloromethane, and the combined extracts were washed with 5 mL of brine, dried (anh. Na_2SO_4), concentrated, and column chromatographed on silica gel using a mixture of hexane and diethyl ether (2:1) as an eluent to give compound **17**.[25]

Yield: 98 mg (76% yield); brown solids, mp 113 – 114 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 (d, *J* = 8 Hz, 1H, C5-H), 7.31 (d, *J* = 8 Hz, 1H, C8-H), 7.23 (t, *J* = 8 Hz, 1H, C7-H), 7.13 (t, *J* = 8 Hz, 1H, C6-H), 4.69 (s, 2H, C4-H), 3.89–3.78 (bs, 2H, C2-H), 3.66 (s, 3H, N-Me) 2.86–2.79 (bs, 2H, C1-H), 1.54 (s, 9H, *t*-Bu).

^{13}C NMR (100 MHz, $CDCl_3$): δ 155.2 (C=O), 137.0, 133.2 (C5a), 125.1, 121.1, 119.1, 117.6, 108.9, 106.7, 79.8 (C-O), 41.5 (C4), 40.8 (C2), 29.1 (N-Me), 28.5 (3C, *t*-Bu), 22.4 (C1).

Catalytic oxidative coupling of 17 and 18. Formation of [4+2] adduct, *tert*-butyl (6a*R**,11b*R**)-3,4-dihydroxy-5-oxo-7-methyl-5*H*,7*H*-6a,11b-(ethanoiminomethano)isochromeno[3,4-b]indole-13-carboxylate (20).

To a solution of 40 mg (0.14 mmol) of **17** and 25 mg (0.16 mmol) of **18** in 0.2 mL of DMF, were added 27 μL (2.3 μmol; 2 mol%) of Cu/Au (3:1)-PVP (50 mM in DMF) and 29 μL (0.28 mmol; 2 equiv.) of 30% H_2O_2. After stirring at 25 °C for 24 h, the solution was diluted with 1 mL of aqueous $Na_2S_2O_5$, and extracted three times with dichloromethane (15 mL each). The combined extract was washed with water and brine, dried (anh. Na_2SO_4), concentrated and column chromatographed on silica gel using a gradient mixture of hexane and diethyl ether to give 2.4 mg (6% recovery) of starting material **17** and compound **20**.

Yield: 37.5 mg (61% yield); pale yellow solids, mp 226 – 227 °C

^{1}H NMR (600 MHz, $CDCl_3$), two rotamers (from Boc group) are present: δ 11.60 (s, 1H, OH), 7.30–7.25 (m, 2H, Ar-H), 7.25–7.21 (m, 1H, Ar-H), 6.84–6.79 (m, 2H, Ar-H), 6.73 (d, *J* = 7.6 Hz, 1H, Ar-H), 5.83–5.67 (bs, 1H, OH), 4.70 (d, *J* = 14 Hz, 1H, C12-H), 4.17 (d, *J* = 14 Hz, 1H, C12-H), 3.05 (s, 3H, NMe), 3.00–2.90 (m, 1H), 2.80–2.75 (m, 1H), 2.57–2.48 (m, 1H), 2.03–1.95 (m, 1H), 1.49 & 1.38 (2s, 9H, *t*-Bu).

^{13}C NMR (150 MHz, $CDCl_3$), two rotamers: δ 168.6 (C=O lactone), 153.5 (C=O Boc), 150.2 (Ar, C-O), 148.4 (Ar), 144.8 (Ar), 130.8 (Ar), 129.2 (Ar), 127.5 (Ar), 122.9 (Ar), 120.3 (Ar), 120.1 (Ar), 117.8 (Ar), 109.1 (Ar), 108.8 (Ar), 107.3 (Ar), 80.6 & 80.4 (O-

$\underline{C}Me_3$), 50.7 (C12), 49.8 & 48.6 (C11b), 41.2 & 40.3 (C14), 29.7 (N-Me), 28.4 (C15), 28.8 & 28.0 (3C, Me_3).

MS (ESI, MeOH): m/z (%) = 439.2 ($M + H^+$, 30).

HRMS-ESI: m/z $[M + H]^+$ calcd for $C_{24}H_{27}N_2O_6^+$: 439.1869, found: 439.1867.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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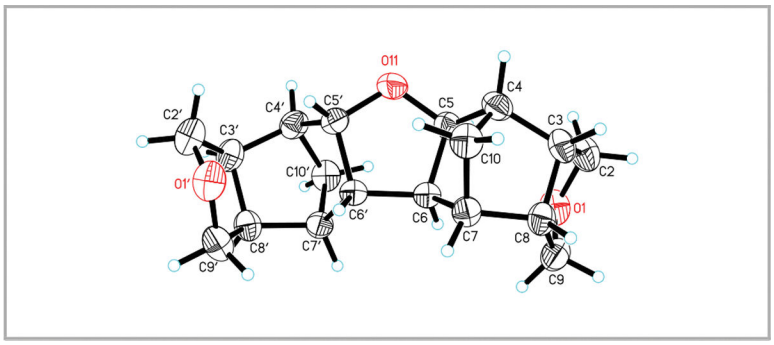


Figure 1.

Molecular structure of dodecahydro-1,4:6,9-dimethanodibenzofurano[2,3-b:7,8-b’]bisoxolane (**5**), obtained from single-crystal X-ray analysis. CCDC 2118275. Selected bond lengths (Å) and angles (°): O1-C2 1.427(3), O1-C9 1.431(3), C3-C8 1.562(3), C5-O11 1.433(2), C5-C6 1.549(2), C5-H5 1.0000, C6-C7 1.542(2), O11-C5’ 1.433(2); C2-O1-C9 105.07(16), O1-C2-C3 106.16(16), O1-C2-H2A 110.5, C5-C4-C3 110.26(15), O11-C5-C6 107.90(14), C4-C5-C6 103.53(14), O11-C5-H5 111.2, C6’-C6-C7 113.72(17), C7-C6-C5 102.81(14), C9-C8-C7 117.63(15).

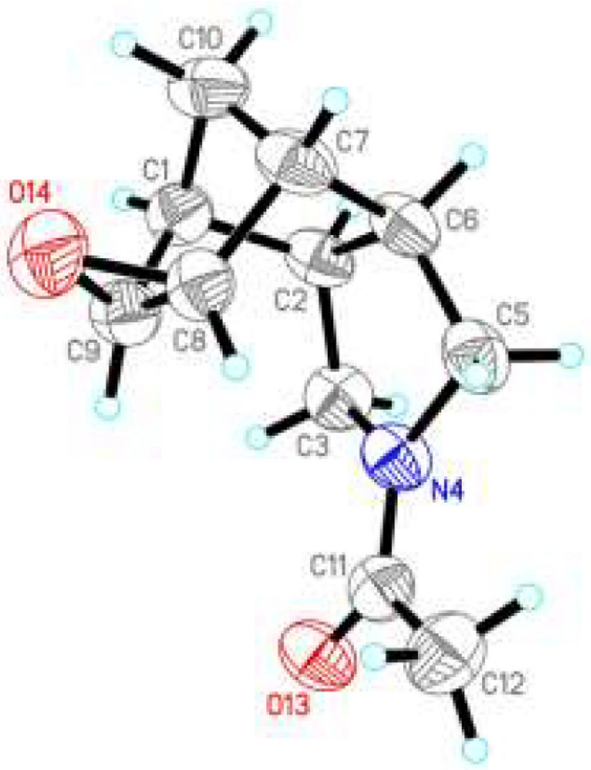


Figure 2.

Molecular structure of *N*-acetyl-4-axa-tricyclo[5.2.1.0]-8,9-*exo*-epoxydecane (**11**), obtained from single-crystal X-ray analysis. CCDC 2212632. Selected bond lengths (Å) and angles (°): C1-C2 1.550(8), C1-C9 1.511(7), C1-C10 1.536(7), C2-C3 1.514(7), C3-N4 1.466(6), N4-C11 1.348(6), C9-O14 1.448(6), C11-O13 1.236(6); C9-C1-C2 105.8(4), C9-C1-C10 102.3(4), C3-C2-C1 117.3(4), N4-C3-C2 104.4(4), C3-N4-C5 110.4(4), O14-C8-C9 59.4(3), C7-C10-C1 94.9(4), C9-O14-C8 60.8(3).

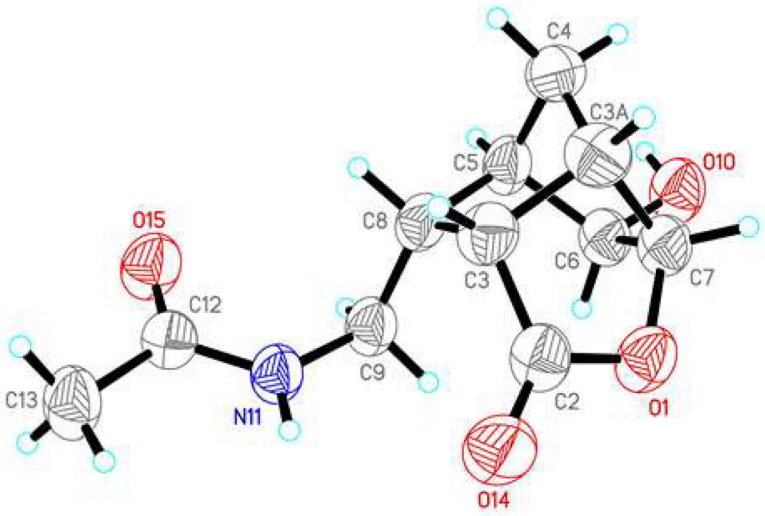


Figure 3.

Molecular structure of (3S*,3aS*,5S*,6aS*,7S*)-hexahydro-6-hydroxy-8-[(N-acetylamino)methyl]-3,5-methano-2H-cyclopenta[b]furan-2-one (**13**), obtained from single-crystal X-ray analysis. CCDC 2212630. Selected bond lengths (Å) and angles (o): O1-C2 1.353(5), O1-C7 1.449(5), C3-C3A 1.541(6), C3A-C4 1.514(7), C3A-C7 1.542(6), C6-C7 1.532(6), C8-C9 1.518(6), C9-N11 1.459(5); C2-O1-C7 108.7(3), O1-C2-C3 109.6(4), C3-C3A-C7 97.6(3), C4-C3A-C3 105.1(4), C6-C5-C8 110.4(3), O10-C6-C5 112.9(4), O10-C6-C7 107.6(3), O1-C7-C3A 105.2(3), C5-C8-C3 102.2(3), N11-C12-C13 116.5(4).

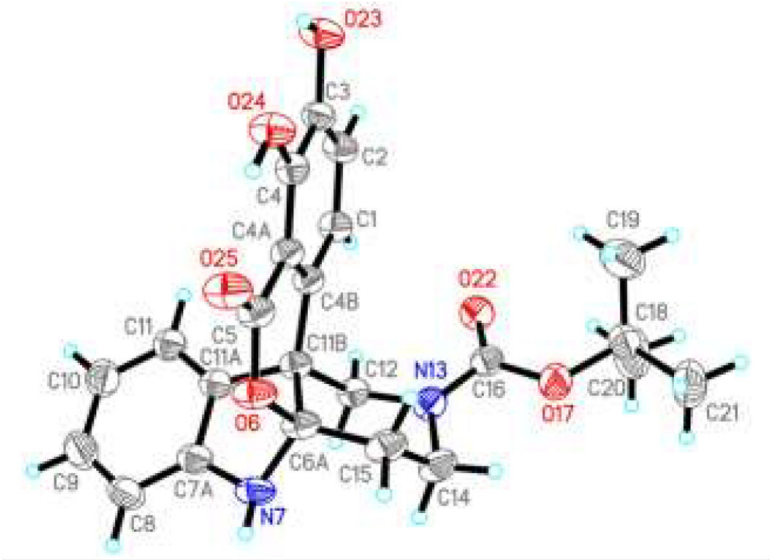
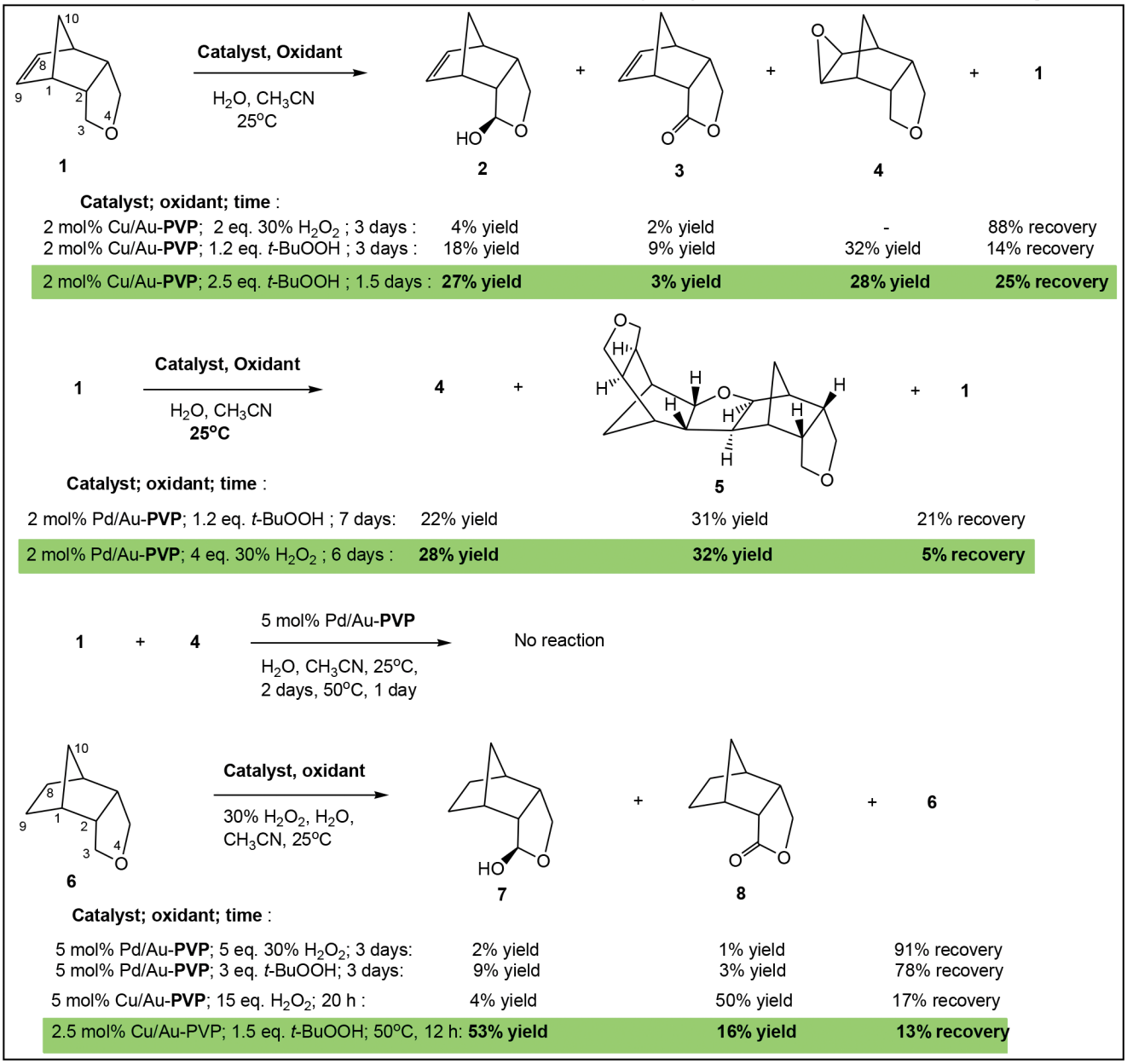


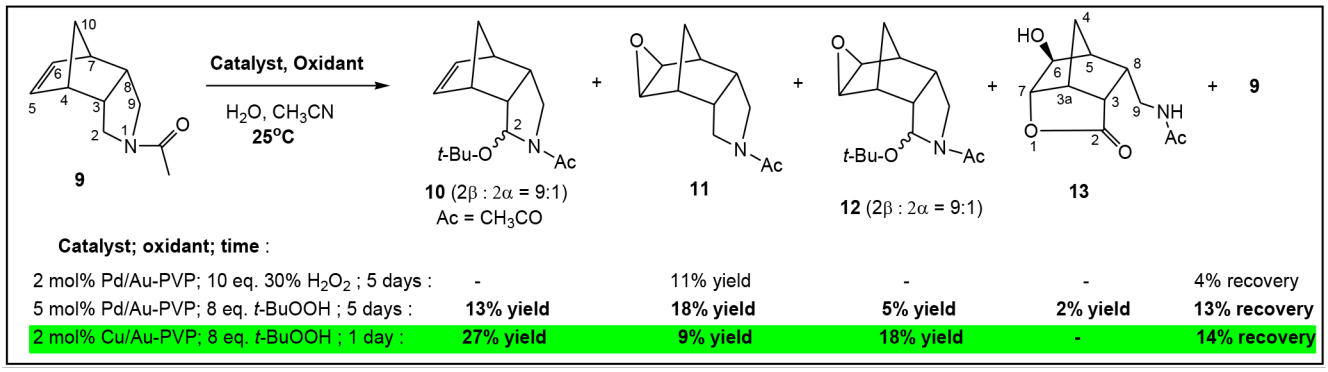
Figure 4.

Molecular structure of tert-butyl (6aR*,11bR*)-3,4-dihydroxy-5-oxo-5H,7H-6a,11b-(ethanoiminomethano)isochromeno[3,4-b]indole-13-carboxylate (**19**), obtained from single-crystal X-ray analysis. CCDC 2212631. Selected bond lengths (Å) and angles (o): O6-C6A 1.4917(13), N7-C6A 1.4294(16), N7-C7A 1.3999(18), C4A-C4B 1.4116(15), C4B-C11B 1.5155(15), C7A-C11A 1.3981(16), C11A-C11B 1.5224(17), C11B-C12 1.5528(15); C5-O6-C6A 122.54(9), C4-C4A-C5 118.34(10), C4B-C4A-C5 121.38(10), O6-C6A-C15 106.15(10), N7-C6A-O6 105.65(9), C11A-C7A-N7 109.69(11), C7A-C11A-C11B 107.45(10), C4B-C11B-C6A 112.23(9).

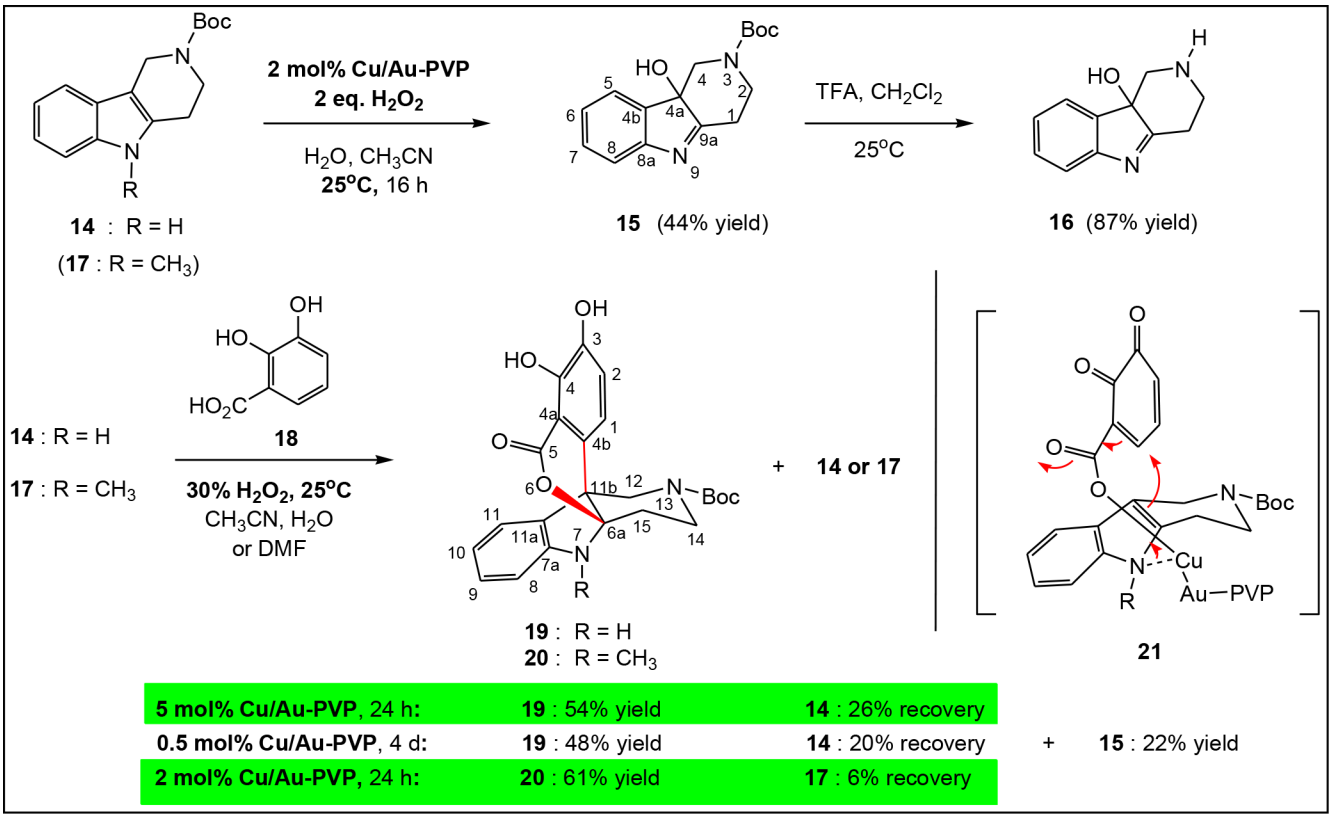


Scheme 1.

Catalytic oxidations of compounds **1** and **6** using bimetallic nanoclusters as catalysts and H_2O_2 or *t*-BuOOH as an oxidant.

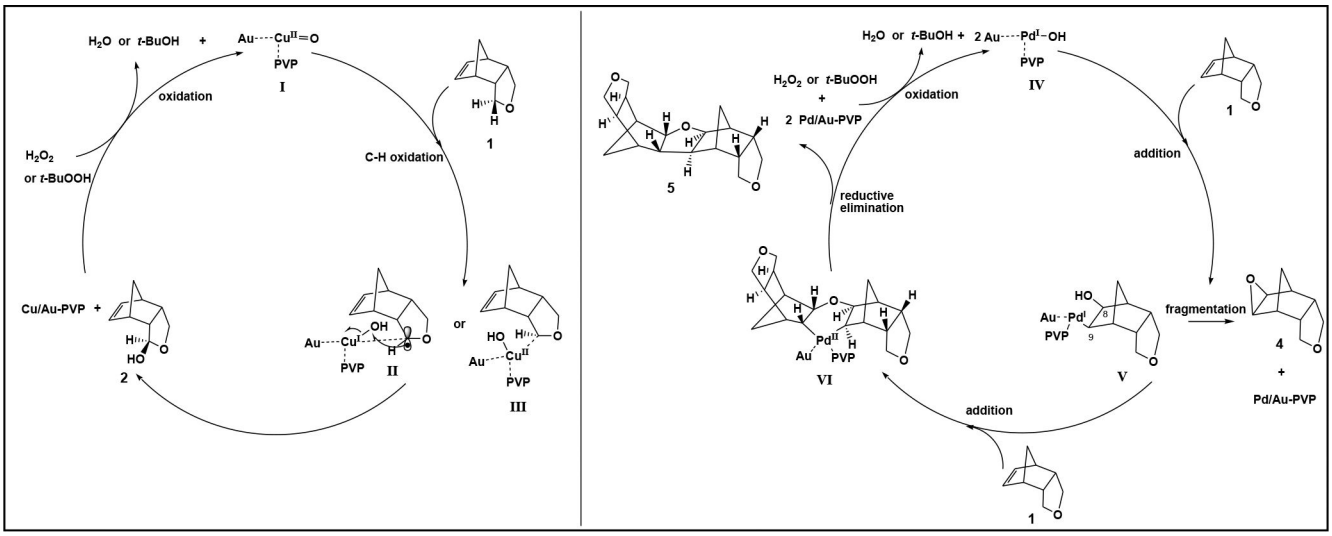


Scheme 2.
Catalytic oxidation of hexahydro-4,7-methanoisoindole 9.



Scheme 3.

Catalytic oxidations of 1,2,3,4-tetrahydro-γ-carbolines **14** and **17**.



Scheme 4.

Proposed mechanism for the oxidation of **1** with Cu/Au or Pd/Au-PVP and H_2O_2 or *t*-BuOOH.

Table 1

Formula, crystal data, method of collection, and methods of structure solution and refinement of x-ray structures of **5**, **11**, and **13**.

Molecules	**5**	**11**	**13**
Formula	$C_{18}H_{24}O_3$	$C_{11}H_{15}NO_2$	$C_{11}H_{15}NO_4$
Fw	288.38	193.24	225.24
T (K)	200(2)	250(70)	240(10)
λ (Å)	1.54178	1.54184	1.54184
Crystal syst	orthorhombic	Orthorhombic	monoclinic
space group	$P2_12_12/c$	$P2_12_12E_1$	P1 21/n 1
a (Å)	10.265(2)	7.956(2)	6.0505(7)
b (Å)	11.241(3)	10.109(2)	7.4705(11)
c (Å)	6.1497(13)	11.708(2)	22.805(2)
α (deg)	90	90	90
β (deg)	90	90	91.028(9)
γ (deg)	90	90	90
V (Å^3)	709.6(3)	941.6(4)	1030.6(2)
Z	4 (molecules)	4 (molecules)	4 (molecules)
diffractometer	Bruker Platinum 135; Cu rotating anode/optical mirrors	Rigaku XtaLAB Synergy-S; Cu microfocus sealed X-ray source	Rigaku XtaLAB Synergy-S; Cu microfocus sealed X-ray source
d_{calcd} (Mg/m^3)	1.350	1.363	1.452
absorption coeff (mm^{-1})	0.718	0.756	0.927
F(000)	312	416	480
20 range (deg)	5.837–69.701	5.783–67.218	3.877–76.389
reflections collected	4011	5236	5565
independent reflections/R_{int}	1244/0.0392	1652/0.0854	1977/0.0961
% completeness /theta(deg)	95.6/66.000	99.3/67.218	98.9/67.684
abs corr	Multi-scan	Semi-empirial from equiv.	Gaussian
max, min transm	0.7532, 0.5417	1.00000, 0.39137	1.000, 0.909
least squares refinement method	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2
Data /restraints/ parameters	1244 / 0 / 101	1652/0/128	1977 / 0 / 147
GOF (on F^2)	1.081	0.976	0.984

Molecules	5	11	13
R1(obsd); wR_2(all)[a]	0.0373; 0.0915	0.0515; 0.1019	0.0735; 0.1705
max./min. residual electron density ($e^-/Å^3$)	0.196/-0.213	0.148/-0.172	0.306/-0.282

[a] $R1 = \Sigma \, ||F0| - |Fc|| \, / \, \Sigma \, |F0|$;. $wR2 = \{ \Sigma \, [w(F0^2 - Fc^2)^2] \, / \, \Sigma \, [w(F0^2)^2] \}^{1/2}$

Table 2

Formula, crystal data, method of collection, and methods of structure solution and refinement of x-ray structures of **19**.

Molecules	**19**
Formula	$C_{23}H_{24}N_2O_6$
Fw	424.44
T (K)	200(10)
λ (Å)	1.54184
Crystal syst	Triclinic
space group	P-1
a (Å)	9.07945(15)
b (Å)	10.76059(17)
c (Å)	11.1521(2)
α (deg)	89.4381(14)
β (deg)	82.5928(15)
γ (deg)	86.8687(13)
V (Å^3)	1078.86(3)
Z	2 (molecules)
diffractometer	Rigaku XtaLAB Synergy-S; Cu microfocus sealed X-ray source
dcalcd (Mg/m^3)	1.307
abs coeff (mm^{-1})	0.789
F(000)	448
0 range (deg)	3.997–79.883
reflections collected	22748
independent reflections/R_{int}	4593/0.0306
% completeness /theta(deg)	100.0/67.684
absorption correction	Semi-empirical from equiv.
max, min transm	1.00000, 0.78634
least squares refinement method	Full-matrix on F^2
data/restraints/ params	4593 / 0/376
GOF (on F^2)	1.048
R1(obsd); wR_2(all)[a]	0.0372; 0.0972
max./min. residual electron density (e$^-$/Å^3)	0.209/−0.237

[a] $R_1 = \Sigma \, ||F_0| - |F_c|| \, / \, \Sigma \, |F_0|$;. $wR_2 = \{ \Sigma \, [w(F_0^2 - F_c^2)^2] \, / \, \Sigma \, [w(F_0^2)^2] \}^{1/2}$