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Ligand- and Brønsted acid/base-switchable reaction pathways in gold(I)-catalyzed cycloisomerizations of allenoic acids†

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Gold-promoted cyclizations of 2,2-diaryl substituted γ-allenoic acids were found to give three isomeric lactone products, each of which could be obtained selectively by exploiting Brønsted acid/base and ligand effects. Simple 5-*exo*-*trig* cyclization products were favored by strong donor ligands or base additives, whereas weak donor ligands and a Brønsted acid additive gave isomeric enelactones resulting from double bond migration. Further optimization afforded a class of medicinally relevant bridged tricyclic lactones *via* a tandem hydroacyloxylation/hydroarylation process. Kinetic studies and control experiments indicated that the initial 5-*exo*-*trig* cyclization product serves as a branch point for further isomerization to the other lactone products *via* cooperative gold(I)/Brønsted acid catalysis.

Introduction

Gold(I) complexes catalyze a diverse array of transformations initiated by π-electrophilic activation of alkynes, allenes, and alkenes toward attack by heteroatom or carbon-based nucleophiles.[1] Although applications of gold catalysis in the synthesis of complex natural products have begun to appear,[2] wider adoption may be hindered by the mechanistic intricacy of these processes, which limits predictive ability.[3,4] Gold-mediated reactions can often evolve along divergent mechanistic pathways that are sensitive to ligand effects, substrate structure, or reaction conditions.[5] Furthermore, there is much evidence that Brønsted acid—either deliberately introduced or generated *in situ* from the nucleophile—can significantly affect the outcomes of gold-catalyzed transformations.[6] Several reports have indicated enhanced rates and/or yields in gold-catalyzed reactions with added Brønsted acid, presumably due to accelerated protodeauration.[7] In other cases, added Brønsted acid changes the reaction stereoselectivity[8] or opens new reaction pathways that do not occur with gold alone. The latter can involve cascade reactions, in which gold-catalyzed steps are followed by Brønsted acid catalysis,[9] or may result from Au^{I}-assisted Brønsted acid catalysis.[10] Brønsted acid can also serve to generate active gold(I) species when basic anionic ligands are present.[11] It is important to identify and control these various Brønsted acid effects on gold catalysis in order to maximize catalyst efficiency and to enable optimization of potentially competing reaction pathways.

Gold-catalyzed cycloisomerizations of alkynes[12] and allenes[13,14] containing pendent carboxylic acids as internal nucleophiles have been relatively little investigated[15] in comparison to related intramolecular hydrofunctionalizations involving amines and alcohols.[16] In particular, only three limited reports of gold-catalyzed hydroacyloxylations of allenoic acids appeared prior to our study, each of them utilizing the same single substrate, which contains an unsubstituted $-CH_2CH_2-$ linkage between the allene and the carboxylic acid.[13,17] In one study, bimetallic diphosphine gold(I)/chiral silver phosphate catalyst systems were employed to achieve varying degrees of enantioselectivity.[13a,18] More recently, it was reported that chiral silver(I) phosphate salts alone are effective catalysts for cyclizations of four γ-allenoic acids bearing geminal diphenyl groups adjacent to the carboxylic acid, even at room temperature.[15d] In these prior reports, only the γ-lactones resulting from simple 5-*exo*-*trig* cyclization were observed.

With a goal of developing modular routes to lactones that could form the cores of medicinally relevant organic molecules,[19] we examined gold-catalyzed cycloisomerizations of 2,2-diaryl allenoic acids using an expanded series from this known

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substrate class.[15d,20,21] A special goal was to identify and optimize any products resulting from alternative reaction pathways. A few reports have shown that different cyclization products can be obtained in some types of intramolecular allene hydrofunctionalizations upon changing the catalytic metal.[22] We hypothesized that ligand effects could be utilized to achieve similar results with allenoic acids, given literature precedent for ligand control of regioselectivities in some related gold-catalyzed cycloisomerizations of functionalized alkynes[5a–c,23] and allenes[24] involving internal nucleophiles other than carboxylic acids. During these studies, we found that gold-catalyzed cyclizations of several 2,2-diaryl-substituted γ-allenoic acids lead to three isomeric lactone products, each of which can be selected by exploiting Brønsted acid/base effects in combination with ligand effects. One product is a tricyclic δ-lactone resulting from an unprecedented tandem hydroacyloxylation/hydroarylation process. Evidence of cooperativity between Au^I and Brønsted acid has been found in two of the catalytic reaction pathways.

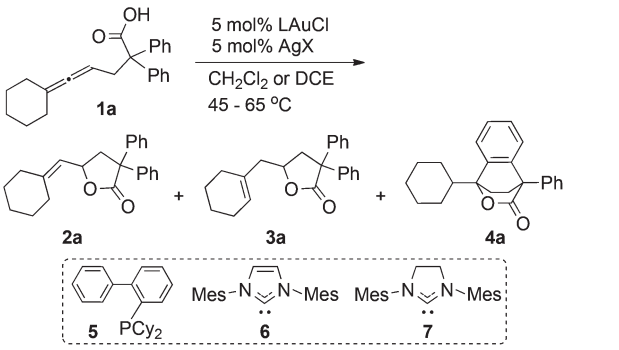
Results and discussion

During an initial screen of *in situ*-generated cationic Au^I complexes bearing common ancillary ligands in the catalytic cycloisomerization of known 2,2-diphenyl γ-allenoic acid substrate **1a**,[15d] two additional products were observed alongside the expected 5-*exo-trig* cyclization product **2a** (Table 1). Catalysts containing PPh_3 or CyJohnPhos (**5**) afforded **2a** as the major product, along with ~30% yields of the double bond isomerized enelactone **3a** (entries 1,2), which has not been previously reported. Switching to the more strongly donating N-heterocyclic carbene ligands IMes (**6**) and SIMes (**7**) nearly eliminated the isomerized product and provided improved yields of **2a** (entries 3,4). The structure of **2a** was confirmed by X-ray diffraction analysis,† and the structure of **3a** was assigned on the basis of ^1H–^{13}C 2D NMR correlation spectroscopy (HMQC and HMBC; see the ESI†).

When poorly donating $P(OPh)_3$ was used as a ligand, formation of **2a** was substantially reduced, and a third product was observed in addition to **3a** (Table 1, entry 5). The ^1H NMR spectrum of this compound showed an absence of olefinic protons, and X-ray crystallography revealed it to be tricyclic δ-lactone **4a** (Fig. 1),† which arises from an apparent tandem hydroacyloxylation/hydroarylation process. Although several metal-catalyzed tandem reactions that combine heteroatom addition to a carbon–carbon π-bond with hydroarylation have been reported,[25] such reactions have rarely afforded bridged ring structures,[25e,f] and there are no examples involving carboxylic acid nucleophiles.[26,27] Furthermore, the tricyclic lactone core of **4a** is found in the bioactive natural product carnosol,[28] suggesting that this tandem cyclization process could have value in medicinal chemistry.[29] A screen of silver salt activators (entries 6–10) revealed that replacing the SbF_6^- counterion with BF_4^- increased the yield of **4a** to 45% at 65 °C (entry 10), so the combination of $(PhO)_3PAuCl$ (**8**) and $AgBF_4$ was selected for further optimization.

Given the acidic functional group of allenoic acid **1a**, we hypothesized that protons might play an important role in the reaction pathways leading to **3a** and **4a**. Therefore, we examined the effects of co-catalytic amounts of Brønsted base (NEt_3) or Brønsted acid (*p*-toluene sulfonic acid hydrate, $TsOH{\cdot}H_2O$) on the product distribution (Table 2). Addition of 5 mol% NEt_3 completely suppressed the formation of **3a** and **4a** and afforded near quantitative yields of **2a** (Table 2, entry 1), although higher amounts of base resulted in a lower yield (entry 2). By contrast, increasing amounts of $TsOH{\cdot}H_2O$ led to

Table 1 Ligand and counterion effects on product distribution in catalytic cycloisomerizations of allenoic acid **1a**[a]



Entry	L	X^-	t (h)	Yield **2a**[b] (%)	Yield **3a**[b] (%)	Yield **4a**[c] (%)
1[d]	PPh_3	SbF_6^-	4.0	67	29	—
2[d]	**5**	SbF_6^-	5.0	58	31	—
3[d]	**6**	SbF_6^-	6.0	83	7	—
4[d]	**7**	SbF_6^-	3.0	88	<2	—
5[d]	$P(OPh)_3$	SbF_6^-	4.0	2	70	20
6[e]	$P(OPh)_3$	SbF_6^-	4.0	<2	63	30
7[e]	$P(OPh)_3$	OTf^-	6.0	10	60	12
8[e]	$P(OPh)_3$	NTf_2^-[f]	4.5	92	5	0
9[e]	$P(OPh)_3$	$BAr^F{}_4^-$[g]	7.0	40	45	0
10[e]	$P(OPh)_3$	BF_4^-	3.5	—	50	45

[a] Reaction conditions: **1a** (0.30 mmol), LAuCl (5 mol%), AgX (5 mol%), solvent (2.0 mL). [b] **2a** and **3a** obtained as an inseparable mixture; ratio determined by ^1H NMR. [c] Isolated yield. [d] In CH_2Cl_2 at 45 °C. [e] In DCE at 65 °C. [f] $LiNTf_2$ was used. [g] $BAr^F{}_4^-$ = tetrakis[3,5-bis(trifluoromethyl)-phenyl]borate.

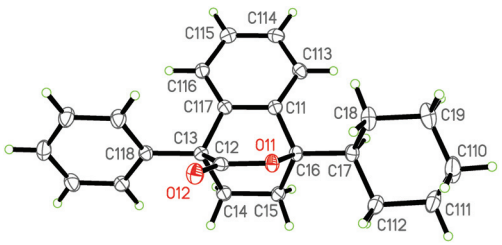


Fig. 1 X-ray crystal structure of **4a** with 50% probability ellipsoids. A second, crystallographically independent molecule with a nearly identical conformation is also present in the asymmetric unit.

Table 2 Brønsted acid/base effects on product distribution in catalytic cycloisomerizations of allenoic acid **1a**[a]

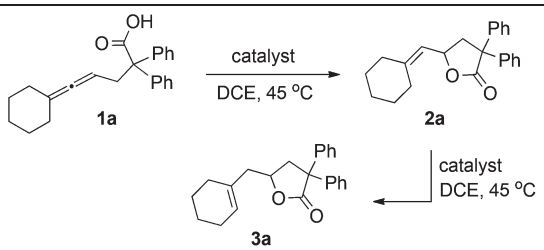
Entry	Additive	t (h)	Yield **2a**[b] (%)	Yield **3a**[b] (%)	Yield **4a**[c] (%)
1[d]	NEt_3 (5 mol%)[e]	3.0	95	—	—
2[d]	NEt_3 (20 mol%)[e]	8.0	65	—	—
3[f]	$TsOH{\cdot}H_2O$ (5 mol%)	4.0	86	7	—
4[f]	$TsOH{\cdot}H_2O$ (20 mol%)	4.0	61	31	—
5[f]	$TsOH{\cdot}H_2O$ (20 mol%)	24	—	93	—

[a] Reaction conditions: **1a** (0.30 mmol), $(PhO)_3PAuCl$ (5 mol%), $AgBF_4$ (5 mol%), solvent (2.0 mL), 45 °C. [b] **2a** and **3a** obtained as an inseparable mixture; ratio determined by ^1H NMR. [c] Isolated yield. [d] In CH_2Cl_2. [e] NEt_3 added as a 1.0 M stock solution in DCE. [f] In DCE.

correspondingly higher quantities of isomerized enelactone **3a** (entries 3,4) while still disfavoring formation of **4a**. With 20 mol% $TsOH{\cdot}H_2O$ and 5 mol% **8**/$AgBF_4$ at extended reaction times, **3a** was obtained exclusively in 93% yield (entry 5).

In order to gain further insights into the effects of Brønsted acid and base additives on gold-catalyzed cycloisomerizations of **1a**, the rates of these reactions were studied under various conditions (Table 3). For these experiments, a pre-activated cationic gold catalyst, nominally formulated as $[(PhO)_3PAu]BF_4$ (≡[Au]),[30] was generated *in situ* by treating **8** with $AgBF_4$ in DCE, followed by filtration of residual silver salts to preclude any background catalysis by Ag^I.[15d] Monitoring of reaction products over time by ^1H NMR spectroscopy revealed complete conversion of **1a** to **2a** within 2 min at 45 °C in the presence of

Table 3 Measured initial rates of formation of **2a** and **3a**, starting from **1a**[a]



Entry	Au catalyst[b]	Additive	Initial rate of formation (mM min^{-1}) **2a**	**3a**[c]
1	5 mol% [Au]	None	>100[d]	0.04(5)
2	5 mol% [Au]	TsOH[e] (20 mol%)	>100[d]	0.39(6)
3	—	TsOH[e] (20 mol%)	11.4(7)	0.20(1)
4	5 mol% [Au]	NEt_3 (5 mol%)	17.5(2)	—
5	5 mol% **8**	TsOH[e] (20 mol%), $AgBF_4$ (5 mol%)[f]	>100[d]	0.51(8)
6	—	$AgBF_4$ (5 mol%)	6.6(2)	—

[a] Reaction conditions: **1a** (0.30 mmol), DCE (1.5 mL), 45 °C. [b] Preactivated gold catalyst [Au] was prepared by reaction of **8** with $AgBF_4$, followed by removal of AgCl by filtration. [c] Rate measurement began after formation of **2a** was complete. [d] Formation of **2a** was complete within 2 min. [e] $TsOH{\cdot}H_2O$ used. [f] AgCl was not filtered off.

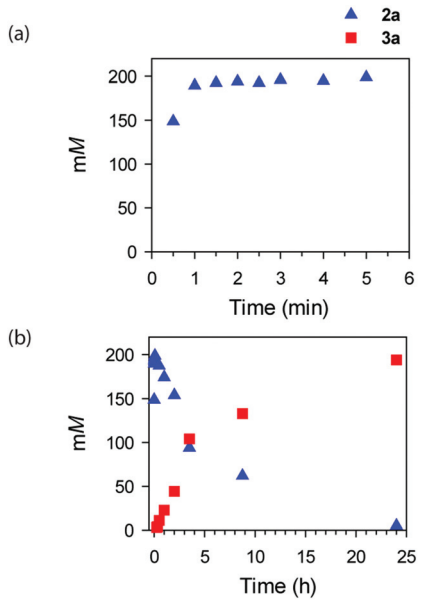
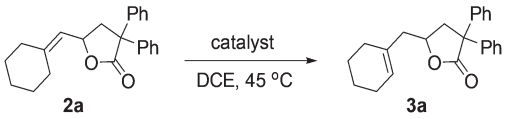


Fig. 2 Product concentrations *versus* time for the catalytic cycloisomerization of **1a** with 5 mol% cationic [Au] plus 20 mol% $TsOH{\cdot}H_2O$: (a) first five minutes; (b) over 24 h.

5 mol% [Au], either with or without 20 mol% $TsOH{\cdot}H_2O$ added. Subsequently, **2a** was transformed into **3a** at a significantly faster rate [0.39(6) mM min^{-1}] with 5 mol% gold catalyst plus 20 mol% $TsOH{\cdot}H_2O$ than with gold catalyst alone [0.04(5) mM min^{-1}] (Table 3, entries 1,2).[31] Fig. 2 illustrates the rapid initial formation of **2a**, followed by slow isomerization to **3a**, for the reaction involving gold catalyst plus added $TsOH{\cdot}H_2O$. A control experiment with 20 mol% $TsOH{\cdot}H_2O$ in the absence of [Au] (Table 3, entry 3) showed that purely acid-catalyzed formation of **2a** (60 min for completion) and **3a** [0.20(1) mM min^{-1}] also occurs, but at significantly slower rates. In addition, isolation of products from the Brønsted acid-catalyzed reaction (20 mol% $TsOH{\cdot}H_2O$), using conditions identical to those used for the gold-catalyzed reactions listed in Table 2, revealed incomplete conversion to **3a** even after 24 h (14% and 80% respective yields of **2a** and **3a**). Addition of NEt_3 to the cationic [Au] catalyst slowed the formation of **2a** considerably but led to no observable **3a** (entry 4), consistent with the clean formation of **2a** achieved with added NEt_3 in the optimization studies (Table 2).

An additional concern was the possible role of silver in these catalytic processes, given that cycloisomerizations of **1a** and three similar allenoic acids were reported to be facile with Ag^I phosphate salts as catalysts.[15d] An experiment utilizing 5 mol% [Au] catalyst and 20 mol% TsOH, but without removal of the AgCl formed upon catalyst pre-activation (Table 3, entry 5), revealed a somewhat higher rate for formation of **3a** [0.51(8) mM min^{-1}] compared with the corresponding reaction in which AgCl was filtered off (Table 3, entry 2). Thus, background catalysis by heterogeneous silver salt apparently contributes to, but does not dominate, the isomerization pathway leading to **3a**. $AgBF_4$ alone (5 mol%, entry 6) catalyzed the

Table 4 Measured initial rates of formation of **3a**, starting from **2a**[a]



2a **3a**

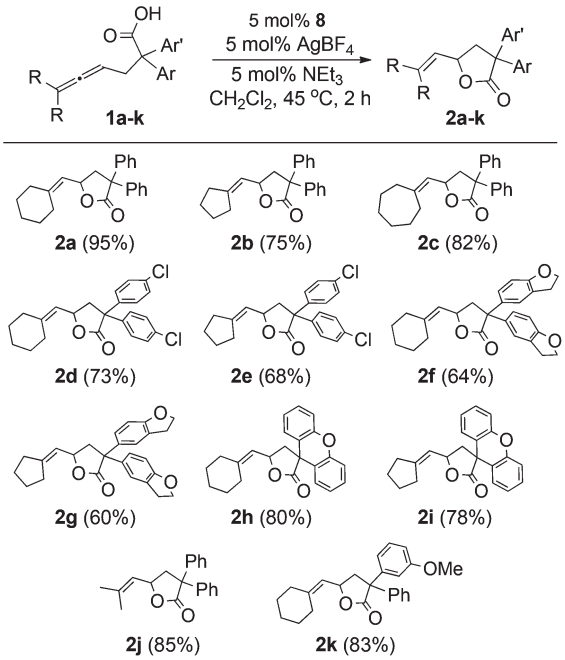
Entry	Au catalyst[b]	Additive	Initial rate of **3a** formation (mM min^{-1})
1	5 mol% [Au]	TsOH (20 mol%)	0.88(2)
2	—	TsOH (20 mol%)	0.26(1)
3	5 mol% [Au]	none	0.002(1)
4	—	TsOH (20 mol%), $AgBF_4$ (5 mol%)	0.23(1)

[a] Reaction conditions: DCE, **2a** (0.18 M), 45 °C. [b] Preactivated gold catalyst [Au] was prepared by reaction of **8** with $AgBF_4$, followed by removal of AgCl by filtration.

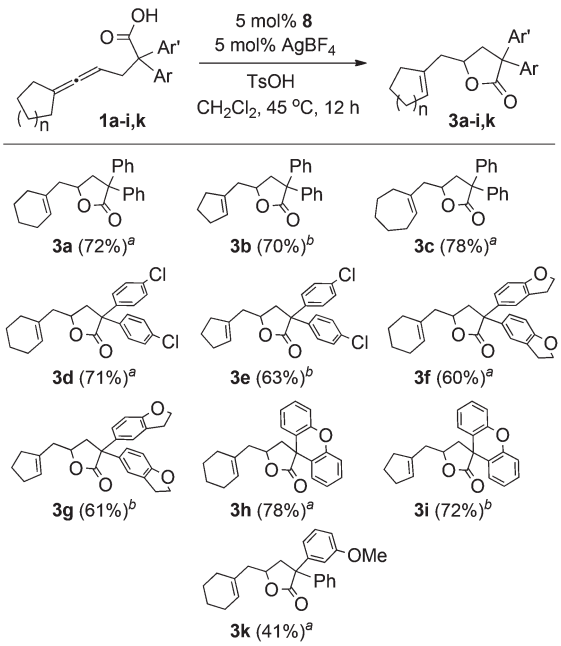
cyclization of **1a** to **2a** more slowly than 20 mol% Brønsted acid (entry 3) and did not catalyze further isomerization to **3a**.

Given the apparent intermediacy of **2a** in the formation of **3a** from **1a**, further kinetic studies examined the rate of isomerization of purified **2a** to **3a** under catalytic conditions (Table 4). Conversion of **2a** to **3a** occurred at a relatively fast rate with 5 mol% cationic [Au] plus 20 mol% TsOH [0.88(2) mM min^{-1}] (entry 1), whereas the Brønsted acid-catalyzed reaction with 20 mol% TsOH alone was substantially slower [0.26(1) mM min^{-1}] (entry 2). The higher rate for formation of **3a** from **2a** (Table 4, entry 1) *versus* **1a** (Table 3, entry 2) under the same conditions was postulated to reflect partial catalyst deactivation or decomposition in the reaction starting from **1a**. With 5 mol% [Au] and no added acid, the transformation of **2a** to **3a** barely occurred (entry 3), affording less than a 3% yield of **3a** after 24 h. These experiments suggest a mechanistic scenario in which cooperative gold/Brønsted acid catalysis is required for efficient formation of **3a**, subsequent to the initial cycloisomerization of **1a** to **2a**. Notably, the TsOH-catalyzed isomerization of **2a** to **3a** was not faster in the presence of $AgBF_4$ (entry 4), indicating that this type of cooperativity apparently does not extend to homogeneous Ag^I catalysts.

The ability to select competing pathways to two isomeric lactone products by addition of simple acid/base additives is notable, given that only nonisomerized enelactones such as **2a** were obtained in previous studies of metal-catalyzed γ-allenoic acid cyclizations.[13a–c,15d,32] Double bond isomerizations have been previously reported to occur in conjunction with Au^I-promoted nucleophilic additions to alkenes,[33] dienes,[10a] and alkynes,[34] but cooperativity between gold and Brønsted acid in these reactions has only rarely been investigated.[10a] These observations enabled us to formulate general conditions for the selective synthesis of either nonisomerized or double bond isomerized enelactones, in synthetically useful yields, for a family of allenoic acids containing differently sized carbocycles at the allene terminus and/or chlorine- or oxygen-substituted 2-aryl groups (Schemes 1 and 2). Enelactones of type **2** were cleanly obtained by adding 5 mol% NEt_3 to the **8**/$AgBF_4$ catalyst system, which effectively suppressed the double-bond

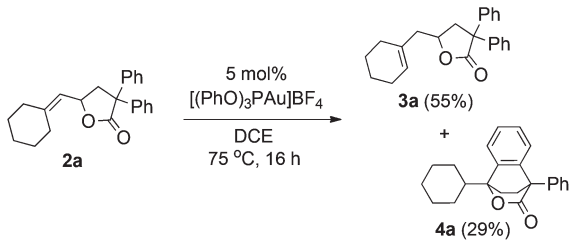


Scheme 1 Selective catalytic 5-*exo*-*trig* cyclizations of allenoic acids **1a–k** to enelactones **2a–k**.



Scheme 2 Selective catalytic synthesis of double-bond isomerized enelactones **3a–i,k**. [a] 20 mol% TsOH·H_2O. [b] 5 mol% TsOH·H_2O.

isomerization process (**2a–k**, Scheme 1). Addition of 20 mol% TsOH·H_2O (5 mol% was sufficient for cyclopentylidene substrates **1b,e,g,i**) facilitated selective formation of the isomerized analogues of type **3**, although extended reaction times of 12 h were needed to obtain optimal yields (**3a–i** and **3k**, Scheme 2). Substrate **1j** (R = Me, Ar = Ph) did not afford a



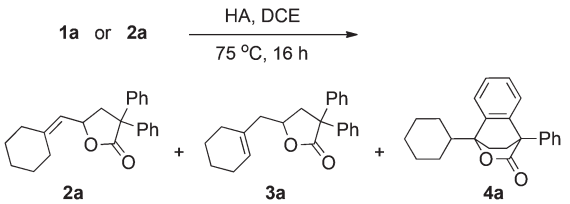
Scheme 3 Gold-catalyzed isomerization of **2a** at 75 °C, showing isolated yields. No **2a** was recovered; the remaining mass balance reflects decomposition to unidentifiable material.

double bond isomerized product of type **3** due to the lack of a ring that could host a thermodynamically favored internal alkene. Notably, products **2** and **3** could not be chromatographically separated for substrates **1a–i,k**, reinforcing the importance of selective catalytic routes to the two distinct isomers.

As no products of hydroarylation without lactonization were observed with **1a**, we hypothesized that the formation of tricyclic lactone **4a** might occur *via* the intermediacy of hydroacyloxylation products **2a** and/or **3a**. Subjecting a purified sample of enelactone **2a** to the preactivated [Au] catalyst at an elevated temperature of 75 °C in DCE for 16 h afforded a substantial amount of **4a** (29% isolated yield), in addition to a 55% yield of **3a** (Scheme 3). Submission of **3a** to the same catalytic conditions resulted in no detectable formation of **4a**; ^{1}H NMR analysis of the product mixture indicated 88% recovery of unreacted **3a**, with only a trace (<1%) of **2a** present. Thus, **4a** is likely formed *via* the intermediacy of **2a**.

Although the transformation of **2a** into **4a** represents a formal alkene hydroarylation, it seems unlikely that this occurs *via* Au^{I}-based carbophilic activation of the carbon–carbon double bond toward arene attack, given the geometric constraints imposed by the five-membered lactone ring of **2a** and the scant literature precedent for such a reaction.[35] Gold-catalyzed additions of arenes to nonconjugated alkenes are rare and mostly limited to examples involving electron-rich aromatic rings.[36] Furthermore, a closely related tricyclic ether was reported to form upon heating an analogous allenol with 20 mol% TsOH·H_2O or TfOH,[37] suggesting that Brønsted acid catalysis may also be important in the formation of **4a**.[38] Therefore, we examined reactions of **1a** and **2a** with catalytic amounts of Brønsted acids at 75 °C (Table 5). No formation of **4a** was observed with either TsOH·H_2O or aqueous HBF_4, and conversion to **3a** was not complete with the latter (entries 1–3). However, HBF_4·OEt_2 led to small amounts of **4a** (entries 4,5), and **4a** was the only product obtained when the stronger Brønsted acid TfOH was employed, although yields were still modest (entries 9,11). The similar yields of **4a** obtained from both **1a** and **2a** using 20 mol% HBF_4·OEt_2 (entries 4,5) or TfOH (entries 9,11) as the catalyst further support the intermediacy of **2a** in this reaction. These results lead to the conclusion that a very strong Brønsted acid, at least as strong as $[HOEt_2]^+$ ($pK_a \leq -3.6$), is required to achieve formation of **4a**.

Table 5 Isomerizations of **1a** and **2a** with catalytic Brønsted acid[a]

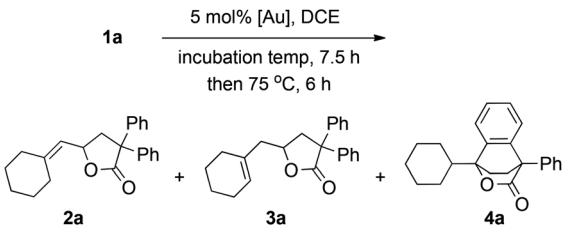


Entry	sm	HA[b]	Yield **2a**[c] (%)	Yield **3a**[c] (%)	Yield **4a**[d] (%)
1	**2a**	TsOH·H_2O	—	91	—
2	**1a**	HBF_4(aq)[e]	63	26	—
3	**2a**	HBF_4(aq)[e]	56[f]	34	—
4	**1a**	HBF_4·OEt_2[g]	—	84	9
5	**2a**	HBF_4·OEt_2[g]	—	81	11
6	**1a**	TfOH (1 mol%)	—	85	—
7	**1a**	TfOH (5 mol%)	—	86	—
8	**1a**	TfOH (10 mol%)	—	91	—
9	**1a**	TfOH (20 mol%)	—	—	52
10	**1a**	TfOH (50 mol%)	—	—	37
11	**2a**	TfOH (20 mol%)	—	—	59

[a] Reaction conditions: **1a** or **2a** (0.30 mmol), DCE (2.0 mL), 75 °C, 16 h. [b] 20 mol% HA, except as noted. [c] **2a** and **3a** obtained as an inseparable mixture; ratio determined by ^{1}H NMR. [d] Isolated yield. [e] 48 wt% HBF_4. [f] Unreacted **2a** recovered. [g] 51–57 wt% HBF_4.

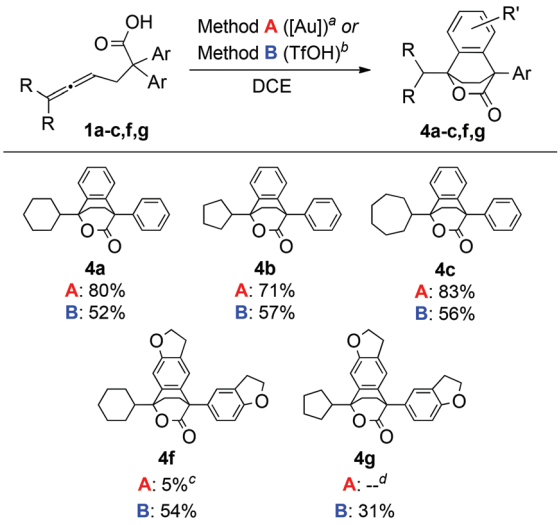
Because efficient formation of **4a** under purely Brønsted acid catalysis was elusive, we developed an alternative Au^{I}-promoted procedure involving an initial low-temperature incubation period followed by heating at 75 °C. A −20 °C incubation temperature proved optimal (Table 6). We postulate that the low temperature step suppresses catalyst deactivation processes while allowing buildup of a small steady-state concentration of strong Brønsted acid, equivalent to unsolvated HBF_4 ($pK_a \sim -10.3$ in DCE[39]). TfOH is a reasonable surrogate for this putative Brønsted acid given its similarly low pKa in DCE (∼−11.4).[39] Notably, a 20 mol% loading of TfOH was found to be optimal with no gold catalyst present (Table 5,

Table 6 Optimization of gold-promoted formation of tricyclic lactone **4a**[a]

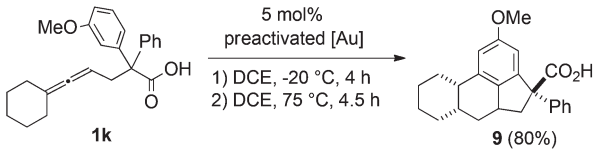


Entry	Incubation temp (° C)	Yield **2a** (%)	Yield **3a**[b] (%)	Yield **4a**[b] (%)
1	25 °C	—	80	12
2	0 °C	—	60	37
3	−20 °C	—	18	80

[a] Reaction conditions: 5 mol% cationic [Au] (prepared *in situ* from **8** + $AgBF_4$ followed by filtration), **1a** (0.30 mmol), DCE (2.0 mL). [b] Isolated yield.



Scheme 4 Synthesis of tandem hydroacyloxylation/hydroarylation products **4**: Optimized conditions *versus* TfOH-catalyzed conditions. [a] 5 mol% cationic [Au], DCE, 2–8 h at −20 °C, then 3–7 h at 75 °C. [b] 20 mol% TfOH, DCE, 75 °C, 16 h. [c] NMR yield; inseparable mixture with **2f** (2%) and **3f** (93%). [d] No **4g** obtained.



Scheme 5 Double hydroarylation of allenoic acid **1k**.

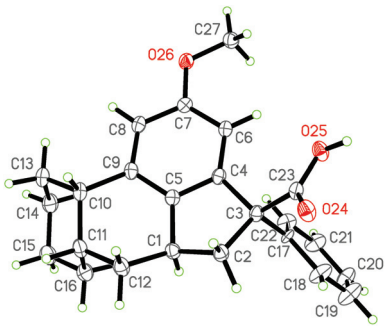


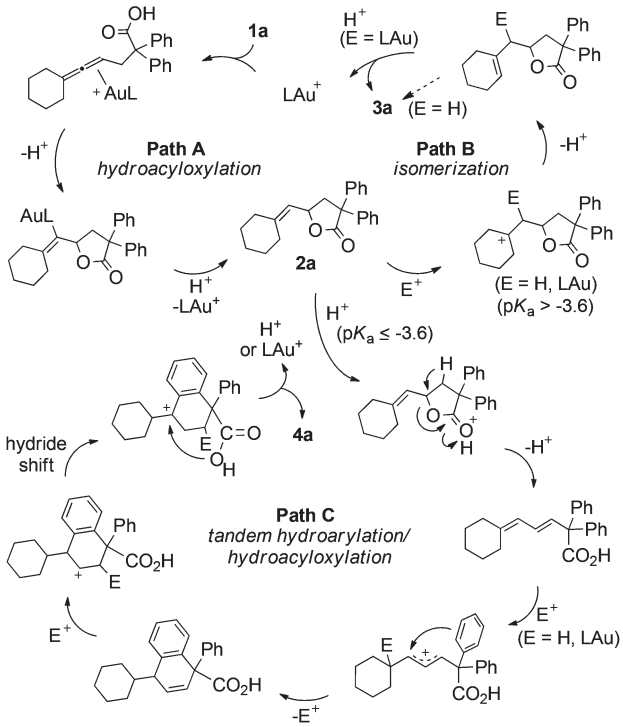
Fig. 3 X-ray crystal structure of **9** with 50% probability ellipsoids. The phenyl group (C17–C22) is disordered, with only the major orientation shown.

entries 6–10), whereas the maximum Brønsted acid concentration that can be formed in the incubation phase of the gold-promoted process is 5 mol%. The improved yields of **4a** obtained under the latter conditions, despite the lower concentration of Brønsted acid, suggest that the optimal reaction conditions involve cooperative gold/Brønsted acid catalysis rather than purely Brønsted acid catalysis that is initiated by gold.[38]

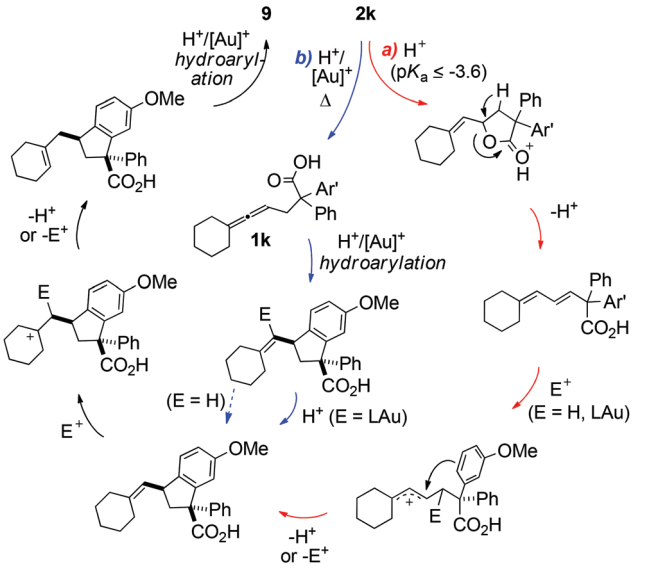
The optimized protocol (Method A, Scheme 4) afforded good yields of tricyclic lactones from allenoic acids **1a–c**, demonstrating that the gold/Brønsted acid-catalyzed tandem process is potentially generalizable, at least with unsubstituted phenyl groups present. However, substrates with an inflexible xanthene moiety in place of 2,2-diaryl substituents (**1h,i**) were unable to undergo hydroarylation, and most others with functionalized aryls (**1d–g**) gave only varying amounts of **3** but no isolable **4** under these conditions, suggesting high sensitivity to the aryl group substitution pattern in this transformation. An alternative, gold-free protocol using 20 mol% TfOH as the catalyst (Method B) provided substantially poorer yields of **4** in most cases (**4a–4c**, Scheme 4). However, this method gave isolable tricyclic lactone in two cases in which the gold-based system was ineffective (**4f**, **4g**), albeit in modest yields, indicating that the simple Brønsted acid catalyst is complementary to the gold-based system for some substrate types.

Whereas hydroarylation is accompanied by oxygen addition in the formation of tricyclic lactones **4a–c,f,g**, the behavior of unsymmetrically substituted allenoic acid **1k** shows that the hydroacyloxylation step can be bypassed when suitably located resonance donor groups are present. Under conditions that gave **4** with other allenoic acids, **1k** yielded a tetracyclic acid **9** resulting from an apparent double hydroarylation occurring in tandem with double bond isomerization (Scheme 5 and Fig. 3).† Although similar double intramolecular hydroarylations of allenes have been reported using $Bi(OTf)_3$ as a catalyst,[40] we are not aware of any precedent for this transformation involving transition metal catalysts. The tetracyclic core of **9** is found in a class of bioactive terpenoid quinone methides,[41] highlighting the potential synthetic value of this cycloisomerization.

To account for the combined effects of ligand and Brønsted acid in allenoic acid cyclizations, we propose the mechanistic scenario depicted in Scheme 6. Lactone **2** is generated rapidly from **1** by a gold-mediated oxygen addition/protodeauration sequence (Path A) and remains as the major product in the absence of a suitably activating ligand and/or added proton source. Isomerization of **2** to **3** occurs *via* carbocation formation and H^+ elimination, following attack on the alkene by Brønsted acid or electrophilic $[L\text{-}Au]^+$ (Path B).[42] The synergistic effect of TsOH with gold on the rate of isomerization to **3** may result from Lewis acid activation of the Brønsted acid,[10] accelerated protodeauration with higher H^+ concentration, or both. With sufficiently strong Brønsted acid present ($pK_a \leq -3.6$), protonation of the lactone can compete kinetically with alkene activation, shifting the reaction manifold toward tandem hydroacyloxylation/hydroarylation (Path C). A plausible mechanism[43] involves elimination from the protonated lactone[44] to yield a diene, which in turn is protonated or aurated to yield an allylic carbocation that can undergo attack by an aryl group.[45] Further reaction of H^+ or LAu^+ with the resulting 1,4-dihydronaphthalene derivative, followed by a 1,2-hydride shift and attack of oxygen on the tertiary carbocation, furnishes the tricyclic lactone product **4**. The increased electrophilicity of Au^I resulting from weak ligand donicity is important



Scheme 6 Mechanistic rationale for competing reaction pathways of allenoic acids.



Scheme 7 Possible mechanisms for the formation of **9** (Ar′ = 3-MeO-C_6H_4).

in both Paths B and C, manifesting the isolobal relationship of LAu^+ to H^+.[46] However, an additional role of $P(OPh)_3$ in promoting Path C is evidently to slow the protodeauration of the organogold species formed upon initial cyclization of **1a**,[47] thereby leading to a controlled buildup of very strong Brønsted acid (equivalent to unsolvated HBF_4) that is a key cocatalyst in this reaction pathway. Added NEt_3 suppresses Paths B and C due to the key role of protons in both mechanisms.

Path C differs from the mechanism proposed for a similar acid-catalyzed isomerization of a γ-allenol, in which the intermediacy of the 5-*exo-trig* cyclization product was not considered.[37] We cannot rule out an alternative mechanism in which the initial cyclization product **2** reverts to allenoic acid **1** at elevated temperature, followed by gold-promoted 6-*endo-dig* hydroarylation, H^+ attack at the remaining double bond, and trapping of the resulting carbocation by the carboxylic acid. However, this would involve a typically disfavored initial attack at the central allene carbon,[16a] and no evidence for reversibility in the conversion of **1** to **2** has been observed.[48] In addition, the presence of a bulky L-Au group as "E" in the proposed allylic cation intermediate preceding hydroarylation (Scheme 6) could explain the failure of the larger aryl groups in substrates **1f** and **1g** to yield tricyclic lactones under gold-promoted conditions (Method A, Scheme 4), despite giving modest yields of the hydroarylation products under purely Brønsted acid catalysis (Method B).

To explain the formation of the unexpected double hydroarylation product **9** with substrate **1k** (Scheme 5), we postulate two mechanistic scenarios that share some features with the pathways leading to products **2**–**4** (Scheme 7). The reaction could begin with acid-promoted ring opening of the intermediate lactone **2k** in a mechanism similar to Path C (***a***, Scheme 7), but with the resulting diene undergoing protonation/auration at the less substituted end. This would give a different allyl cation that could undergo attack by the 3-methoxylphenyl group to yield a five-membered ring. Alternatively, **2k** could revert to **1k** upon heating (***b***, Scheme 7), followed by either gold-mediated 5-*exo-trig* hydroarylation or protonation at the central allene carbon and aryl attack at the resulting allylic cation. Either mechanistic pathway (***a*** or ***b***) would be followed by proton- or gold-mediated isomerization of the remaining carbon–carbon double bond (similarly to Path B) and a second hydroarylation to complete the tetracyclic structure. Although these mechanistic pathways are speculative, they both account for the formation of a five-membered carbocycle in **9**, in contrast to the six-membered ring resulting from hydroarylation in tricyclic lactones **4**. The presence of a resonance donor methoxy group at the aryl 3-position is of **1k** is clearly important in promoting the initial 5-*exo-trig* hydroarylation, given that similar reactivity was not observed for **1f** and **1g**, which contain donor groups at the 4-position.

Conclusions

In summary, ligand and Brønsted acid/base effects can be exploited in concert to selectively switch between three isomeric products in Au^I-catalyzed cyclizations of 2,2-diaryl allenoic acids, albeit with limited substrate scope in the case of the tandem hydroacyloxylation/hydroarylation process. The kinetically favored enelactone product **2** serves as a divergence point for distinct mechanistic pathways leading to either alkene isomerization product **3** or bridged tricyclic lactone **4**,

via cooperative gold/Brønsted acid catalyzed processes that are dependent on the strength of the Brønsted acid. The first two reactions provide alkene-appended lactones that could be elaborated into more complex structures, while the third pathway opens access to medicinally relevant bridged polycyclic lactones. These results reinforce previously accumulated evidence[6–11] suggesting that Brønsted acid/base effects should be carefully examined in order to maximize the efficiency and product structural diversity of gold-catalyzed organic reactions.

Experimental section

General experimental details

All manipulations were carried out under nitrogen in dried, distilled solvents unless otherwise noted. Diethyl ether, THF, and hexanes were purified by distillation from sodium benzophenone ketyl. Dichloromethane and DCE were washed with a sequence of concentrated H_2SO_4, deionized water, 5% Na_2CO_3 and deionized water, followed by pre-drying over anhydrous $CaCl_2$, and were then refluxed over and distilled from P_2O_5 under nitrogen. Pyridine and NEt_3 were dried over activated 4 Å molecular sieves and then distilled, degassed, and stored over dried 4 Å sieves under nitrogen. Au(PPh$_3$)Cl,[49] Au(CyJohnPhos)Cl [Au(**5**)Cl],[49] and Au[P(OPh)$_3$]Cl (**8**)[50] were synthesized by a reported procedure[51] starting from Au(THT)Cl.[52] Au(IMes)Cl [Au(**6**)Cl],[53] Au(SIMes)Cl [Au(**7**)Cl],[53] and $AgBAr^F{}_4$[54] were prepared by literature procedures. All gold complexes were ultimately derived from chloroauric acid (99.9%, 49% Au) purchased from Strem. $AgBF_4$ (99%), $AgSbF_6$ (98%), and HBF_4(aq.) (48 wt%) were purchased from Strem. $HBF_4{\cdot}Et_2O$ (51–57 wt%) was purchased from Aldrich. *p*-TsOH·H_2O (99%) and TfOH (99%) were purchased from Acros. Allenoic acid substrates were synthesized by literature procedures (**1a**,**1j**)[15d,22b] or by modifications thereof (see the ESI† for details).[20,21]

Optimized catalytic procedures

Synthesis of nonisomerized enelactones 2a–k. In a nitrogen glovebox, allenoic acid substrate (**1a–k**, 100 mg) was added to 2.0 mL dry CH_2Cl_2 in a 4 mL reaction vial. Precatalyst (PhO)$_3$-PAuCl **8** (5 mol%), $AgBF_4$ (5 mol%) and NEt_3 (5 mol%, as a 1.0 *M* stock solution in DCE) were then introduced. The vial was sealed with a septum cap and placed in a pre-heated aluminum block heater, and the reaction mixture was stirred at 45 °C for 2 h. After complete consumption of starting material as monitored by TLC, the reaction mixture was diluted with 10.0 mL of CH_2Cl_2 and washed with 10.0 mL of water. The organic layer was separated and dried over anhydrous sodium sulfate. The solvent was evaporated under reduced pressure to obtain the crude product, which was purified by flash chromatography on silica.

Synthesis of isomerized enelactones 3a–i. In a nitrogen glovebox, substrate (**1a–i**, 100 mg) was added to 2.0 mL dry CH_2Cl_2 in a 4 mL reaction vial. Precatalyst **8** (5 mol% relative to **1**), $AgBF_4$ (5 mol%) and TsOH·H_2O (5 mol% for **3b**,**3e**,**3g**,**3i**; 20 mol% for others) were then introduced. The vial was sealed with a septum cap and placed in a pre-heated aluminum block heater, and the reaction mixture was stirred at 45 °C for 12 h. After complete consumption of starting material as monitored by TLC, the reaction mixture was diluted with 10.0 mL of CH_2Cl_2 and washed with 10.0 mL of water. The organic layer was separated and dried over anhydrous sodium sulfate. The solvent was evaporated under reduced pressure to obtain the crude product, which was purified by flash chromatography on silica.

Synthesis of tricyclic lactones 4a–d and tetracyclic acid 9 (Method A). In a nitrogen glovebox, precatalyst **8** (5 mol% relative to **1**) and $AgBF_4$ (5 mol%) were added to 2.0 mL of dry DCE in a 4 mL reaction vial. The precatalyst mixture was stirred for 30 min at 25 °C, and the AgCl precipitate was then removed by three successive filtrations through celite. The filtrate was placed in a fresh 4 mL reaction vial, and the substrate (**1a–c**,**1k**; 100 mg) was introduced. The vial was sealed with a septum cap, and several layers of PTFE tape were wrapped around the cap seal for protection. The reaction mixture was stirred at −20 °C (dry ice/CCl_4 bath) under rigorously dry conditions until the starting material had been consumed as monitored by TLC (2–8 h). The reaction mixture was then heated at 75 °C for an additional 3–7 h. The reaction mixture was cooled to room temperature and loaded directly onto a silica pad for column chromatographic purification.

Brønsted acid-catalyzed synthesis of tricyclic lactones 4f,g (Method B). Reaction setup followed Method A, but with no pre-activation step and no −20 °C incubation period. After addition of TfOH (20 mol%) to a preheated (75 °C) solution of substrate, the reaction mixture was heated with stirring for 16 h, followed by workup.

Kinetic procedures

Typical kinetic procedure with allenoic acid 1a. Substrate **1a** (100 mg, 0.30 mmol), TsOH·H_2O (11.5 mg, 0.060 mmol) and mesitylene (4.0 μL; NMR internal standard) were added to a 4 mL reaction vial, which was closed with a septum screw-cap. A catalyst stock solution was prepared by mixing **8** (33 mg, 0.060 mmol) and $AgBF_4$ (11.5 mg, 0.060 mmol) in 1.5 mL of dry DCE, stirring for 15 min, and filtering three times through celite to remove the AgCl precipitate. The filtrate was diluted to a volume of 2.0 mL. A 0.5 mL aliquot of this solution was syringed into the vial containing the substrate, followed by 1.0 mL of pre-heated (45 °C) DCE, and the vial was placed in a pre-heated aluminum block reactor with magnetic stirring. At periodic intervals, 20 μL aliquots were withdrawn and added to 0.60 mL of a $CDCl_3$ solution containing methylisocyanide[55] (25 mM), in order to deactivate the gold catalyst. Reaction aliquots were stored at −4 °C until analysis. Product concentrations were determined by ^{1}H NMR integration of product resonances *versus* mesitylene. The catalyst deactivation procedure was verified by adding fresh substrate **1a** to a deactivated aliquot containing product **2a** in 0.25 mM MeNC–$CDCl_3$. After 12 h at 25 °C, no change in the concentration of **2a** and no formation of **3a** were observed.

Substrate **1a** is only partially soluble in DCE, but dissolution occurred concomitant with its conversion to **2a**. In cases in which the rates were slow enough to be measured, the appearance of **2a** followed pseudo zero-order kinetics, consistent with a constant equilibrium concentration of **1a** in solution. Kinetic plots for formation of **3a** were consistent with reactions that are pseudo first-order in **2a** (see the ESI† for plots). Initial rates were determined by least-squares fitting of product concentration *versus* time plots over the linear region, with uncertainties reported at the 95% confidence level.

Typical kinetic procedure with enelactone 2a. Enelactone **2a** (60 mg, 0.18 mmol), $TsOH{\cdot}H_2O$ (7.0 mg, 0.036 mmol) and mesitylene (2.5 μL; NMR internal standard) were added to a 4 mL reaction vial, which was closed with a septum screw-cap. A catalyst stock solution was prepared by mixing **8** (19.5 mg, 0.036 mmol) and $AgBF_4$ (7.0 mg, 0.036 mmol) in 1.5 mL of dry DCE, stirring for 15 min, and filtering three times through celite to remove the AgCl precipitate. The filtrate was diluted to a total volume of 2.0 mL. A 0.5 mL aliquot of this solution was syringed into the vial containing the substrate, followed by 0.5 mL of pre-heated (45 °C) DCE, and the vial was placed in a pre-heated aluminum block reactor with magnetic stirring. Data collection and analysis were performed as in kinetic experiments with **1a**.

Product characterization

5-(Cyclohexylidenemethyl)-3,3-diphenyldihydrofuran-2(3*H*)-one (2a). R_f 0.50 (1 : 9 acetone–hexanes); colourless viscous oil, yield 95 mg (95%). ^{1}H and ^{13}C NMR data were in agreement with published values.[15d]

5-(Cyclopentylidenemethyl)-3,3-diphenyldihydrofuran-2(3*H*)-one (2b). R_f 0.52 (1 : 4 diethyl ether–hexanes); white solid, yield 75 mg (75%). ^{1}H and ^{13}C NMR data were in agreement with published values.[15d]

5-(Cycloheptylidenemethyl)-3,3-diphenyldihydrofuran-2(3*H*)-one (2c). R_f 0.49 (1 : 4 diethyl ether–hexanes); white solid, m.p. = 111–112 °C, yield 82 mg (82%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43–7.36 (m, 4H), 7.34–7.29 (m, 5H), 7.28–7.22 (m, 1H), 5.28 (dt, J = 8.8, 1.2 Hz, 1H), 5.06 (ddd, J = 9.6, 8.4, 5.2, 1H), 3.07 (dd, J = 13.0, 5.2 Hz, 1H), 2.69 (dd, J = 13.2, 10.4 Hz, 1H), 2.36–2.20 (m, 4H), 1.63–1.46 (m, 8H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 177.4, 150.4, 142.4, 139.9, 129.1, 128.5, 127.9, 127.8, 127.5, 127.3, 122.3, 73.8, 58.4, 44.5, 37.9, 30.6, 29.7, 29.1, 28.7, 27.3. IR (neat): ν 2970 (w), 2918 (w), 1901 (w), 1757 (s), 1647 (w) cm^{-1}. HRMS (ESI-orbitrap, $[C_{24}H_{26}O_2 + H]^+$) calc. 347.2011, found *m*/*z* 347.2016.

3,3-Bis(4-chlorophenyl)-5-(cyclohexylidenemethyl)dihydrofuran-2(3*H*)-one (2d). R_f 0.57 (1 : 4 diethyl ether–hexanes); viscous yellow oil, yield 73 mg (73%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36–7.20 (m, 8H), 5.17 (d, J = 8.4 Hz, 1H), 5.05 (ddd, J = 10.4, 8.4, 4.8 Hz, 1H), 2.95 (dd, J = 13.2, 4.8 Hz, 1H), 2.63 (dd, J = 13.2, 10.4 Hz, 1H), 2.20–2.03 (m, 4H), 1.59–1.48 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 176.6, 149.3, 140.3, 138.2, 134.2, 133.6, 129.4, 129.2, 128.8, 128.7, 118.4, 73.4, 57.5, 44.4, 37.1, 29.7, 28.3, 27.9, 26.5. IR (neat): ν 2979 (w), 2926 (w), 1908 (w), 1750 (s), 1640 (w) cm^{-1}. HRMS (ESI-orbitrap, $[C_{23}H_{22}Cl_2O_2 + Na]^+$) calc. 423.0894, found *m*/*z* 423.0898.

3,3-Bis(4-chlorophenyl)-5-(cyclopentylidenemethyl)dihydrofuran-2(3*H*)-one (2e).[56] R_f 0.55 (1 : 4 diethyl ether–hexanes); white solid, m.p. = 103–104 °C, yield 68 mg (68%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37–7.21 (m, 8H), 5.38–5.34 (m, 1H), 4.95–4.89 (m, 1H), 3.00 (dd, J = 13.0, 5.2 Hz, 1H), 2.64 (dd, J = 13.2, 10.4 Hz, 1H), 2.39–2.26 (m, 3H), 2.24–2.15 (m, 1H), 1.72–1.54 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 176.6, 153.2, 140.4, 138.2, 134.2, 133.6, 129.4, 129.2, 128.8, 128.8, 117.0, 75.8, 57.5, 44.0, 34.2, 29.4, 26.3, 26.0. IR (neat): ν 2977 (w), 2922 (w), 1909 (w), 1752 (s), 1647 (w) cm^{-1}. HRMS (ESI-orbitrap, $[C_{22}H_{20}Cl_2O_2 + Na]^+$) calc. 409.0738, found *m*/*z* 409.0736.

5-(Cyclohexylidenemethyl)-3,3-bis(2,3-dihydrobenzofuran-5-yl)dihydrofuran-2(3*H*)-one (2f). R_f 0.45 (3 : 7 ethyl acetate–hexanes); viscous yellow oil, yield 64 mg (64%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.20 (s, 1H), 7.14 (s, 1H), 7.13 (dd, J = 8.4, 2.4 Hz, 1H), 6.97 (dd, J = 8.4, 2.4 Hz, 1H), 6.77 (d, J = 8.4 Hz, 1H), 6.69 (d, J = 8.4 Hz, 1H), 5.39–5.35 (m, 1H), 4.95–4.88 (m, 1H), 4.56 (quintet, J = 8.8 Hz, 4H), 3.17 (dt, J = 13.6, 8.8 Hz, 4H), 2.98 (dd, J = 13.0, 5.2 Hz, 1H), 2.60 (dd, J = 12.4, 10.8 Hz, 1H), 2.39–2.28 (m, 3H), 2.26–2.15 (m, 1H), 1.72–1.58 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 178.2, 159.7, 159.2, 148.5, 135.0, 132.0, 128.1, 127.3, 126.9, 124.8, 124.5, 119.1, 109.3, 108.8, 73.4, 75.6, 71.7, 71.6, 57.6, 45.4, 37.1, 29.9, 29.9, 29.7, 28.4, 27.4, 26.6. IR (neat): ν 2948 (w), 2763 (w), 1755 (s), 1685 (w), 1616 (m) cm^{-1}. HRMS (ESI-orbitrap, $[C_{27}H_{28}O_4 + Na]^+$) calc. 439.1885, found *m*/*z* 439.1886.

5-(Cyclopentylidenemethyl)-3,3-bis(2,3-dihydrobenzofuran-5-yl)dihydrofuran-2(3*H*)-one (2g). R_f 0.40 (3 : 7 ethyl acetate–hexanes); white solid, m.p. 154–155 °C, yield 60 mg (60%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.22 (s, 1H), 7.14–7.12 (m, 2H), 6.98 (dd, J = 8.4 Hz, 1H), 6.77 (dd, J = 8.4 Hz, 1H), 6.69 (dd, J = 8.4 Hz, 1H), 5.39–5.36 (m, 1H), 4.95–4.89 (m, 1H), 4.58 (t, J = 8.8, Hz, 2H), 4.54 (t, J = 8.8, Hz, 2H),3.19 (t, J = 8.8, Hz, 2H), 3.15 (t, J = 8.8, Hz, 2H), 2.98 (dd, J = 12.8, 4.8 Hz, 1H), 2.60 (dd, J = 12.8, 4.8 Hz, 1H), 2.39–2.28 (m, 3H), 2.26–2.15 (m, 1H), 1.72–1.58 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 178.2, 159.7, 159.2, 152.4, 135.1, 132.0, 128.1, 127.4, 127.4, 126.9, 124.8, 124.5, 117.6, 109.3, 108.8, 75.7, 75.6, 71.7, 57.5, 44.9, 34.1, 29.9, 29.9, 29.4, 26.3, 26.0. IR (neat): ν 3050 (w), 2967 (m), 2929 (w), 1917 (w), 1755 (s), 1567 (m) cm^{-1}. HRMS (ESI-orbitrap, $[C_{26}H_{26}O_4 + Na]^+$) calc. 425.1729, found *m*/*z* 425.1729.

5-(Cyclohexylidenemethyl)-4,5-dihydro-2*H*-spiro[furan-3,9′-xanthen]-2-one (2h).[56] R_f 0.55 (3 : 7 ethyl acetate–hexanes); viscous yellow oil, yield 80 mg (80%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35–7.12 (m, 8H), 5.44 (ddd, J = 10.0, 8.4, 6.0 Hz, 1H), 5.25 (d, J = 8.4 Hz, 1H), 2.72 (dd, J = 13.6, 6.4 Hz, 1H), 2.31–2.12 (m, 4H), 2.26 (dd, J = 13.6, 10.0 Hz, 1H), 1.64–1.48 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 177.3, 151.7, 151.0, 148.8, 129.3, 129.0, 127.5, 125.9, 124.3, 124.1, 123.7, 122.9, 119.0, 117.6, 116.7, 73.8, 50.8, 50.3, 37.1, 29.8, 28.4, 28.0, 26.6. IR (neat): ν 2955 (w), 2769 (w), 1909 (w), 1751 (s), 1685 (w), 1616 (m) cm^{-1}. HRMS (ESI-orbitrap, $[C_{23}H_{22}O_3 + Na]^+$) calc. 369.1467, found *m*/*z* 369.1465.

5-(Cyclopentylidenemethyl)-4,5-dihydro-2*H*-spiro[furan-3,9′-xanthen]-2-one (2i).[56] R_f 0.49 (3 : 7 ethyl acetate–hexanes); white solid, m.p. = 150–151 °C, yield 78 mg (78%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35–7.26 (m, 3H), 7.23 (dd, J = 3.2, 1.2 Hz, 1H), 7.21–7.20 (m, 1H), 7.18–7.12 (m, 3H), 5.44–5.40 (m, 1H), 5.32–5.26 (m, 1H), 2.74 (dd, J = 13.2, 6.0 Hz, 1H), 2.48–2.19 (m, 4H), 2.26 (dd, J = 13.6, 10.0 Hz, 1H), 1.78–1.59 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 177.3, 152.9, 151.7, 151.0, 129.3, 129.0, 127.4, 125.9, 124.3, 124.1, 123.7, 122.9, 117.6, 117.6, 116.7, 76.2, 50.2, 34.2, 29.4, 26.4, 26.0. IR (neat): ν 3055 (w), 2969 (m), 2922 (w), 1913 (w), 1755 (s), 1599 (m) cm^{-1}. HRMS (ESI-orbitrap, $[C_{22}H_{20}O_3 + Na]^+$) calc. 355.1310, found m/z 355.1316.

5-(2-Methylprop-1-en-1-yl)-3,3-diphenyldihydrofuran-2(3*H*)-one (2j). R_f 0.55 (1 : 4 diethyl ether–hexanes); colourless oil, yield 85 mg (85%). ^{1}H and ^{13}C NMR data were in agreement with published values.[15d]

5-(Cyclohexylidenemethyl)-3-(3-methoxyphenyl)-3-phenyldihydrofuran-2(3*H*)-one (2k). R_f 0.48 (1 : 4 diethyl ether–hexanes); white solid, m.p. = 110–114 °C, yield 83 mg (83%). Mixture of two diastereomers (1 : 1 ratio by ^{1}H NMR); not separable by TLC. ^{1}H NMR (400 MHz, $CDCl_3$; proton count reflects both diastereomers): δ 7.41 (dd, J = 8.4, 1.2 Hz, 2H, both diastereomers), 7.34 (td, J = 6.8, 2.0 Hz, 2H, both diastereomers), 7.33–7.27 (m, 6H, both diastereomers), 7.25–7.20 (m, 2H, both diastereomers), 7.02 (dd, J = 7.6, 1.2 Hz, 1H, one diastereomer), 6.95 (t, J = 2.5 Hz, 1H, one diastereomer), 6.91–6.90 (m, 1H, one diastereomer), 6.89–6.84 (m, 2H, both diastereomers), 6.77 (dd, J = 8.0, 2.4 Hz, 1H, one diastereomer), 5.21 (d, J = 8.4 Hz, 1H, one diastereomer), 5.21 (d, J = 8.4 Hz, 1H, one diastereomer), 5.13–5.05 (m, 2H, both diastereomers), 3.78 (s, 3H, one diastereomer), 3.75 (s, 3H, one diastereomer), 3.05 (dd, J = 4.8, 3.2 Hz, 1H, one diastereomer), 3.01 (dd, J = 4.8, 3.2 Hz, 1H, one diastereomer), 2.69 (dd, J = 10.4, 5.6 Hz, 1H, one diastereomer), 2.65 (dd, J = 10.4, 5.6 Hz, 1H, one diastereomer), 2.28–2.06 (m, 8H, both diastereomers), 1.61–1.49 (m, 12H, both diastereomers). ^{13}C NMR (101 MHz, $CDCl_3$): δ 177.3, 177.2, 160.1, 159.6, 148.7, 148.7, 143.9, 142.3, 141.4, 139.8, 130.0, 129.4, 129.1, 128.5, 127.8, 127.8, 127.5, 127.3, 120.2, 119.8, 119.0, 114.4, 113.9, 113.0, 112.4, 73.5, 73.4, 58.4, 58.4, 55.4, 55.4, 44.8, 44.8, 37.1, 29.8, 29.7, 28.4, 27.9, 26.6. HRMS (ESI-orbitrap, $[C_{24}H_{26}O_3 + Na]^+$) calc. 385.1780, found m/z 385.1777.

5-(Cyclohex-1-en-1-ylmethyl)-3,3-diphenyldihydrofuran-2(3*H*)-one (3a). To obtain optimal yields, a reaction time of 24 h and 20 mol% TsOH were used. R_f 0.50 (1 : 9 acetone–hexanes); viscous yellow oil, yield 93 mg (93%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39–7.34 (m, 4H), 7.33–7.27 (m, 5H), 7.26–7.20 (m, 1H), 5.52–5.51 (m, 1H), 4.49–4.42 (m, 1H), 3.01 (dd, J = 12.8, 4.8 Hz, 1H), 2.59 (dd, J = 13.2, 10.4 Hz, 1H), 2.47 (dd, J = 14.4, 6.4 Hz, 1H), 2.26 (dd, J = 14.4, 6.4 Hz, 1H), 1.99–1.92 (m, 4H), 1.63–1.50 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 177.3, 142.4, 140.0, 132.7, 129.0, 128.5, 127.8, 127.8, 127.5, 127.3, 125.2, 76.2, 58.2, 43.7, 43.6, 29.0, 25.4, 22.9, 22.3. IR (neat): ν 2923 (s), 2857 (m), 1951 (w), 1755 (s), 1609 (w) cm^{-1}. HRMS (ESI-orbitrap, $[C_{23}H_{24}O_2 + Na]^+$) calc. 355.1674, found m/z 355.1670.

5-(Cyclopent-1-en-1-ylmethyl)-3,3-diphenyldihydrofuran-2-(3*H*)-one (3b). R_f 0.52 (1 : 4 diethyl ether–hexanes); viscous yellow oil, yield 70 mg (70%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42–7.34 (m, 4H), 7.34–7.22 (m, 6H), 5.51–5.49 (m, 1H), 4.55–4.48 (m, 1H), 3.07 (dd, J = 13.2, 5.2 Hz, 1H), 2.64 (dd, J = 14.8, 6.4 Hz, 1H), 2.63 (dd, J = 13.2, 10.4 Hz, 1H), 2.46 (dd, J = 14.8, 6.4 Hz, 1H), 2.35–2.26 (m, 4H), 1.92–1.84 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 177.1, 142.3, 140.0, 138.8, 129.0, 128.4, 127.8, 127.8, 127.6, 127.4, 127.2, 76.0, 58.2, 43.7, 36.8, 35.7, 32.6, 23.5. IR (neat): ν 2929 (s), 2862 (m), 1953 (w), 1748 (s), 1608 (w) cm^{-1}. HRMS (ESI-orbitrap, $[C_{22}H_{22}O_2 + H]^+$) calc. 319.1698, found m/z 319.1697.

5-(Cyclohept-1-en-1-ylmethyl)-3,3-diphenyldihydrofuran-2-(3*H*)-one (3c). R_f 0.49 (1 : 4 diethyl ether–hexanes); white solid, m.p. = 95–96 °C, yield 78 mg (78%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41–7.32 (m, 4H), 7.32–7.22 (m, 6H), 5.67 (t, J = 6.4 Hz, 1H), 4.48–4.41 (m, 1H), 3.02 (dd, J = 13.0, 5.2 Hz, 1H), 2.61 (dd, J = 13.2, 10.4 Hz, 1H), 2.55 (d, J = 14, 6.8 Hz, 1H), 2.30 (d, J = 14, 6.8 Hz, 1H), 2.15–2.07 (m, 4H), 1.73 (quintet, J = 6.0 Hz, 2H), 1.52–1.48 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 177.3, 142.5, 140.0, 139.1, 130.6, 129.0, 128.5, 127.9, 127.8, 127.5, 127.3, 73.8, 58.2, 45.6, 43.7, 33.2, 32.5, 28.5, 27.1, 26.7. IR (neat): ν 2926 (s), 2857 (m), 1952 (w), 1750 (s), 1602 (w) cm^{-1}. HRMS (ESI-orbitrap, $[C_{24}H_{26}O_2 + H]^+$ calc. 347.2011, found m/z 347.2015.

3,3-Bis(4-chlorophenyl)-5-(cyclohex-1-en-1-ylmethyl)dihydrofuran-2(3*H*)-one (3d). R_f 0.54 (1 : 4 diethyl ether–hexanes); viscous yellow oil, yield 71 mg (71%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36–7.32 (m, 2H), 7.30–7.27 (m, 4H), 7.25–7.22 (m, 2H), 5.54–5.51 (m, 1H), 4.47–4.40 (m, 1H), 2.95 (dd, J = 12.8, 4.8 Hz, 1H), 2.56 (dd, J = 13.2, 10.4 Hz, 1H), 2.48 (dd, J = 14.4, 6.4 Hz, 1H), 2.26 (dd, J = 14.4, 5.6 Hz, 1H), and 2.00–1.92 (m, 4H), 1.64–1.51 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 176.5, 140.4, 138.2, 134.1, 133.6, 132.5, 129.3, 129.2, 128.8, 128.8, 125.5, 76.2, 57.3, 43.5, 43.4, 29.0, 25.4, 22.9, 22.3. IR (neat): ν 2926 (s), 1899 (w), 1759 (s), 1593 (m) cm^{-1}. HRMS (ESI-orbitrap, $[C_{23}H_{22}Cl_2O_2 + Na]^+$) calc. 423.0894, found m/z 423.0890.

3,3-Bis(4-chlorophenyl)-5-(cyclopent-1-en-1-ylmethyl)dihydrofuran-2(3*H*)-one (3e). R_f 0.55 (1 : 4 diethyl ether–hexanes); white solid, m.p. = 96–97 °C, yield 63 mg (63%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 (dt, J = 8.8, 2.0 Hz, 2H), 7.30–7.26 (m, 4H), 7.23 (dt, J = 8.8, 2.0 Hz, 2H), 5.48 (br. s, 1H), 4.51–4.44 (m, 1H), 2.97 (dd, J = 13.2, 4.8 Hz, 1H), 2.63 (dd, J = 15.0, 7.2 Hz, 1H), 2.56 (dd, J = 13.2, 10.4 Hz, 1H), 2.44 (dd, J = 15.0, 5.6 Hz, 1H), 2.34–2.24 (m, 4H), 1.87 (quintet, J = 7.2 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 176.4, 140.4, 138.5, 138.3, 134.2, 133.7, 129.4, 129.2, 128.8, 128.0, 76.1, 57.3, 43.5, 36.7, 35.7, 32.6, 23.5. IR (neat): ν 2929 (s), 2851 (m), 1901 (w), 1761 (s), 1593 (m) cm^{-1}. HRMS (ESI-orbitrap, $[C_{22}H_{20}Cl_2O_2 + Na]^+$) calc. 409.0738, found m/z 409.0737.

5-(Cyclohex-1-en-1-ylmethyl)-3,3-bis(2,3-dihydrobenzofuran-5-yl)dihydrofuran-2(3*H*)-one (3f). R_f 0.49 (3 : 7 ethyl acetate–hexanes); viscous yellow oil, yield 60 mg (60%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.19–7.13 (m, 2H), 7.10 (dd, J = 8.4, 1.2 Hz, 1H), 6.97 (dd, J = 8.4, 1.2 Hz, 1H), 6.77 (d, J = 6.8, Hz,

1H), 6.72 (d, J = 15.6, 1H), 5.52 (br. s, 1H), 4.56 (dt, J = 14.0, 8.8 Hz, 4H), 4.47–4.40 (m, 1H), 3.17 (dd, J = 13.2, 8.8 Hz, 4H), 2.93 (dd, J = 13.0, 5.2 Hz, 1H), 2.51 (dd, J = 12.8, 10.0 Hz, 1H), 2.47 (dd, J = 15.0, 6.8 Hz, 1H), 2.25 (dd, J = 14.2, 5.8 Hz, 1H), 2.03–1.94 (m, 4H), 1.66–1.53 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 178.2, 159.7, 159.3, 135.2, 132.9, 132.1, 129.4, 128.8, 128.1, 127.4, 127.0, 125.2, 124.8, 124.5, 109.3, 108.9, 76.2, 71.7, 71.6, 57.4, 44.5, 43.7, 29.9, 29.1, 25.4, 23.0, 22.4. IR (neat): ν 3058 (w), 2962 (m), 2922 (w), 1901 (w), 1758 (s), 1598 (m) cm^{-1}. HRMS (ESI-orbitrap, $[C_{27}H_{28}O_4 + Na]^+$) calc. 439.1885, found m/z 439.1883.

5-(Cyclopent-1-en-1-ylmethyl)-3,3-bis(2,3-dihydrobenzofuran-5-yl)dihydrofuran-2(3*H*)-one (3g). R_f 0.40 (3 : 7 ethyl acetate–hexanes); viscous yellow oil, yield 61 mg (61%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.19–7.18 (m, 1H), 7.14–7.13 (m, 1H), 7.10 (dd, J = 8.4, 2.0 Hz, 1H), 6.98 (dd, J = 8.4, 2.0 Hz, 1H), 6.75 (d, J = 8.4 Hz, 1H), 6.70 (d, J = 8.4 Hz, 1H), 5.49–5.47 (m, 1H), 4.57 (t, J = 8.8, Hz, 2H), 4.54 (t, J = 8.8, Hz, 2H), 4.51–4.44 (m, 1H), 3.18 (t, J = 8.8, Hz, 2H), 3.16 (t, J = 8.8, Hz, 2H), 2.96 (dd, J = 13.2, 4.8 Hz, 1H), 2.62 (dd, J = 14.8, 6.0 Hz, 1H), 2.52 (dd, J = 13.2, 10.4 Hz, 1H), 2.43 (dd, J = 14.8, 6.0 Hz, 1H), 2.33–2.25 (m, 4H), 1.87 (quintet, J = 8.0 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 178.2, 159.7, 159.2, 152.4, 135.1, 132.0, 128.1, 127.4, 127.4, 126.9, 124.8, 124.5, 117.6, 109.3, 108.4, 75.7, 71.7, 71.6, 57.5, 44.9, 34.1, 29.9, 29.9, 29.4, 26.4, and 26.0. IR (neat): ν 3051 (w), 2967 (m), 2926 (w), 1934 (w), 1757 (s), 1567 (m) cm^{-1}. HRMS (ESI-orbitrap, $[C_{26}H_{26}O_4 + Na]^+$) calc. 425.1729, found m/z 425.1731.

5-(Cyclohex-1-en-1-ylmethyl)-4,5-dihydro-2*H*-spiro[furan-3,9′-xanthen]-2-one (3h). R_f 0.50 (3 : 7 ethyl acetate–hexanes); viscous yellow oil, yield 78 mg (78%). ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.41–7.27 (m, 4H), 7.23–7.17 (m, 4H), 5.59 (br s, 1H), 5.06–4.99 (m, 1H), 2.80 (dd, J = 13.6, 7.2 Hz, 1H), 2.53 (dd, J = 13.6, 7.2 Hz, 1H), 2.40 (dd, J = 14.0, 5.2 Hz, 1H), 2.33 (dd, J = 14.0, 10.0 Hz, 1H), 2.05–1.94 (m, 4H), 1.62–1.50 (m, 4H). ^{13}C NMR (101 MHz, DMSO-d_6): δ 176.8, 150.4, 149.4, 132.8, 129.4, 129.2, 127.8, 126.4, 124.4, 124.3, 124.1, 123.0, 122.4, 116.9, 116.3, 76.5, 48.6, 48.0, 43.2, 28.3, 24.7, 22.4, 21.8. IR (neat): ν 2973 (w), 2934 (m), 2859 (w), 1902 (w), 1767 (s), 1493 (m) cm^{-1}. HRMS (ESI-orbitrap, $[C_{23}H_{22}O_3 + Na]^+$) calc. 369.1467, found m/z 369.1451.

5-(Cyclopent-1-en-1-ylmethyl)-4,5-dihydro-2*H*-spiro[furan-3,9′-xanthen]-2-one (3i). R_f 0.49 (3 : 7 ethyl acetate–hexanes); viscous yellow oil, yield 72 mg (72%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34–7.28 (m, 2H), 7.22–7.11 (m, 6H), 5.51 (br. s, 1H), 4.88–4.80 (m, 1H), 2.73 (dd, J = 14.2, 6.0 Hz, 1H), 2.71 (dd, J = 13.4, 6.4 Hz, 1H), 2.50 (dd, J = 14.0, 6.4 Hz, 1H), 2.31 (t, J = 7.6 Hz, 4H), 2.23 (dd, J = 13.2, 10.0 Hz, 1H), 1.92–1.84 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 177.2, 151.6, 150.8, 138.4, 129.3, 129.0, 128.2, 127.4, 125.8, 124.3, 124.1, 123.6, 122.8, 117.6, 116.8, 76.5, 50.0, 49.9, 37.3, 35.8, 32.6, 23.5. IR (neat): ν 3057 (w), 2969 (m), 2920 (w), 1904 (w), 1750 (s), 1561 (m) cm^{-1}. HRMS (ESI-orbitrap, $[C_{22}H_{20}O_3 + Na]^+$) calc. 355.1310, found m/z 355.1318.

5-(Cyclohex-1-en-1-ylmethyl)-3-(3-methoxyphenyl)-3-phenyldihydrofuran-2(3*H*)-one (3k). R_f 0.48 (1 : 4 diethyl ether–hexanes); viscous oil, yield 41 mg (41%). Mixture of two diastereomers (1 : 1 ratio by ^{1}H NMR); not separable by TLC. ^{1}H NMR (400 MHz, $CDCl_3$; proton count reflects both diastereomers): δ 7.37–7.21 (m, 5H, both diastereomers), 6.99 (dd, J = 8.0, 1.6 Hz, 1H, one diastereomer), 6.93 (t, J = 2.4 Hz, 1H, one diastereomer), 6.90–6.86(m, 2H, both diastereomers), 6.85 (d, J = 2.4 Hz, 1H, one diastereomer), 6.83 (d, J = 2.8 Hz, 1H, one diastereomer), 6.80 (d, J = 2.8 Hz, 1H, one diastereomer), 6.78 (d, J = 2.4 Hz, 1H, one diastereomer), 5.52 (s, 1H, both diastereomers), 4.51 (m, 1H, both diastereomers), 3.77 (s, 3H, one diastereomer), 3.75 (s, 3H, one diastereomer), 3.04 (m, 1H, both diastereomers), 2.62 (m, 1H, both diastereomers), 2.50 (dd, 14, 7.2 Hz, 1H both diastereomers), 2.28 (dd, J = 14, 5.6 Hz, 1H, both diastereomers), 1.99 (m, 8H, both diastereomers), 1.64 (m, 12H, both diastereomers). ^{13}C NMR (125 MHz, $CDCl_3$): δ 177.3, 177.2, 160.1, 159.6, 144.0, 142.3, 141.3, 139.8, 132.7, 130.0, 129.5, 129.0, 128.5, 127.8, 127.5, 127.3, 125.3, 125.2, 120.3, 119.8, 114.4, 113.9, 112.9, 112.2, 76.3, 76.2, 58.2, 58.1, 55.4, 47.4, 43.8, 43.6, 29.1, 25.4, 22.9, 22.3. HRMS (ESI-orbitrap, $[C_{24}H_{26}O_3 + H]^+$) calc. 363.1960, found m/z 363.1945.

1-Cyclohexyl-4-phenyl-1,2,3,4-tetrahydro-1,4-(epoxymethano)-naphthalen-9-one (4a). Method A; reaction time 7.5 h at −20 °C, then 6 h at 75 °C. R_f 0.58 (1 : 4 acetone–hexanes); white solid, m.p. = 232–233 °C, yield 80 mg (80%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52–7.47 (m, 4H), 7.46–7.41 (m, 1H), 7.40 (d, J = 8.8 Hz, 1H), 7.29 (dt, J = 7.5, 1.2 Hz, 1H), 7.17 (dt, J = 7.68, 1.2 Hz, 1H), 6.64 (d, J = 7.6 Hz, 1H), 2.55–2.47 (m, 2H), 2.42–2.35 (m, 1H), 2.21–2.14 (m, 2H), 2.11–2.05 (m, 1H), 1.98–1.89 (m, 2H), 1.82–1.77 (m, 1H), 1.69 (t, J = 10.4 Hz, 1H), 1.62–1.49 (m, 2H), 1.47–1.38 (m, 2H), 1.36–1.28 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 174.4, 141.9, 138.7, 135.7, 129.7, 128.3, 128.1, 128.0, 126.9, 124.4, 122.3, 85.4, 53.2, 28.8, 27.5, 27.0, 26.8, 26.8, 26.5. IR (neat): ν 2933 (m), 2851 (m), 1952 (w), 1737 (s), 1600 (w) cm^{-1}. HRMS (ESI-orbitrap, $[C_{23}H_{24}O_2 + H]^+$) calc. 333.1855, found m/z 333.1851.

1-Cyclopentyl-4-phenyl-1,2,3,4-tetrahydro-1,4-(epoxymethano)-naphthalen-9-one (4b). Method A; reaction time 5 h at −20 °C, then 7 h at 75 °C. R_f 0.35 (1 : 4 diethyl ether–hexanes); white solid, m.p. = 231–234 °C (decomp), yield 71 mg (71%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52–7.40 (m, 6H),7.29 (td, J = 15.2, 1.2 Hz, 1H), 7.18 (td, J = 15.2, 1.2 Hz, 1H), 6.64 (dd, J = 7.6, 0.8 Hz, 1H), 2.91 (quintet, J = 8.8 Hz, 1H), 2.57–2.43 (m, 2H), 2.20–2.14 (m, 1H), 2.13–1.96 (m, 2H), 1.90–1.79 (m, 3H), 1.77–1.68 (m, 3H), 1.67–1.58 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 174.6, 141.5, 139.6, 135.8, 129.7, 128.3, 128.2, 128.0, 127.0, 124.2, 122.3, 85.7, 53.5, 42.2, 30.5, 27.9, 27.9, 27.3, 26.6, 26.3. IR (neat): ν 2951 (w), 2865 (w), 1739 (s), 1601 (w), 1477 (m) cm^{-1}. HRMS (ESI-orbitrap, $[C_{22}H_{22}O_2 + H]^+$) calc. 319.1698, found m/z 319.1697.

1-Cycloheptyl-4-phenyl-1,2,3,4-tetrahydro-1,4-(epoxymethano)-naphthalen-9-one (4c). Method A; reaction time 3 h at −20 °C, then 5 h at 75 °C. R_f 0.37 (1 : 4 diethyl ether–hexanes); white solid, m.p. = 218–219 °C, yield 83 mg (83%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51–7.40 (m, 5H), 7.38–7.26 (m, 2H), 7.18 (t, J = 7.6 Hz, 1H), 6.65 (d, J = 7.6 Hz, 1H), 2.58–2.50 (m, 3H), 2.22–1.56 (m, 14H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 174.5, 141.9,

139.5, 135.7, 129.7, 128.3, 128.1, 128.0, 126.9, 124.4, 122.1, 87.3, 53.2, 40.7, 29.2, 29,2, 28.1, 27.7, 27.2. IR (neat): ν 3042 (w), 2946 (w), 1864 (w), 1739 (s), 1610 (w), 1486 (m) cm^{-1}. HRMS (ESI-orbitrap $[C_{24}H_{26}O_2 + H]^+$) calc. 347.2011, found *m*/*z* 347.1991.

9-Cyclohexyl-6-(2,3-dihydrobenzofuran-5-yl)-1,2,6,7,8,9-hexahydro-9,6-(epoxymethano)naphtho[2,1-*b*]furan-11-one (4f). Method B. R_f 0.42 (2 : 8 ethyl acetate–hexanes); viscous yellow oil, yield 54 mg (54%). ^1H NMR (400 MHz, $CDCl_3$): δ 7.57 (s, 1H), 7.25 (d, J = 8 Hz, 2H), 6.76 (d, J = 8 Hz, 1H), 6.70 (d, J = 8 Hz, 1H), 4.59–4.54 (m, 4H), 3.25–3.18 (m, 4H), 2.73–2.70 (m, 1H), 2.21–2.14 (m, 2H), 2.09–1.98 (m, 3H), 1.67–1.66 (m, 1H), 1.66–1.63 (m, 1H), 1.44–1.35 (m, 1H), 1.44–1.24 (m, 3H), 1.12–1.03 (m, 2H), 0.88–0.81 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 178.6, 159.2, 158.8, 133.7 (2C), 130.6 (2C), 126.9 (2C), 124.0, 109.0 (2C), 84.3, 71.4, 56.9, 53.0, 52.0, 36.0, 32.0, 30.3, 30.0, 29.9, 26.8, 23.8, 21.0. IR (neat): ν 2932 (m), 2857 (m), 1762 (s), 1614 (w), 1492 (m), 1235 (m) cm^{-1}. HRMS (ESI-orbitrap, $[C_{27}H_{28}O_4 + Na]^+$) calc. 439.1885, found *m*/*z* 439.1874.

9-Cyclopentyl-6-(2,3-dihydrobenzofuran-5-yl)-1,2,6,7,8,9-hexahydro-9,6-(epoxymethano)naphtho[2,1-*b*]furan-11-one (4g). Method B. R_f 0.45 (2 : 8 ethyl acetate–hexanes); viscous yellow oil, yield 31 mg (31%). ^1H NMR (400 MHz, $CDCl_3$): δ 7.61 (s, 1H), 7.31 (s, 1H), 7.04 (d, J = 8 Hz, 1H), 6.77 (d, J = 8 Hz, 1H), 6.71 (d, J = 8 Hz, 1H), 4.60–4.54 (m, 4H), 3.26–3.18 (m, 4H), 2.83–2.79 (m, 1H), 2.45 (t, J = 8 Hz, 2H), 2.13–1.26 (m, 9H), 0.88–0.81 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 177.8, 159.2, 159.1, 134.2, 131.6, 128.4, 127.4, 127.2, 126.9, 124.6, 124.1, 109.0, 108.9, 96.0, 76.8, 71.5, 58.0, 56.6, 48.8, 38.4, 34.2, 30.4, 30.0, 30.0, 28.2, 22.4. IR (neat): ν 2926 (m), 2855 (m), 1762 (s), 1616 (w), 1491 (m), 1231 (m) cm^{-1}. HRMS (ESI-orbitrap, $[C_{26}H_{26}O_4 + Na]^+$) calc. 425.1729, found *m*/*z* 425.1719.

2-Methoxy-4-phenyl-4,5,5a,6,6a,7,8,9,10,10a-decahydroacephenanthrylene-4-carboxylic acid (9). Method A; reaction time 4 h at −20 °C, then 4.5 h at 75 °C. R_f 0.49 (3 : 4 diethyl ether–hexanes); white solid, m.p. = 292–295 °C (decomp), yield 80 mg (80%). ^1H NMR (400 MHz, $CDCl_3$): δ 7.32–7.22 (m, 5H), 7.11 (d, J = 1.6 Hz, 1H), 6.81 (d, J = 1.6 Hz, 1H), 3.82 (s, 3H), 2.91–2.85 (m, 1H), 2.83–2.76 (m, 1H), 2.64–2.54 (m, 2H), 2.29–2.26 (m, 1H), 2.04–2.01 (m, 1H), 1.93–1.87 (m, 1H), 1.70–1.63 (m, 2H), 1.52–1.39 (m, 3H), 1.38–1.25 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 178.9, 159.9, 142.0, 141.2, 138.8, 136.8, 128.5, 127.4, 127.3, 111.4, 109.0, 63.5, 55.8, 48.4, 38.5, 36.2, 34.1, 33.2, 28.8, 28.2, 25.9, 22.4. IR (neat): ν 3282 (br), 2928 (m), 2957 (m), 1710 (m) cm^{-1}. HRMS (ESI-orbitrap, $[C_{24}H_{26}O_3 + H]^+$) calc. 363.1960, found *m*/*z* 363.1957.

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