The Journal of Organic Chemistry

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J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.5b00887 • Publication Date (Web): 16 Jun 2015

The Journal of Organic Chemistry is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

An Alternative to Precious Metals: $Hg(ClO_4)_2{\cdot}3H_2O$ as a Cheap and Water-Tolerant Catalyst for the Cycloisomerization of Allenols

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Abstract: $Hg(ClO_4)_2{\cdot}3H_2O$, a cheap, water-tolerant, and stable salt, catalyzes the cycloisomerization reaction or α-allenols to 2,5-dihydrofurans in an efficient and selective manner. The reaction is general and can be applied to differently functionalized substrates, including alkyl-substituted, aryl-substituted, enantiopure, and tertiary allenols. Besides, density functional theory (DFT) calculations were performed to obtain an insight into various aspects of the controlled reactivity of α-allenols under mercury catalysis. They suggest a dual activation of the allenol by the Hg-complex that drives the reaction to the chemoselective formation of 2,5-dihydrofurans.

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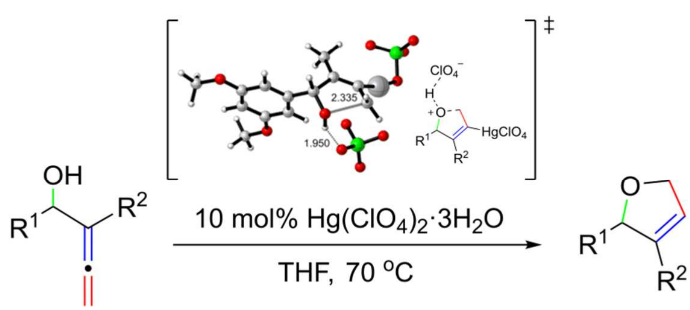


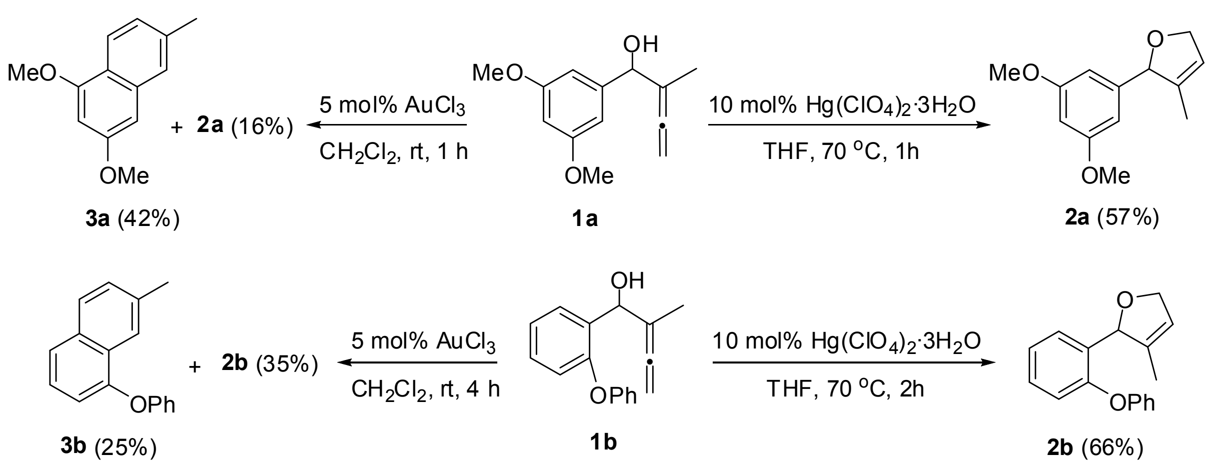
INTRODUCTION

The last decade has seen an increasing use of allene derivatives as versatile building blocks in synthetic chemistry, in large part due to their interesting reactivity patterns which allows the preparation of relevant products in a controlled manner.[1] On the other hand, the development of synthetic methods for the preparation of oxacycles is important because they are present in a wide range of natural products and biologically active molecules.[2] Among the possibilities, transition metal-catalyzed intramolecular nucleophilic addition of the hydroxyl group across the allene moiety in allenols is intriguing from the point of view of regioselectivity as well as it being one of the most rapid and convenient methods for the preparation of oxacycles owing to its atom-economy and efficiency.[1] Despite that this field was initiated by mercury salts serving as promoters in stoichiometric or sub-stoichiometric amounts,[3] the discovery of platinum- and especially gold-based precatalysts[4,5] has displaced mercury,[6] probably invoking toxicity issues.[7] However, from a scientific point of view, prejudices coming from popularly accepted suppositions must be taken with care,[8] because a particular element can be toxic or not depending on the compound considered.[9,10] From an economic point of view, the common practice of using 5% loading in gold catalysis makes its use often impractical in larger scale synthesis in fields such as medicinal chemistry and material science. Compared with noble-metal catalysts, extremely expensive and with diminishing reserves, mercury-based methods have obvious economic attractiveness. In light of these facts, we decide to investigate the catalytic profile of $Hg(ClO_4)_2 \cdot 3H_2O$,[11] a cheap, water-tolerant, and stable salt,[12,13] for the cycloisomerization of allenols.

RESULTS AND DISCUSSION

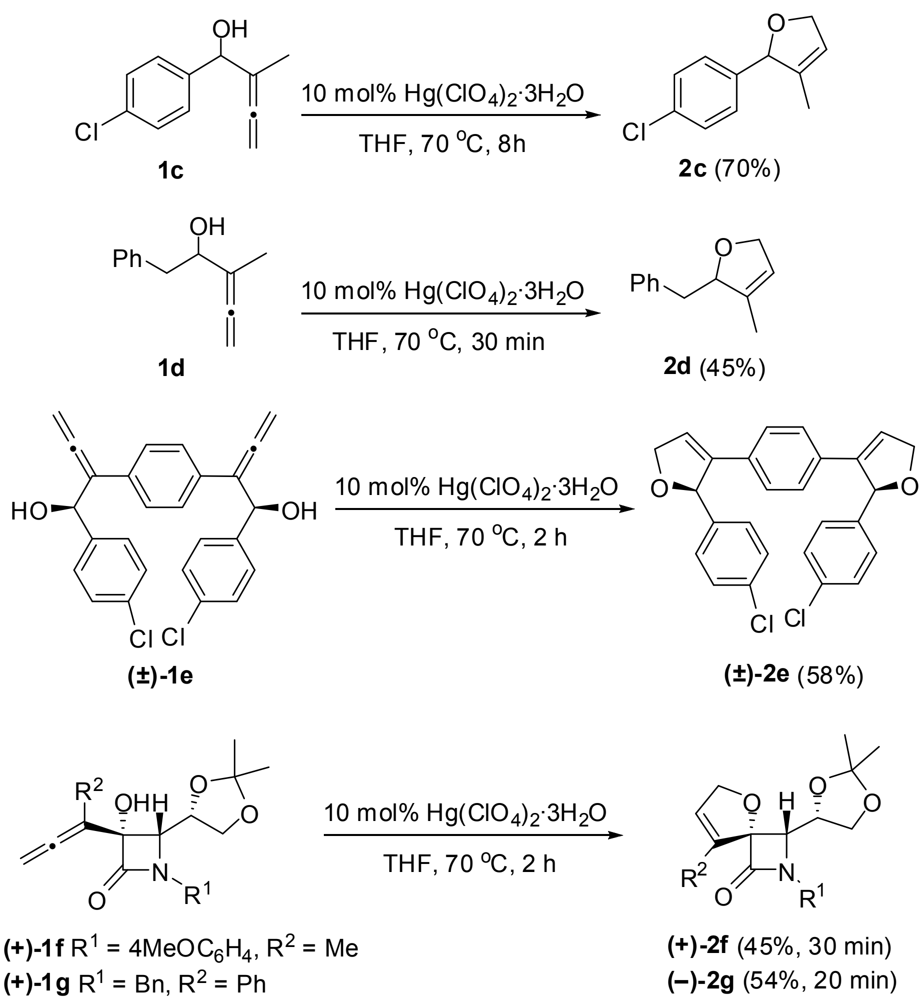
Starting allenols **1a–l** were prepared from the appropriate carbonyl derivative via regiocontrolled indium-mediated Barbier-type carbonyl–allenylation reaction in aqueous media adopting our previously reported methodology.[14] Allene **1a** was chosen as a model substrate for Hg(II)-catalyzed cycloetherification reactions. To screen the reactivity of the α-allenol moiety, several conditions were screened. While $Hg(ClO_4)_2 \cdot 3H_2O$ could catalyze the heterocyclization reaction of **1a** to 2,5-dihydrofuran **2a** in several solvents such as 1,2-dichloroethane, acetonitrile, and THF, the mercury-based catalytic system gave the desired product **2a** in low yield when DMF or THF–H_2O (1:1) were used (Table S1 in the Supporting Information). Treatment of α-allenol **1a** with $Hg(ClO_4)_2 \cdot 3H_2O$ (10 mol%) in THF at 70°C on a sealed tube afforded the best yield of the corresponding adduct **2a**, from a 5-*endo* oxycyclization, as a single isomer (Scheme 1). Interestingly, under gold catalysis α-allenol **1a** delivered fused bicycle **3a**, carbocyclization adduct, in addition to 2,5-dihydrofuran **2a** (Scheme 1). A similar reaction course was encountered through the use of α-allenol **1b**. The $AuCl_3$-catalyzed reaction afforded a separable mixture of 2,5-dihydrofuran **2b** and naphthalene **3b**, while the $Hg(ClO_4)_2 \cdot 3H_2O$-catalyzed reaction was totally selective towards the oxycyclization adduct **2b** (Scheme 1). Thus, it has been shown that $Hg(ClO_4)_2 \cdot 3H_2O$ is a more selective cycloetherification catalyst than $AuCl_3$. Different Hg(II) salts such as $HgCl_2$, $Hg(AcO)_2$, and $Hg(TfO)_2$ were also tested. The corresponding dihydrofuran was the major reaction product under catalytic $Hg(TfO)_2$ conditions. However, the use of either 10 mol% $HgCl_2$ or 10 mol% $Hg(AcO)_2$ did not get the reaction to completion. Dihydrofuran adducts **2** were afforded as minor products along with degradation products. Comparatively, the use of mercurium salts different to $Hg(ClO_4)_2.3H_2O$ led to limited reactivity.

Scheme 1. Gold- versus mercury-catalyzed cyclization reaction of α-allenols 1a and 1b.



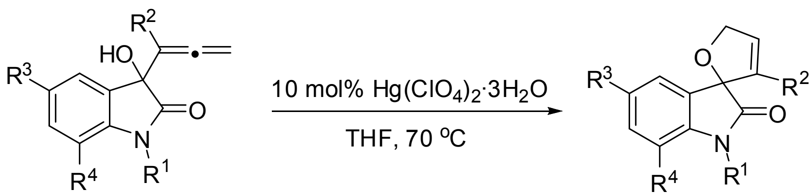
Under the optimized reaction conditions, we investigated the generality of the mercury-catalyzed transformation of differently substituted α-allenols **1c–m**. As shown in Scheme 2 and Scheme 3, the above process serves as a general approach to 2,5-dihydrofurans **2c–m**. Nicely, bis(α-allenol) **1e** undergoes the double transformation to give bi(2,5-dihydrofuran) **2e**. To assess scope, the even more challenging enantiopure allenyl-tethered 2-azetidinones **1f** and **1g** were tested as cyclization precursors, giving the desired spirocyclic dihydrofuran-β-lactams **2f** and **2g**. Notably, despite that Lewis acids are well known for their ability to promote acetonide cleavage, no traces of diols were detected from tertiary α-allenols **1f** and **1g** (Scheme 2).[15]

Scheme 2. Controlled mercury-catalyzed oxycyclization of α-allenols 1c–g.



Encouraged by the above results, 3-allenyl 3-hydroxyoxindoles **1h–m** were studied to determine the applicability of the Hg(II)-catalyzed method (Table S2 in the Supporting Information) for the preparation of the spiroindolinone framework,[16] which is an important structural motif in biologically relevant compounds.[17] Nicely, 2-indolinone-tethered allenic alcohols **1h–m** responded well to the oxycyclization reaction, affording reasonable yields of spiroindolinones **2h–m** (Scheme 3).

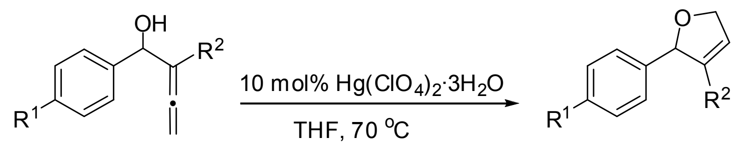
Scheme 3. Controlled mercury-catalyzed oxycyclization of 2-indolinone-tethered α-allenols 1h–m.



1h R^1 = H, R^2 = Me, R^3 = R^4 = H — **2h** (80%; 1.5 h)
1i R^1 = H, R^2 = 4-MeOC_6H_4, R^3 = R^4 = H — **2i** (56%; 1.5 h)
1j R^1 = Me, R^2 = Me, R^3 = R^4 = H — **2j** (75%; 3 h)
1k R^1 = Me, R^2 = Ph, R^3 = R^4 = H — **2k** (67%; 3 h)
1l R^1 = Me, R^2 = Me, R^3 = Cl, R^4 = H — **2l** (73%; 2 h)
1m R^1 = Me, R^2 = Me, R^3 = H, R^4 = Cl — **2m** (87%; 1 h)

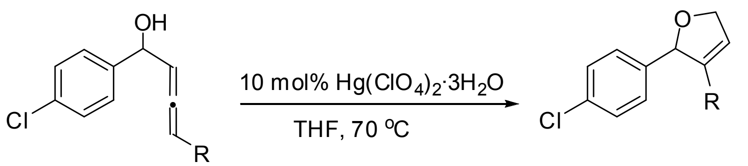
Since the above examples bear either electron donating or weakly electron withdrawing groups, we prepared cyano- and carboxyethyl-allenol derivatives **1n** and **1o**. Pleasingly, exposure of each of these electron-poor substrates to the mercury salt gave the corresponding 2,5-dihydrofurans **2n** and **2o** in good yields (Scheme 4). By contrast, if an ester group is placed at the terminal carbon of the allene, such as in allenol **1p**, the cycloetherification reaction did not proceed (Scheme 4). Likewise, exposure of allenol **1q** with a mono-substituted allene moiety under the optimized conditions did not give rise to the expected heterocycle (Scheme 4). It should be noted that we observed a similar unselective process for the $AuCl_3$-catalyzed reaction of unsubstituted allenol **1q**.

Scheme 4. Mercury-catalyzed reaction of α-allenols 1n–q.



1n R^1 = CN, R^2 = Ph
1o R^1 = COOMe, R^2 = Me

2n (63%, 4 h)
2o (72%, 1.5 h)

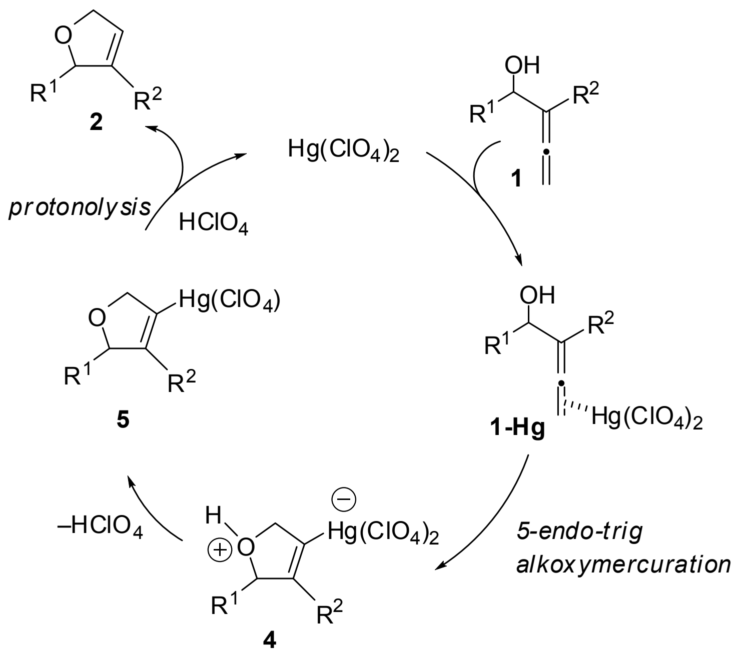


1p R = COOEt
1q R = H

(degradation products, 8h)
(degradation products, 4h)

A possible mechanism for the catalytic achievement of dihydrofurans **2** involving a mercury-based carbophilic π-acid may proceed through initial η-coordination of the metal to the distal double bond of allenols **1** leading to species **1-Hg**. Next, 5-*endo*-trig alkoxymercuration forms zwitterionic dihydrofurans **4**. Loss of $HClO_4$ in intermediates **4** generates neutral vinylmetal species **5**. Protonolysis of the carbon–mercury bond of **5** liberates dihydrofurans **2** with concomitant regeneration of the Hg(II) catalytic species (Scheme 5).

Scheme 5. Initially proposed mechanistic explanation for the mercury-catalyzed cycloetherification of allenols 1.



Density functional theory (DFT) calculations have been carried out to rationalize the divergent chemoselectivity observed for the Hg- and Au-catalyzed reactions of α-allenols **1a** and **1b**.

These metals are known as excellent π-activators and, more generally, soft Lewis acids. These properties make them superior as catalysts to other transition and non-transition metals for the addition of carbon and heteroatom nucleophiles to unsaturated C–C bonds.[18] Au(III) complexes form 16e^- square-planar structures, which is typical of a metal complex with a d^8 electron count, with a vacant coordination site that easily admit extra-coordination to a new molecule (to give an 18e^- species). In contrast, the Hg(II) species is a d^{10} that prefers to form 14e^- linear complexes. The existence of these linear complexes is explained by the high stabilization of the 6s orbital compared to the 6p: since the LUMO is exclusively composed by the 6s and the 6p orbitals, it has more s-character. Thus, sp-hybridization occurs, giving the linear structure for the metal center. In this case, the access of the reactants must be preceded by the release of the ligands since: a) no oxidative addition is possible, and b) associative addition hardly occurs since π-back donation from the Hg(II) cation is disfavored.[10] These general trends make important differences in the catalytic behavior of both metal-complexes in the cycloisomerization of α-allenols **1**.

Thus, the activation of the allene moiety of **1a** by $Hg(ClO_4)_2$ proceeds with the release of ClO_4^- species from a metal coordination site which is occupied by η^2-coordination of the distal double bond of the allene to give a linear complex, **1a**-Hg (Figure 1). Remarkably, the inspection of the transition structure for the 5-*endo*-trig alkoxymercuration (**TS1**) reveals that the released counteranion ClO_4^- forms an hydrogen-bond with the nucleophile. It suggests a dual activation by the catalyst, as both the electrophile and nucleophile are activated for the intramolecular heterocyclization. This effect is supported by the low activation barrier computed ($\Delta G^{\#}$ = 2.6 kcal/mol). Moreover, it should be noted that **TS1** leads to **5**, not to **4** as proposed in Scheme 4, since the hydroxylic proton is captured by the counteranion, to form $HClO_4$, simultaneously to the formation of the C–O bond. Thus, the vinylmetal **5** is H-bonded to $HClO_4$ through the ether oxygen. The formation of this intermediate structure is highly exothermic (ΔG = –23.2 kcal/mol), so this step is probably irreversible. The subsequent protonolysis step of the carbon–mercury bond of **5** liberates dihydrofuran **2a** with regeneration of the linear $Hg(ClO_4)_2$ catalytic species. This step takes place through **TS2**, –12.9 kcal/mol below **1a**-Hg, and it is strongly exothermic (ΔG = –31.1 kcal/mol). Therefore, this cycloetherification proceeds through a two-step mechanism involving dual activation of the precursor by the catalyst.

In order to verify the ability of the Hg-counteranion to H-bond and its role onto selectivity, we have performed further calculations with $Hg(OTf)_2$ and $Hg(BF_4)_2$. In the former case, slightly higher barriers than for $Hg(ClO_4)_2$ have been computed for the two possible cyclizations (3.3 and 5.9 kcal/mol, for **TS1** and **TS1'**, respectively), which suggest a lower reactivity and the same selectivity. For the catalyst with the less basic anion BF_4^-, however, both barriers are similarly higher (5.9 and 6.5 kcal/mol, for **TS1** and **TS1'**, respectively). Moreover, the evolution of **TS1** leads to an intermediate where the H remains partially attached to the oxygen (1.167 Å vs 1.568 for $Hg(OTf)_2$ and 1.722 Å for $Hg(ClO_4)_2$).

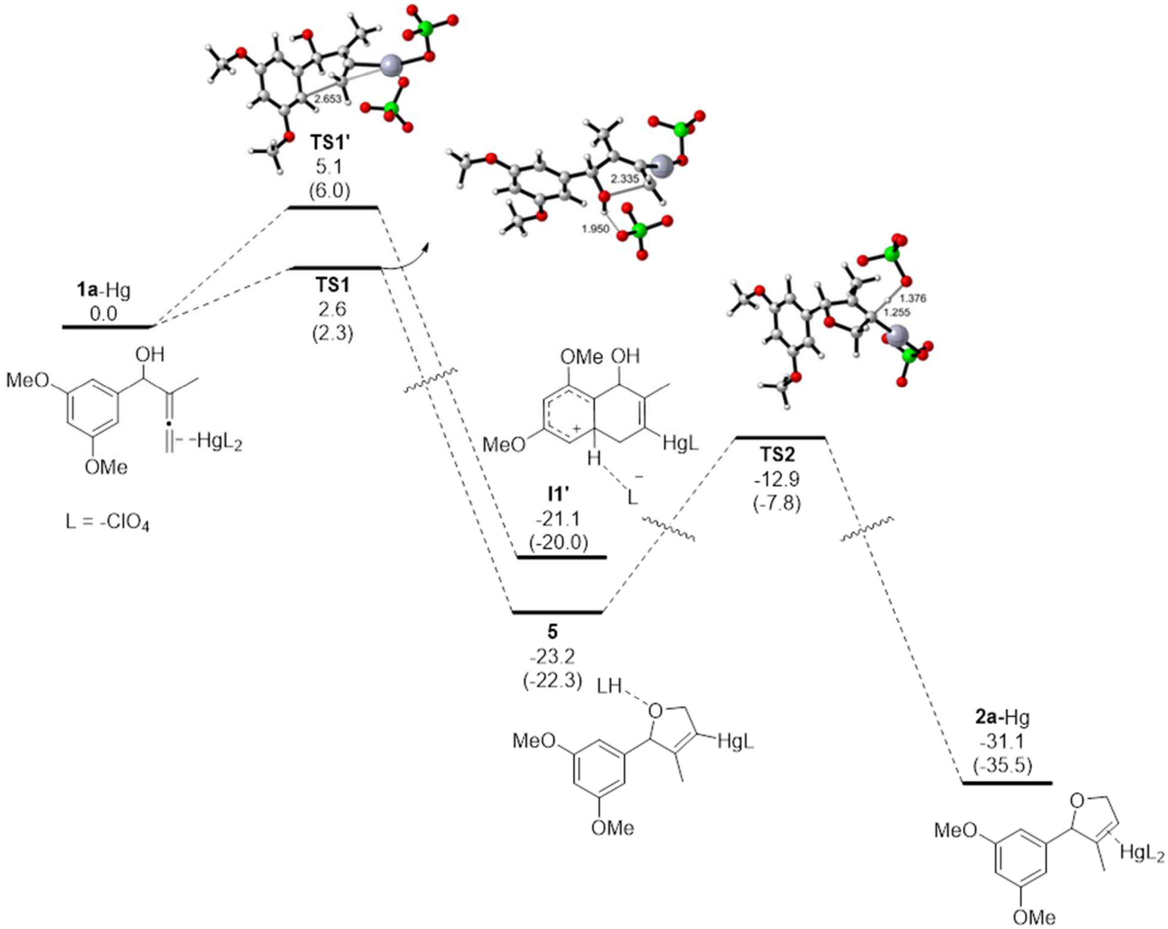


Figure 1. Computed reaction profile (PCM(THF)-M06/6-31+G(2d,p)/SDD(Hg)//M06/6-31+G(2d,p)/SDD(Hg) level) for the cycloisomerization of allenol **1a** catalyzed by $Hg(ClO_4)_2$. Gas-phase results are shown in parenthesis. Relative free energies are given in kcal/mol and bond lengths in the transition states in angstroms.

The plausible hydroarylation to form naphthalene should take place probably via initial 6-*endo*-trig cyclization of **1a**-Hg following a Friedel–Crafts-type mechanism.[19] This carbocyclization step affords the Wheland-type intermediate **I1’** through the transition structure **TS1’** (Figure 1), 2.5 kcal/mol higher in energy than **TS1**. In addition, the intermediate **I1’** is 2.1 kcal/mol less stable than **5**. Hence, the 5-*endo*-trig oxycyclization is the preferred cyclization mode from kinetic and thermodynamic viewpoints, and these energy differences clearly support the chemoselective formation of the 2,5-dihydrofuran skeleton under $Hg(ClO_4)_2$ catalysis.

On the other hand, the $AuCl_3$ complex presents a vacant coordination site that can be occupied by the allene moiety to form a square-planar complex, **1a**-Au. Thus, the 5-*endo*-trig oxycyclization step takes places with an activation barrier of 4.9 kcal/mol and drives to a zwitterionic intermediate, **I1$_{Au}$**, 6.2 kcal/mol more stable than the reactant complex **1a**-Au (Figure 2). Amazingly, the calculations show that the nucleophillic addition of the arene to the gold(III)-activated allene is more favourable, requiring an activation free energy of only 1.5 kcal/mol *via* transition state **TS1'$_{Au}$**. Moreover, the formation of the Wheland-type intermediate **I1'$_{Au}$** is strongly exothermic (by 27.7 kcal/mol), and hence likely irreversible. This step leads to a C–C bond formation between the allene and the aromatic core. The formation of the naphthalene framework **3a** then takes place via stepwise rearomatization. Thus, calculations suggest that **I1'$_{Au}$** drives to **I2'$_{Au}$** (ΔG = –27.0 kcal/mol), through a deprotonation process assisted by a chloride ligand via **TS2'$_{Au}$** ($\Delta G^{\#}$ = –5.8 kcal/mol). Then, the released HCl promotes the protonation of the hydroxylic substituent and formation of a water molecule. This step proceeds through **TS3'$_{Au}$** ($\Delta G^{\#}$ = –10.8 kcal/mol), which shows the advanced formation of the O–H bond (1.033 Å) and breaking of the O–C bond (2.031 Å). The subsequent step is the aromatization through a deprotonation process assisted by the chloride anion. The transition state **TS4'$_{Au}$** for this step needs a low activation energy ($\Delta G^{\#}$ = –13.0 kcal/mol), and drives to the formation of the aromatic intermediate **I4'$_{Au}$** and HCl in a strongly exothermic step (ΔG = –54.1 kcal/mol) due to the high stability of the aromatic bicycle.[20] Finally, this intermediate undergoes demetalation by protonolysis to yield the hydroarylation product and regenerates the gold(III) catalyst. This transformation occurs via **TS5'$_{Au}$** ($\Delta G^{\#}$ = –34.2 kcal/mol), and leads to the expected formation of naphthalene **3a**-Au (ΔG = –63.7 kcal/mol). Therefore, the favoured reaction of α-allenols **1** under Au(III)-catalysis proceeds through initial π-complexation of the allene moiety, which triggers the nucleophilic attack of the arene *via* an *endo*-trig carbocyclization pathway in a Friedel–Crafts-type mechanism.

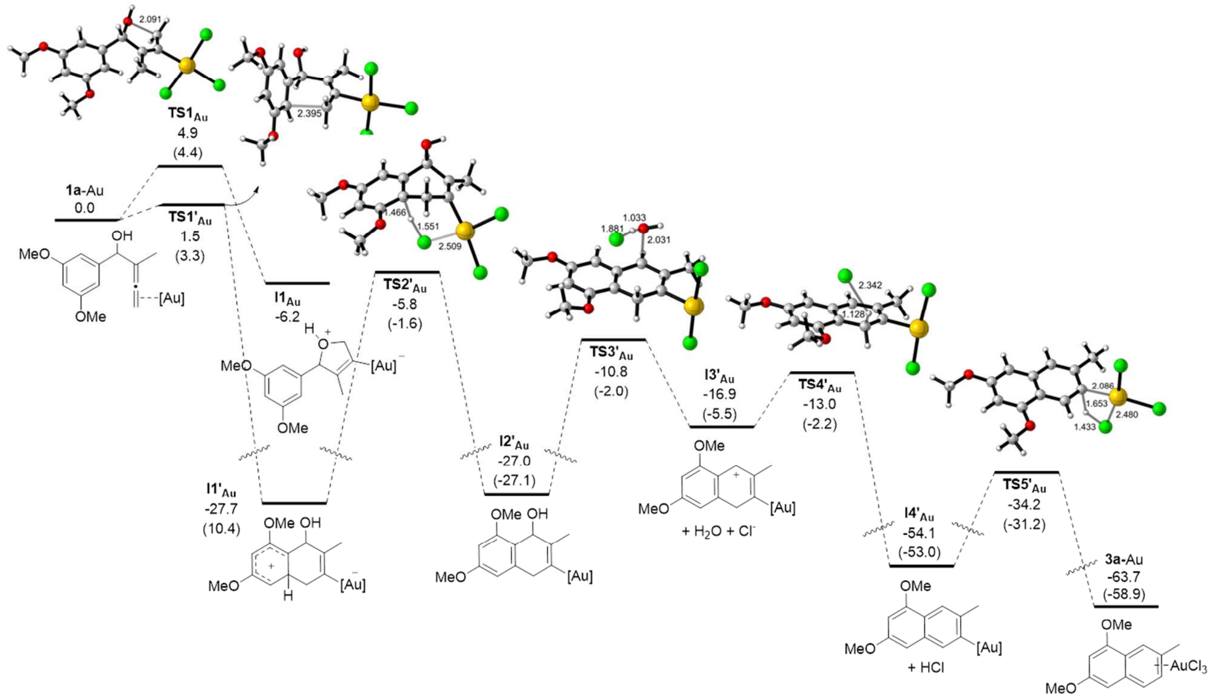


Figure 2. Computed reaction profile (PCM(CH_2Cl_2)-M06/6-31+G(2d,p)/SDD(Au)//M06/6-31+G(2d,p)/SDD(Au) level) for the cycloisomerization of allenol **1a** catalyzed by $AuCl_3$. Gas-phase results are shown in parenthesis. Relative free energies are given in kcal/mol and bond lengths in the transition states in angstroms.

Conclusions

In conclusion, $Hg(ClO_4)_2 \cdot 3H_2O$, a cheap, water-tolerant, and stable salt,[21] catalyzes the heterocyclization reaction or α-allenols.[22] Thus, differently functionalized 2,5-dihydrofurans can be obtained in an efficient and selective manner. The possibility of using optically active substrates as well as substrates of increased steric demand, such as tertiary α-allenols, expands the attractiveness of the method. Besides, density functional theory (DFT) calculations were performed to obtain an insight into various aspects of the controlled reactivity of α-allenols under mercury catalysis. They suggest a dual activation of the allenol by the Hg-complex that drives the reaction to the chemoselective formation of 2,5-dihydrofurans.

Experimental Section

General methods: NMR spectra were recorded at 25 ^{o}C on a 300 or a 700 MHz instruments. Chemical shifts are given in ppm relative to TMS (^{1}H, 0.0 ppm), or $CDCl_3$ (^{13}C, 76.9

ppm). Low and high resolution mass spectra were taken on a QTOF LC/MS spectrometer using the electronic impact (EI) or electrospray modes (ES). Specific rotation $[\alpha]_D$ is given in 10^{-1} deg cm^2 g^{-1} at 20 °C, and the concentration (*c*) is expressed in g per 100 mL. All commercially available compounds were used without further purification.

Previously unreported α-allenic alcohols 1b and (±)-1e were prepared adopting our general procedure.[14] 2-Methyl-1-(2-phenoxyphenyl)buta-2,3-dien-1-ol 1b. From 235 mg (2.19 mmol) of 2-phenoxybenzaldehyde, and after chromatography of the residue using hexanes/ethyl acetate (8:1) as eluent gave compound **1b** (337 mg, 61%) as a colorless oil; ^{1}H-NMR (300 MHz, $CDCl_3$, 25 °C) δ: 7.49 (dd, *J* = 7.5, 1.8 Hz, 1H), 7.33 (t, *J* = 7.6 Hz, 2H), 7.25 (td, *J* = 8.0, 1.8 Hz, 1H), 7.16 (td, *J* = 7.4, 1.2 Hz, 1H), 7.10 (t, *J* = 7.4 Hz, 1H), 6.98 (d, *J* = 7.6 Hz, 2H), 6.88 (dd, *J* = 8.0, 1.2 Hz, 1H), 5.42 (m, 1H), 4.74 (qu, *J* = 3.1 Hz, 2H), 2.56 (d, *J* = 6.0 Hz, 1H), 1.65 (t, *J* = 3.1 Hz, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$, 25 °C) δ: 205.0, 157.4, 154.3, 133.0, 129.7 (2C), 128.8, 128.3, 123.7, 123.0, 119.1, 118.3 (2C), 102.1, 77.7, 70.0, 15.0; IR ($CHCl_3$, cm^{-1}): ν 3419, 3065, 1483, 1230, 751, 691; HRMS (ES): calcd for $C_{17}H_{16}O_2$ $[M]^+$: 252.1150; found: 252.1147.

(*SR*)-1-(4-chlorophenyl)-2-(4-((RS)-1-(4-chlorophenyl)-1-hydroxybuta-2,3-dien-2-yl)phenyl)buta-2,3-dien-1-ol (±)-1e. From 169 mg (1.2 mmol) of 4-chlorobenzaldehyde, and after chromatography of the residue using hexanes/ethyl acetate (2:1) as eluent, gave compound (±)-**1e** (120 mg, 45%) as a yellow oil; ^{1}H-NMR (300 MHz, acetone-δ_6, 25 °C) δ: 7.48 (d, *J* = 8.5 Hz, 4H), 7.31 (d, *J* = 8.5 Hz, 4H), 5.77 (d, *J* = 5.0 Hz, 2H), 5.11 (m, 4H), 4.96 (d, *J* = 5.0 Hz, 2H); ^{13}C-NMR (75 MHz, acetone-δ_6, 25 °C) δ: 210.0 (2C), 143.4 (2C), 133.9 (2C), 133.0 (2C), 129.3 (4C), 128.8 (4C), 128.0 (4C), 110.2 (2C), 80.0, 79.9, 72.8 (2C); IR ($CHCl_3$, cm^{-1}): ν 3397, 1937, 1701, 1089, 1014; HRMS (ES): calcd for $C_{26}H_{20}Cl_2O_2$ $[M]^+$: 434.0840; found: 434.0829.

4-(1-Hydroxy-2-phenylbuta-2,3-dienyl)benzonitrile 1n. From 200 mg (1.5 mmol) of 4-formylbenzonitrile, and after chromatography of the residue using hexanes/ethyl acetate (4:1) as eluent, gave compound **1n** (157 mg, 44%) as a colorless oil; ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC) δ: 7.62 (d, *J* = 8.4 Hz, 2H), 7.55 (d, *J* = 8.4 Hz, 2H), 7.30 (m, 5H), 5.80 (s, 1H), 5.22 (m, 2H), 2.44 (br s, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$, 25 ºC) δ: 207.9, 147.2, 133.2, 132.0, 128.6, 127.5, 127.3, 126.8, 118.7, 111.4, 109.3, 81.3, 72.1; IR ($CHCl_3$, cm^{-1}): ν 3455, 2230, 1711, 853; HRMS (ES): calcd for $C_{17}H_{13}NO$ $[M]^+$: 247.0997; found: 247.0992.

Methyl 4-(1-hydroxy-2-methylbuta-2,3-dienyl)benzoate 1o. From 330 mg (2.0 mmol) of methyl 4-formylbenzoate, and after chromatography of the residue using hexanes/ethyl acetate (5:1) as eluent, gave compound **1o** (284 mg, 65%) as a colorless oil; ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC) δ: 7.98 (d, *J* = 8.2 Hz, 2H), 7.42 (d, *J* = 8.2 Hz, 2H), 5.18 (s, 1H), 4.84 (m, 2H), 3.88 (s, 3H), 2.77 (br s, 1H) 1.54 (t, *J* = 3.1 Hz, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$, 25 ºC) δ: 205.0, 166.9, 147.0, 129.5, 129.2, 126.3, 101.9, 77.4, 74.3, 51.9, 13.9; IR ($CHCl_3$, cm^{-1}): ν 3471, 1720, 1279, 1112; HRMS (ES): calcd for $C_{13}H_{14}O_3$ $[M]^+$: 218.0943; found: 218.0939.

General procedure for the $Hg(ClO_4)_2$·$3H_2O$-catalyzed reaction of allenols 1. Preparation of dihydrofurans 2. $Hg(ClO_4)_2$·$3H_2O$ (0.014 mmol) was added to a solution of the appropriate allenol **1** (0.14 mmol) in THF (2.5 mL). The reaction mixture was stirred at 70 ºC on a sealed tube until the starting material disappeared as indicated by TLC. The mixture was concentrated under vacuum, and purified by flash column chromatography eluting with ethyl acetate/hexanes mixtures. Spectroscopic and analytical data for pure forms of compounds **2** follow.

2-(3,5-Dimethoxyphenyl)-3-methyl-2,5-dihydrofuran 2a. From 34 mg (0.15 mmol) of allenol **1a**, and after chromatography of the residue using hexanes/ethyl acetate (6:1) as eluent, gave compound **2a** (19 mg, 57%) as a colorless oil; ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC) δ: 6.44 (d, *J* = 2.2 Hz, 2H), 6.40 (m, 1H), 5.63 (m, 1H), 5.41 (m, 1H), 4.84 (m, 1H), 4.70 (m, 1H), 3.79 (s, 6H), 1.58 (m, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$, 25 ºC) δ: 160.9(2C), 143.9, 138.4, 120.8, 104.7

(2C), 99.8, 90.5, 75.4, 55.3 (2C), 12.5; IR ($CHCl_3$, cm^{-1}): ν 1596, 1153; HRMS (ES): calcd for $C_{13}H_{17}O_3$ $[M + H]^+$: 221.1178; found: 221.1175.

3-Methyl-2-(2-phenoxyphenyl)-2,5-dihydrofuran 2b. From 123 mg (0.49 mmol) of allenol **1b**, and after chromatography of the residue using hexanes/ethyl acetate (7:1) as eluent, gave compound **2b** (82 mg, 66%) as a colorless oil; ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC) δ: 7.30 (dd, J = 7.5, 1.7 Hz, 1H), 7.23 (t, J = 8.0 Hz, 2H), 7.15 (t, J = 7.7 Hz, 1H), 7.06 (t, J = 7.4 Hz, 1H), 6.98 (d, J = 6.9 Hz, 1H), 6.89 (d, J = 7.7 Hz, 2H), 6.80 (d, J = 8.0 Hz, 1H), 5.90 (br s, 1H), 5.51 (m, 1H), 4.74 (m, 1H), 4.60 (m, 1H), 1.55 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$, 25 ºC) δ: 157.7, 154.1, 138.5, 133.0, 129.6 (2C), 128.9, 128.5, 124.1, 122.8, 120.7, 119.2, 118.0 (2C), 84.1, 75.4, 12.6; IR ($CHCl_3$, cm^{-1}): ν 3067, 1757, 1483, 1231, 753, 693; HRMS (ES): calcd for $C_{17}H_{16}O_2$ $[M]^+$: 252.1150; found: 252.1147.

2-(4-Chlorophenyl)-3-methyl-2,5-dihydrofuran 2c. From 35 mg (0.18 mmol) of allenol **1c**, and after chromatography of the residue using hexanes/ethyl acetate (5:1) as eluent, gave compound **2c** (25 mg, 70%) as a colorless oil; ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC) δ: 7.32 (d, J = 8.5 Hz, 2H), 7.21 (d, J = 8.5 Hz, 2H), 5.65 (m, 1H), 5.46 (m, 1H), 4.84 (m, 1H), 4.71 (m, 1H), 1.55 (m, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$, 25 ºC) δ: 140.0, 138.1, 133.5, 128.5 (2C), 128.2 (2C), 121.0, 89.8, 75.5, 12.4; IR ($CHCl_3$, cm^{-1}): ν 1730, 1684, 1091; HRMS (ES): calcd for $C_{11}H_{12}ClO$ $[M + H]^+$: 195.0577; found: 195.0579.

2-Benzyl-3-methyl-2,5-dihydrofuran 2d. From 43 mg (0.24 mmol) of allenol **1d**, and after chromatography of the residue using hexanes/ethyl acetate (9:1) as eluent, gave compound **2d** (19 mg, 45%) as a colorless oil; ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC) δ: 7.27 (m, 5H), 5.44 (q, J = 1.6 Hz, 1H), 4.88 (m, 1H), 4.46 (m, 2H), 3.01 (dd, J = 14.2, 3.9 Hz, 1H), 2.72 (dd, J = 14.2, 6.8 Hz, 1H), 1.74 (q, J = 1.6 Hz, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$, 25 ºC) δ: 138.2, 137.5, 129.4 (2C), 128.0 (2C), 126.0, 121.3, 88.1, 74.4, 40.4, 12.7; IR ($CHCl_3$, cm^{-1}): ν 1759, 1081, 1027; HRMS (ES): calcd for $C_{12}H_{14}O$ $[M]^+$: 174.1045; found: 174.1041.

1-((*RS*)-2-(4-Chlorophenyl)-2,5-dihydrofuran-3-yl)-4-((*SR*)-2-(4-chlorophenyl)-2,5-dihydrofuran-3-yl)benzene (±)-2e. From 41 mg (0.09 mmol) of allenol (±)-**1e**, and after chromatography of the residue using hexanes/ethyl acetate (4:1) as eluent, gave compound (±)-**2e** (23 mg, 58%) as a colorless solid; mp 78–80 ºC; ^{1}H-NMR (700 MHz, $CDCl_3$, 25 ºC) δ: 7.27 (m, 8H), 7.09 (s, 4H), 6.45 (d, J = 1.7 Hz, 1H), 6.42 (d, J = 1.7 Hz, 1H), 6.00 (m, 2H), 4.92 (m, 2H), 4.84 (m, 2H); ^{13}C-NMR (175 MHz, $CDCl_3$, 25 ºC) δ: 139.9 (2C), 139.2 (2C), 134.0 (2C), 131.8, 131.6, 129.0 (2C), 128.9(2C), 128.8 (4C), 126.5 (2C), 126.4 (2C), 123.7, 123.6, 87.3, 87.2, 75.3 (2C); IR ($CHCl_3$, cm^{-1}): ν 1720, 1091, 1014; HRMS (ES): calcd for $C_{26}H_{20}Cl_2O_2$ $[M]^+$: 434.0840; found: 434.0842.

(3*S*,4*R*)-3-((*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl)-2-(4-methoxyphenyl)-8-methyl-5-oxa-2-azaspiro[3.4]oct-7-en-1-one (+)-2f. From 30 mg (0.087 mmol) of allenol (+)-**1f**, and after chromatography of the residue using hexanes/ethyl acetate (1:1) as eluent, gave compound (+)-**2f** (15 mg, 45%) as a yellow solid; mp 95–97 ºC; $[\alpha]_D$: +6.0 (c 0.53 in $CHCl_2$); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC) δ: 7.72 (d, J = 9.1 Hz, 2H), 6.88 (d, J = 9.1 Hz, 2H), 5.80 (q, J = 1.5 Hz, 1H), 4.82 (dt, J = 13.0, 1.9 Hz, 1H), 4.61 (dt, J = 13.0, 1.9 Hz, 1H), 4.46 (m, 1H), 4.26 (dd, J = 8.6, 7.1 Hz, 1H), 4.08 (d, J = 8.6 Hz, 1H), 3.80 (s, 3H), 3.55 (dd, J = 8.6, 6.3 Hz, 1H), 1.76 (q, J = 1.9 Hz, 3H), 1.54 (s, 3H), 1.34 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$, 25 ºC) δ: 165.9, 156.5, 132.7, 130.9, 124.8, 119.7 (2C), 114.0 (2C), 109.8, 99.6, 77.2, 76.3, 66.5, 66.3, 55.4, 26.6, 24.6, 10.9; IR ($CHCl_3$, cm^{-1}): ν 1752; HRMS (ES): calcd for $C_{19}H_{24}NO_5$ $[M + H]^+$: 346.1654; found: 346.1665.

(3*SR*,4*RS*)-2-Benzyl-3-((*S*)-2,2-dimethyl-1,3-dioxolan-4-yl)-8-phenyl-5-oxa-2-azaspiro[3.4]oct-7-en-1-one (–)-2g. From 29 mg (0.074 mmol) of allenol (+)-**1g**, and after chromatography of the residue using hexanes/ethyl acetate (2:1) as eluent, gave compound (–)-**2g**

(16 mg, 54%) as a colorless oil; $[\alpha]_D$: –22.2 (c 0.5 in $CHCl_2$); ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC) δ: 7.20 (m, 10 H), 6.23 (t, *J* = 1.8 Hz, 1H), 4.97 (dd, *J* = 14.1, 1.8 Hz, 1H), 4.83 (d, *J* = 14.4 Hz, 1H), 4.69 (dd, *J* = 14.1, 1.8 Hz, 1H), 4.46 (m, 1H), 4.25 (d, *J* = 14.4 Hz, 1H), 4.13 (dd, *J* = 8.5, 7.0 Hz, 1H), 3.47 (d, *J* = 7.9 Hz, 1H), 3.43 (dd, *J* = 8.5, 6.0 Hz, 1H), 1.33 (s, 3H), 1.31 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$, 25 ºC) δ: 167.9, 158.2, 134.8, 131.2, 129.1, 128.6, 128.4, 128.3, 127.5, 126.9, 126.5, 109.7, 99.8, 77.2, 76.0, 66.3, 64.4, 45.3, 26.5, 24.8; IR ($CHCl_3$, cm^{-1}): ν 1753; HRMS (ES): calcd for $C_{24}H_{26}NO_4$ $[M + H]^+$: 392.1862; found: 392.1875.

3-Methyl-5*H*-spiro[furan-2,3'-indolin]-2'-one 2h. From 30 mg (0.15 mmol) of allenol **1h**, and after chromatography of the residue using hexanes/ethyl acetate (2:1) as eluent, gave compound **2h** (24 mg, 80%) as a yellow oil; ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ^{o}C) δ: 8.76 (br, 1H), 7.25 (td, *J* = 7.7, 1.3 Hz, 1H), 7.19 (m, 1H), 7.05 (td, *J* = 7.5, 1.0 Hz, 1H), 6.89 (d, *J* = 7.8 Hz, 1H), 5.98 (m, 1H), 5.03 (dquin, *J* = 12.4, 2.0 Hz, 1H), 4.94 (dquin, *J* = 12.4, 2.0 Hz, 1H), 1.50 (q, *J* = 2.0 Hz, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$, 25 ^{o}C) δ: 178.3, 141.0, 135.8, 130.0, 128.7, 124.8, 124.7, 123.2, 110.4, 93.0, 76.5, 11.1; IR ($CHCl_3$, cm^{-1}): ν 3256, 1726, 1619; HRMS (ES): calcd for $C_{12}H_{11}NO_2$ $[M]^+$: 201.0790; found: 201.0793.

3-(4-Methoxyphenyl)-5*H*-spiro[furan-2,3'-indolin]-2'-one 2i. From 30 mg (0.10 mmol) of allenol **1i**, and after chromatography of the residue using hexanes/ethyl acetate (2:1) as eluent, gave compound **2i** (16.5 mg, 56%) as a yellow oil; ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ^{o}C) δ: 8.28 (br, 1H), 7.25 (m, 2H), 7.02 (m, 2H), 6.89 (d, *J* = 7.7 Hz, 1H), 6.68 (d, *J* = 8.8 Hz, 1H), 6.54 (t, *J* = 1.8 Hz, 1H), 5.15 (dd, *J* = 13.5, 1.8 Hz, 1H), 5.06 (dd, *J* = 13.5, 1.8 Hz, 1H), 3.70 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$, 25 ^{o}C) δ: 177.5, 159.4, 140.9, 138.4, 130.3, 129.2, 127.4 (2C), 125.6, 125.3, 124.1, 123.4, 113.9 (2C), 110.5, 91.0, 76.0, 55.1; IR ($CHCl_3$, cm^{-1}): ν 1725; HRMS (ES): calcd for $C_{18}H_{15}NO_3$ $[M]^+$: 293.1052; found: 293.1061.

1',3-Dimethyl-5*H*-spiro[furan-2,3'-indolin]-2'-one 2j. From 30 mg (0.14 mmol) of allenol **1j**, and after chromatography of the residue using hexanes/ethyl acetate (4:1) as eluent, gave compound **2j** (22 mg, 75%) as a colorless oil; ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC) δ: 7.32 (td, J = 7.7, 1.2 Hz, 1H), 7.20 (d, *J* = 6.3 Hz, 1H), 7.07 (t, *J* = 7.5 Hz, 1H), 6.82 (d, *J* = 7.7 Hz, 1H), 5.96 (q, *J* = 1.5 Hz, 1H), 5.01 (dt, *J* = 12.4, 1.9 Hz, 1H), 4.90 (dt, *J* = 12.4, 1.9 Hz, 1H), 3.20 (s, 3H), 7.07 (m, 2H), ^{13}C-NMR (75 MHz, $CDCl_3$, 25 ºC) δ: 175.6, 144.0, 135.8, 130.0, 128.3, 124.9, 124.4, 123.1, 108.2, 92.4,76.3, 26.3, 11.1; IR ($CHCl_3$, cm^{-1}): ν 1715; HRMS (ES): calcd for $C_{13}H_{14}NO_2$ $[M + H]^+$: 216.1025; found: 216.1031.

1'-Methyl-3-phenyl-5*H*-spiro[furan-2,3'-indolin]-2'-one 2k. From 25 mg (0.09 mmol) of allenol **1k**, and after chromatography of the residue using hexanes/ethyl acetate (2:1) as eluent, gave compound **2k** (17 mg, 67%) as a yellow solid; mp 144–146 ºC;^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC) δ: 7.26 (td, *J* = 7.7, 1.1 Hz, 1H), 7.19 (m, 2H), 7.07 (m, 2H), 6.97 (td, *J* = 7.5, 0.8 Hz, 1H), 6.91 (m, 2H), 6.78 (d, *J* = 7.9 Hz, 1H), 6.57 (q, *J* = 1.8 Hz, 1H), 5.09 (dd, *J* = 13.6, 1.8 Hz, 1H), 4.99 (dd, *J* = 13.6, 1.8 Hz, 1H), 3.15 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$, 25 ºC) δ: 175.1, 144.0, 139.0, 131.7, 130.4, 128.7, 128.4 (2C), 128.0, 127.5, 126.1 (2C), 124.9, 123.4, 108.5, 90.7, 75.8, 26.4; IR ($CHCl_3$, cm^{-1}): ν 1725, 1612; HRMS (ES): calcd for $C_{18}H_{16}NO_2$ $[M + H]^+$: 278.1181; found: 278.1180.

5'-Chloro-1',3-dimethyl-5*H*-spiro[furan-2,3'-indolin]-2'-one 2l. From 30 mg (0.12 mmol) of allenol **1l**, and after chromatography of the residue using hexanes/ethyl acetate (2:1) as eluent, gave compound **2l** (22 mg, 73%) as a yellow oil; ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC) δ: 7.29 (dd, *J* = 8.3, 2.2 Hz, 1H), 7.18 (d, *J* = 2.2 Hz, 1H), 6.75 (d, *J* = 8.3 Hz, 1H), 5.97 (q, *J* = 1.5 Hz, 1H), 5.00 (dt, *J* = 12.4, 2.0 Hz, 1H), 4.90 (dt, *J* = 12.4, 2.0 Hz, 1H), 3.18 (s, 3H), 1.44 (q, *J* = 2.0 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$, 25 ºC) δ: 175.2, 142.4, 135.2, 130.0, 129.9, 128.6, 125.3, 124.9, 109.2, 92.3, 76.5, 26.4, 11.1; IR ($CHCl_3$, cm^{-1}): ν 1729, 1487; HRMS (ES): calcd for $C_{13}H_{13}ClNO_2$ [M + H]$^+$: 250.0635; found: 250.0612.

7'-Chloro-1',3-dimethyl-5*H*-spiro[furan-2,3'-indolin]-2'-one 2m. From 31 mg (0.12 mmol) of allenol **1m**, and after chromatography of the residue using hexanes/ethyl acetate (4:1) as eluent, gave compound **2m** (26 mg, 87%) as a yellow solid; mp 81–83 ºC; ^{1}H-NMR (300 MHz, $CDCl_3$, 25 °C) δ: 7.25 (m, 1H), 7.09 (dd, J = 7.2, 1.1 Hz, 1H), 6.99 (t, J = 7.7 Hz, 1H), 5.97 (q, J = 1.5 Hz, 1H), 5.00 (dt, J = 12.4, 1.9 Hz, 1H), 4.90 (dt, J = 12.4, 1.9 Hz, 1H), 3.57 (s, 3H), 1.44 (q, J = 1.9 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$, 25 °C) δ: 175.9, 139.7, 135.5, 132.2, 131.2, 125.1, 123.9, 123.0, 115.7, 91.8, 76.5, 29.7, 11.1; IR ($CHCl_3$, cm^{-1}): ν 1734, 1461; HRMS (ES): calcd for $C_{13}H_{12}ClNO_2$ [M]$^+$: 249.0557; found: 249.0551.

4-(3-Phenyl-2,5-dihydrofuran-2-yl)benzonitrile 2n. From 40 mg (0.16 mmol) of allenol **1n**, and after chromatography of the residue using hexanes/ethyl acetate (7:1) as eluent, gave compound **2n** (24 mg, 63%) as a colorless oil; ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC) δ: 7.35 (s, 4H), 7.14 (m, 3H), 7.09 (d, J = 3.0 Hz, 2H), 6.05 (td, J = 4.6, 1.8 Hz, 1H), 5.98 (q, J = 1.9 Hz, 1H), 4.76 (d, J = 1.9 Hz, 1H), 4.74 (m, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$, 25 ºC) δ: 146.7, 141.3, 133.0, 132.7, 129.0, 128.6, 128.5, 127.2, 124.2, 119.0, 112.8, 87.9, 76.1; IR ($CHCl_3$, cm^{-1}): ν 2230, 1758, 843; HRMS (ES): calcd for $C_{17}H_{13}NO$ [M]$^+$: 247.0997; found: 247.1005.

Methyl 4-(3-methyl-2,5-dihydrofuran-2-yl)benzoate 2o. From 40 mg (0.18 mmol) of allenol **1o**, and after chromatography of the residue using hexanes/ethyl acetate (6:1) as eluent, gave compound **2o** (28 mg, 72%) as a colorless oil; ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC) δ: 8.16 (d, J = 8.4 Hz, 2H), 7.17 (m, 2H), 5.38 (m, 1H), 5.13 (q, J = 1.6 Hz, 1H), 4.61 (m, 2H) 3.50 (s, 3H), 1.23 (t, J = 1.3 Hz, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$, 25 ºC) δ: 137.0, 147.9, 138.8, 130.7, 130.5, 127.3, 121.7, 90.5, 76.1, 51.9, 12.6; IR ($CHCl_3$, cm^{-1}): ν 1723, 1281, 1112; HRMS (ES): calcd for $C_{13}H_{14}O_3$ [M]$^+$: 218.0943; found: 218.0938.

$AuCl_3$-catalyzed reaction of allenol 1a. $AuCl_3$ (2 mg, 0.0065 mmol) was added to a solution of allenol **1a** (30 mg, 0.13 mmol) in dichloromethane (3 mL). The reaction mixture was stirred at RT until the starting material disappeared as indicated by TLC. Saturated aqueous sodium bicarbonate (1 mL) was added, before being partitioned between dichloromethane and water. The organic extract was washed with brine, dried ($MgSO_4$), and concentrated under vacuum. Chromatography of the residue using hexanes/ethyl acetate (6:1) as eluent gave 12 mg (42%) of the less polar compound **3a** and 5 mg (16%) of the more polar compound **2a**.

1,3-Dimethoxy-6-methylnaphthalene 3a. Colorless oil; ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC) δ: 8.02 (d, *J* = 8.5 Hz, 1H), 7.46 (s, 1H), 7.14 (dd, *J* = 8.5, 1.2 Hz, 1H), 6.66 (d, *J* = 1.9 Hz, 1H), 6.44 (d, *J* = 1.9 Hz, 1H), 3.96 (s, 3H), 3.90 (s, 3H), 2.48 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$, 25 ºC) δ: 158.2, 156.5, 136.7, 135.2, 125.6, 125.0, 121.7, 119.7, 97.4. 96.7, 55.4, 55.2, 21.6; IR ($CHCl_3$, cm^{-1}): ν 2934, 1633, 1154; HRMS (ES): calcd for $C_{13}H_{14}O_2$ $[M]^+$: 202.0994; found: 202.0998.

$AuCl_3$-catalyzed reaction of allenol 1b. $AuCl_3$ (4 mg, 0.013 mmol) was added to a solution of allenol **1b** (62 mg, 0.24 mmol) in dichloromethane (6 mL). The reaction mixture was stirred at RT until the starting material disappeared as indicated by TLC. Saturated aqueous sodium bicarbonate (2 mL) was added, before being partitioned between dichloromethane and water. The organic extract was washed with brine, dried ($MgSO_4$), and concentrated under vacuum. Chromatography of the residue using hexanes/ethyl acetate (10:1) as eluent gave 22 mg (35%) of the less polar compound **2b** and 14 mg (25%) of the more polar compound **3b**.

7-Methyl-1-phenoxynaphthalene 3b. Colorless oil; ^{1}H-NMR (300 MHz, $CDCl_3$, 25 ºC) δ: 7.66 (s, 1H), 7.45 (d, *J* = 7.6 Hz, 1H), 7.32 (m, 3H), 7.16 (m, 3H), 6.97 (m, 3H), 2.36 (s, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$, 25 ºC) δ: 157.2, 155.0, 138.6, 134.9, 130.6, 130.0 (2C), 129.8 (2C), 127.7, 123.3 (2C), 119.3, 119.1, 118.3 (2C), 25.7; IR ($CHCl_3$, cm^{-1}): ν 3065, 1483, 1235, 752, 693; HRMS (ES): calcd for $C_{17}H_{14}O$ $[M]^+$: 234.1045; found: 234.1041.

Acknowledgment. Support for this work by MINECO and FEDER (Projects CTQ2012-33664-C02-01 and CTQ2012-33664-C02-02) and UCM-BANCO SANTANDER (Project GR3/14) is gratefully acknowledged. E.S. thanks CESGA for the generous allocation of computational resources.

Supporting Information Available: Copies of NMR spectra of new compounds and computational details. This material is available free of charge via the Internet at http://pubs.acs.org.

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(16) A potentially promising subset of the spirooxindole alkaloids are the oxa-spirooxindoles, joining two privileged motifs, the oxacycle and oxindole substructures through a unique spiro-quaternary carbon. Unfortunately, approaches for this interesting hybrid scaffold remain limited. For selected examples, see: (a) Liu, R.; Yu, C.; Xiao, Z.; Li, T.; Wang, X.; Xie, Y.; Yao, C. *Org. Biomol. Chem.* **2014**, *12*, 1885. (b) Xie, X.; Peng, C.; He, G.; Leng, H.-J.; Wang, B.; Huang, W.; Han, B. *Chem. Commun.* **2012**, *48*, 10487. (c) Wang, X.-N.; Zhang, Y.-Y.; Ye, S. *Adv. Synth. Catal.* **2010**, *352*, 1892. (d) Alcaide, B.; Almendros, P.; Martínez del Campo, T.; Quirós, M. T. *Chem. Eur. J.* **2009**, *15*, 3344.

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(21) **CAUTION!** Perchlorates are potentially explosive compounds and should be handled very carefully. We used $Hg(ClO_4)_2{\cdot}3H_2O$ for our experiments and we encountered no problem during handling. $Hg(ClO_4)_2{\cdot}3H_2O$ is a stable salt because: a) 0.006 M solutions (around 22 mg) in different organic solvents (THF, DCE, acetonitrile, and DMF) can be safely heated at 70^{o}C for several hours; b) 10 mg of $Hg(ClO_4)_2{\cdot}3H_2O$ (neat product) can be heated at 200^{o}C with decomposition but not explosion; and c) it did not decompose during storage at room temperature for several weeks. We did not suffer any explosion, but this salt should be handled with care.

(22) The unpurified reaction mixture of allenol **1j** under catalytic $HClO_4$ conditions contained the corresponding rearranged α,β-unsaturated ketone as the major reaction product, along with unidentified impurities. This result should rule out the possibility of Brønsted acid catalysis through adventitious perchloric acid with the use of $Hg(ClO_4)_2{\cdot}3H_2O$.