Gold Catalysis: Desymmetrization in the Furan–Yne Reaction

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Dedicated to Prof. Rolf Huisgen on the occasion of his 90th birthday

Abstract: A series of seven symmetric difuryl-diynes were synthesized by a route delivering an *anti*-configurated product as the major product. The gold-catalyzed conversion of the individual *anti*- and *syn*-diastereomers was investigated. The *anti*-diastereomer in a desymmetrization reaction chemoselectively delivered dihydroindenediols with a furyl and a 2-oxopropyl side chain. The *syn*-diastereomer was completely converted into oligomeric/polymeric material. Thus, it was not necessary to separate the minor amount of the *syn*-diastereomers from the product mixtures in order to isolate the dihydroindenediols.

Key words: alkynes, alcohols, furans, gold, homogeneous catalysis, ketones

The exponential growth of homogeneous gold catalysis in the last decade[1] has led to many new synthetic methods and an increasing number of applications of these methods in total synthesis.[2]

In most examples, two identical functional groups in the substrates will react in an identical manner, as shown for many gold-catalyzed reactions and different substrates.[3]

Based on the gold-catalyzed furan–yne reaction, which usually delivers phenols as products,[4] we have recently investigated changes in the reaction pathway initiated by donors on the alkyne or different lengths of the tether between the furan and alkyne.[5]

Here we report the synthesis of symmetrical difuran-diyne substrates by bidirectional synthesis and their gold-catalyzed conversion with desymmetrization leading to products with only one, rather than the expected two, phenol groups.

Recently, we published the organocatalytic conversion of furfurals **1** into the corresponding furoins **2**, reduction to the 1,2-diol **3**, propargylation to substrates **4**, and subsequent gold-catalyzed transformation to give the bis-phenol derivatives **5**.[6] In the gold-catalyzed step, exclusively cyclization to the five-membered ring product **5**, but not the isomeric six-membered-ring product **6**, was observed (Scheme 1).

We have now prepared the corresponding symmetrical 1,2-dicarbonyl compounds **7** from the unsymmetrical furoins **2** by oxidation. Initially we assumed that we would need an oxidant, such as Dess–Martin periodinane, for this oxidation, but we found that the substrates **2** readily and selectively oxidize in air, only the formation of **2a** was dependent on the oxidant Dess–Martin periodinane[7] (DMP). Thus the formation of the α-furils **7** from furfurals **1** overall is an efficient organocatalyzed dimerization/autoxidation sequence.

Table 1 lists the different substrates **7** prepared in the context of this investigation. The two alkyl derivatives **1c** and **1d** gave low yields of **7c** and **7d**; the same is true for **7e** and **7f**. Thus, these four substrates were not used for the next step. The aryl derivatives **7g–k** were obtained in good yields (entries 7–11). Single crystals could be grown of **7b**, **7j**, and **7l** and these were used for crystal structure analysis (Figure 1). They all show *anti*-conformation of the two carbonyl dipoles. In the case of **7b** the crystal packing causes a slight tilt of the molecule, in **7j** and **7l** the molecules are planar.

The substituted furfurals **1** were either commercially available or conveniently accessible by cross-coupling of 5-bromofuran-2-carbaldehyde (**9**) using the PEPPSI[8] catalyst system (Scheme 2). Good results were obtained for **1j** and **1k** with arylboronic acids, while using alkylboronic acids, the nonbranched butyl group gave **1c** in low yield (9%) and the branched isopropyl group gave no product **1e**. We also tried the Pd-X-Phos[9] and Umicore CX31[10] catalysts in combination with potassium *tert*-butoxide as the base, but the furfurals, in our hands, gave unselective reactions and the products **1** could not be obtained in pure form.

The reaction of the substrates **7** with two equivalents of propargylmagnesium bromide then provided the bis-homopropargylic diols **8** (Table 1). In most cases good yields for the twofold addition could be obtained (entries 1, 2, 7, 9–12); the reaction was unselective only in the case of the bromoarene **7h** (entry 8) and the desired product could not be isolated. Taking into account that after the first addition the intermediate monoketone is sterically quite shielded, the overall yields for the twofold addition are quite good. The diyne substrates **8** were obtained with low diastereoselectivity, the major diastereomer probably originating from a Cram-chelate transition state. The major diastereomer was assigned from crystal structure analysis of the product **8a** (Figure 2), clearly showing the relative configuration of the two stereocenters to be *anti*.[11] The other assignments are based on comparison of the NMR data with the data of **8a**, only in the case of **8i** (entry

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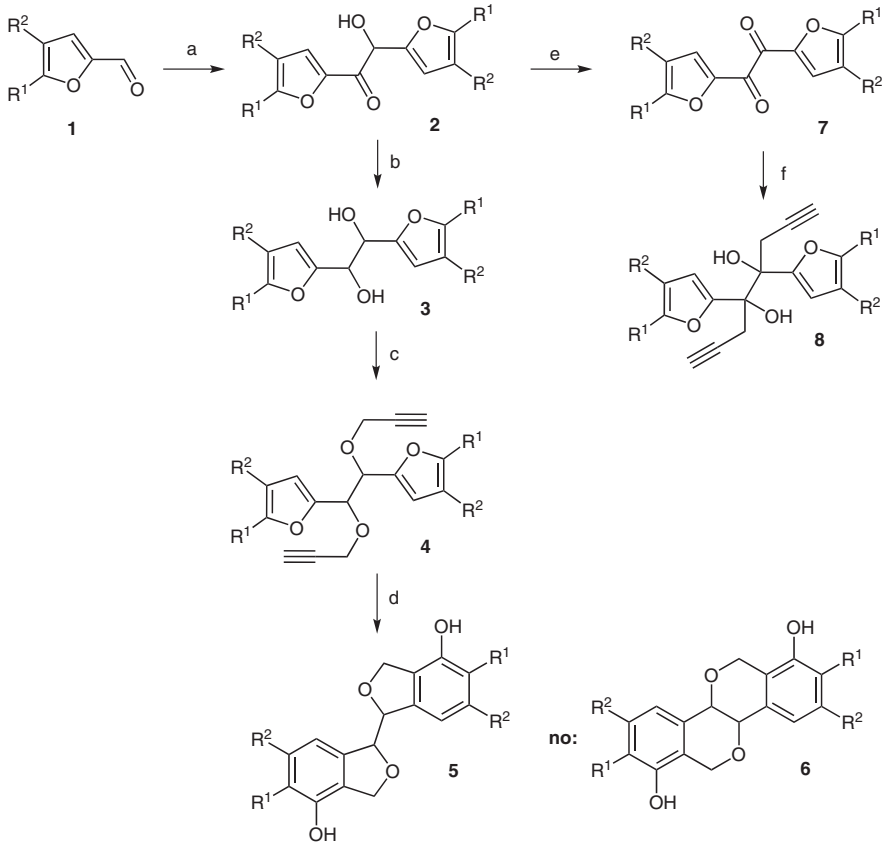


Scheme 1 Known synthesis and conversion of **4** and synthesis of the new substrate type **8**. *Reagents and conditions:* (a) thiazolium or triazolium salt (5 mol%), base; (b) $NaBH_4$, MeOH; (c) $HC{\equiv}CCH_2Br$, NaH, DMF; (d) $AuCl_3$ (5 mol%), CH_2Cl_2; (e) DMP or spontaneous oxidation in air; (f) $HC{\equiv}CCH_2MgBr$ (2 equiv), THF.

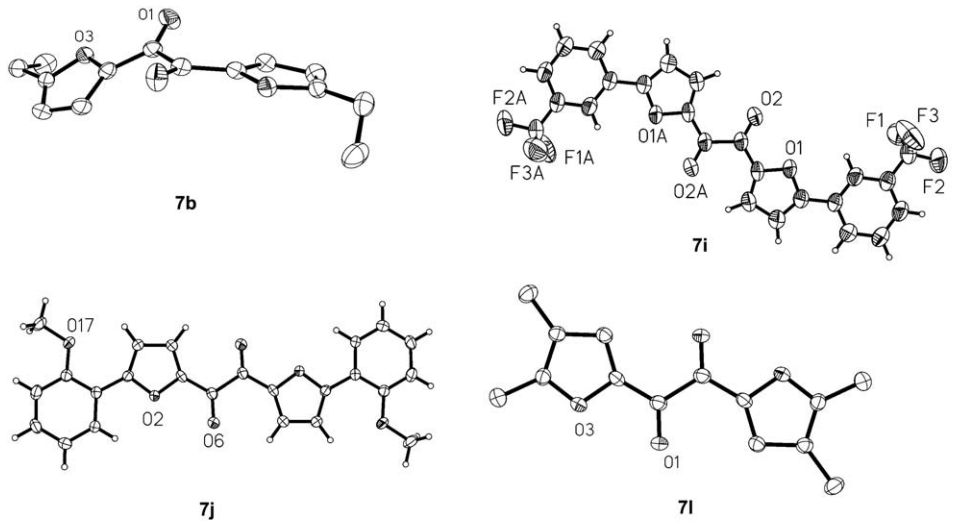


Figure 1 Solid-state structure of **7b** (CCDC 776565), **7i** (CCDC 776566), **7j** (CCDC 776567), and **7l** (CCDC 776568)

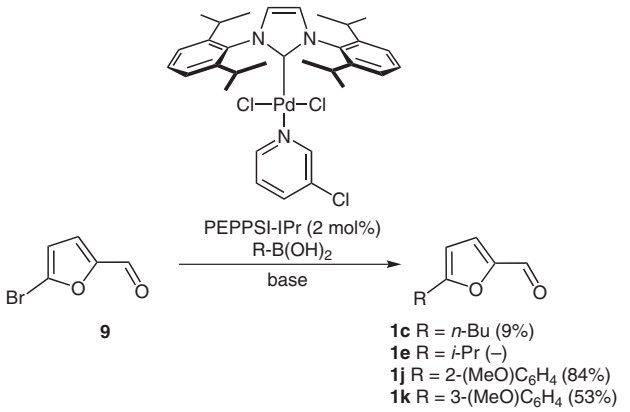
9) did a comparison with the spectroscopic data of **8a** not allow safe assignment of the *anti*/*syn*-diastereomers.

The substrates **8** now in our hands, we first investigated the reaction of the individual diastereomers. Reaction of the *anti*-diastereomer gave selective conversion delivering phenols of type **10**, a reaction that has a loss of symmetry from the substrate to the product (Scheme 3). The product **10** now possesses four different functional groups, namely a phenol, a tertiary alcohol, a ketone, and a furan ring. In these initial examples with pure *anti*-**8** the phenol-type product **10** was isolated in excellent yields; full conversion was reached within a few minutes. The formation of side products could not be detected. Table 2

Table 1 Synthesis of the 1,2-Dicarbonyl Compounds **7** and Twofold Addition of Propargylmagnesium Bromide To Give **8**

Entry	Substrate			Yield (%)		Temp (°C) of	Product **8**[b]	
		R^1	R^2	**2**	**7**[a]	Grignard addition	Yield[b] (%)	Ratio *anti*/*syn*
1	**1a**	Me	H	66[6]	54[c]	–50	67	75:25
2	**1b**	Et	H	–[d]	79	–10	65	54:46
3	**1c**	Bu	H	–[e]	36	–	–	–
4	**1d**	pentyl	H	–[d]	–	–	–[f]	–
5	**1e**	*i*-Pr	H	–[e]	–	–	–	–
6	**1f**	NO_2	H	–	–	–	–	–
7	**1g**	Ph	H	–	92[g]	–20	62	64:36
8	**1h**	4-BrC_6H_4	H	–	78	–20	–	–
9	**1i**	3-$F_3CC_6H_4$	H	98[6]	92	–20	82	57:43[h]
10	**1j**	2-$MeOC_6H_4$	H	–[d]	63	–10	61	54:46
11	**1k**	3-$MeOC_6H_4$	H	–[d]	68	–10	69	65:35
12	**1l**	Me	Me	–[d]	91	–10	59	67:33

[a] Isolated yield, unless otherwise stated oxidation is by air and the yield is over 2 steps from **1**.
[b] Isolated yield.
[c] Oxidation is by DMP, yield over two steps from **1a**.
[d] **1** was directly converted into **7**.
[e] Not converted into **2** as the yield of the Suzuki coupling leading to **1c** was too low.
[f] Not converted into **8** as the yield of **7** was too low.
[g] O_2, yield over two steps from **1g**.
[h] No unambiguous assignment of the diastereomers was possible.



Scheme 2 PEPPSI-catalyzed Suzuki cross-coupling of 5-bromofuran-2-carbaldehyde (**9**)

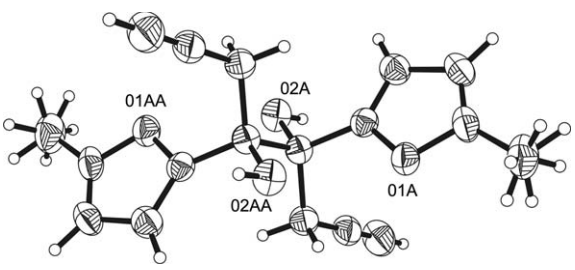
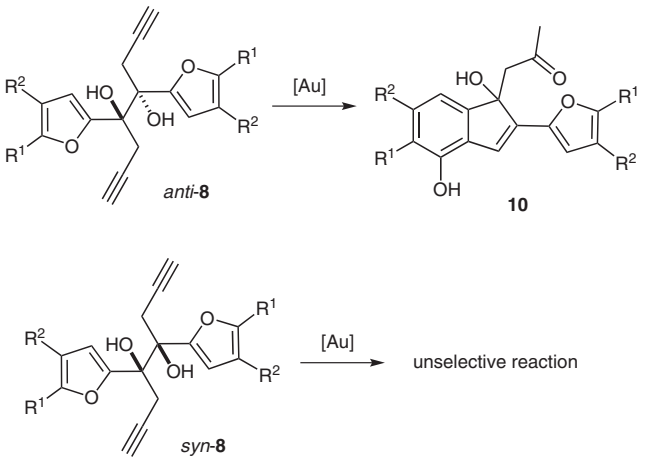


Figure 2 Solid state molecular structure of *anti*-**8a** (CCDC 776569)

summarizes the results with *anti*-**8a**, *anti*-**8b**, and *anti*-**8g**, all of which gave yields of more than 90%.

The *syn*-diastereomer of the substrate reacts completely unselective, ^{1}H NMR of the reaction mixture showed no detectable intermediates and at the end of the reaction no defined products could be isolated (Scheme 3).



Scheme 3 Different selectivity is observed when starting from the individual diastereomers of **8**

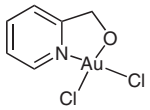
The reaction conditions were varied for the reaction of *anti*-**8a** (Table 3). Monitoring the reactions by ^{1}H NMR showed that gold(III) chloride in dichloromethane (entry

Table 2 Gold-Catalyzed Transformations of *anti*-**8** to the Phenol **10** (5 mol% $AuCl_3$, CH_2Cl_2)

Entry	Substrate	R^1 (R^2 = H)	Time (min)	Product	Yield (%)
1	*anti*-**8a**	Me	5	**10a**	92
2	*anti*-**8b**	Bu	10	**10b**	95
3	*anti*-**8g**	Ph	10	**10i**	95

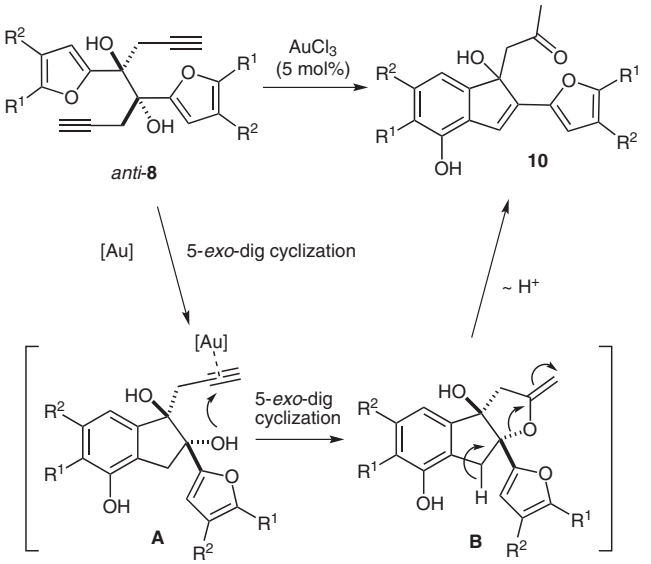
1) represents the best conditions. In chloroform (entry 2) the consumption of the substrate is fast, but unselective and in acetonitrile (entry 3) the isomerization is much slower, but still selective. The other gold catalysts like a pyridine complex[4c] (entry 4) reacted very slowly or, like the gold(I) complex (entry 5), they were unselective.

Table 3 Testing Different Catalysts and Solvents for the Room-Temperature Conversion of Substrate *anti*-**8a** into **10a**

Entry	Catalyst	Solvent, time	Yield (%)
1	5 mol% $AuCl_3$	CH_2Cl_2, 5 min	92
2	5 mol% $AuCl_3$	$CDCl_3$, 5 min	unselective
3	5 mol% $AuCl_3$	CD_3CN, 24 h	90
4	 5 mol%	$CDCl_3$, 24 h	50
5	3 mol% (μ-Cl)-$[Au(PPh_3]_2BF_4$[12]	$CDCl_3$, 24 h	unselective

The reactions of *anti*-**8** probably proceed by a 5-*exo*-dig-cycloisomerization of the first furyl-yne to the intermediate **A** (Scheme 4), the mechanism of this conversion corresponds to the well-known phenol synthesis.[4f] In the next step the gold catalyst could activate the remaining triple bond for another nucleophilic addition, in the *anti*-diastereomer the formation of the enol ether **B** is conceivable (intramolecular competition experiments with furyl and hydroxy nucleophile have shown that the enol ether formation is faster).[13] On the other hand, we cannot exclude that first water is eliminated (creating a conjugation between the aryl and the furyl ring) and then re-added to the alkyne (such gold-catalyzed eliminations have been described).[14] There is no tendency for the elimination of water from the indene derivative **10** under these reaction conditions. We assume that in *anti*-**8** an intramolecular hydrogen bridge between one furan ring and a distal hydroxy group stabilizes a conformation which places the other furyl group close to the alkyne and thus facilitates the first cycloisomerization step (Figure 3, left). In the corresponding *syn*-**8** such an intramolecular hydrogen bridge stabilizes a conformation that prevents cycloisomerization (Figure 3, right), then gold-catalyzed elimination/condensation chemistry[14] takes place and oligomeric/polymeric material is formed.

Finally, we investigated the conversion of mixtures of the two diastereomers, which proceeded nicely. In the case of



Scheme 4 Gold-catalyzed cycloisomerization/desymmetrization of substrates *anti*-**8**

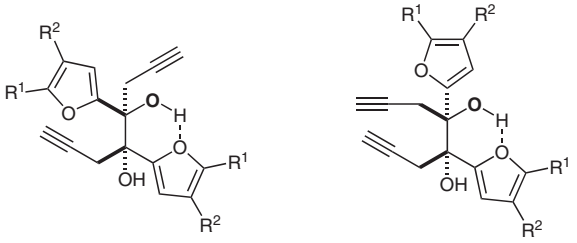


Figure 3 Possible hydrogen bridges in the *anti*- (left) and the *syn*-diastereomers (right) of **8**

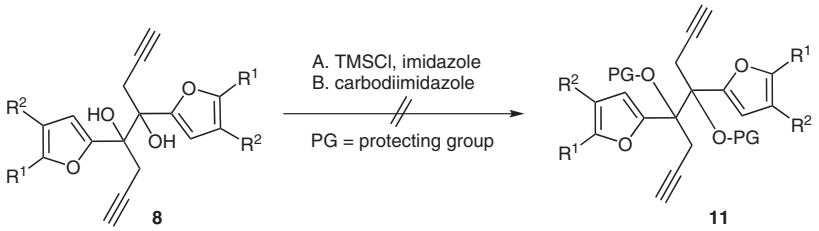
8b a reduced yield was obtained (Table 4, entry 1), which is caused by separation problems in the workup. Compound **8i** gave **10i** in excellent yield (entry 2), however, for **8j–l** separation problems again led to slightly reduced yields (entries 3–5).

Table 4 Gold-Catalyzed Conversion of *anti*/*syn*-Mixtures of **8** into **10**[a]

Entry	Substrate *anti*/*syn*-**8**			Yield[b] (%)
		R^1	R^2	
1	**8b**	Et	H	67
2	**8i**	3-$F_3CC_6H_4$	H	95
3	**8j**	2-$MeOC_6H_4$	H	36
4	**8k**	3-$MeOC_6H_4$	H	76
5	**8l**	Me	Me	72

[a] Reaction conditions: CD_3CN, r.t., 24 h.
[b] Based on the portion of *anti*-**8**.

Efforts to suppress the competing reaction of the hydroxy groups by protecting them failed. The sterically crowded environment did not allow for the successful protection of **8** (Scheme 5).



Scheme 5 The TMS- or carbonate-protection of **8** failed

The gold-catalyzed conversions of the two diastereomers of the difuran-diynes show how the outcome of the gold-catalyzed conversion can depend on the relative configuration of stereocenters in the substrate. The products obtained from the major diastereomers demonstrate desymmetrization, converting the substrate into a product with four quite different functional groups, a phenolic hydroxy group, a tertiary alcohol, a ketone, and one remaining furan ring (the latter, for example, can easily be degraded to a carboxylate[15]). This work complements the recent findings on highly diastereoselective reaction of monofuran diyne substrates.[16]

Commercially available chemicals were used without further purification. THF and Et_2O were dried prior to use. If not indicated otherwise, all reactions were carried out using Schlenk techniques under an atmosphere of nitrogen. Melting points were determined on a Büchi SMP-20 melting point apparatus and are uncorrected. NMR spectra were recorded at r.t. on Bruker ARX500, ARX300 or ARX250 spectrometers. Chemical shifts (δ, ppm) were referenced to residual solvent protons. Signal multiplicities are as follows: s (singlet), br s (broad singlet), d (doublet), t (triplet), q (quartet), quint (quintet), m (multiplet). The multiplicities assigned to the ^{13}C NMR data are based on a combination of DEPT 135 and DEPT 90 spectra and are defined as follows: s (quarternary C), d (CH), t (CH_2), q (CH_3). MS spectra were recorded on Finnigan MAT 90 or Varian 711 instruments. IR spectra were recorded on a Bruker Vector 22 spectrophotometer. The fraction of petroleum ether (PE) used was that with boiling range 70–90 °C.

CCDC 776565–776569 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Organocatalyzed Furil Addition To Give Furoins 7; General Procedure

The published procedure was used for this transformation.[6]

2-Hydroxy-1,2-bis(5-methylfuran-2-yl)ethanone (2a)

Obtained from 5-methylfuran-2-carbaldehyde (**1a**, 10.0 g, 90.8 mmol), Et_3N (3.8 mL, 27.3 mmol) and thiazolium catalyst (142 mg, 4.52 mmol, 5 mol%) in abs EtOH (30 mL). The mixture was stirred under reflux for 3 h and the product was precipitated by addition of cold H_2O and purified by recrystallization (EtOH) to give the product (6.85 g, 31.1 mmol, 69%) as a yellow solid. The spectroscopic data is in accordance with the literature.[17]

^1H NMR (300 MHz, $CDCl_3$): δ = 2.24 (d, *J* = 1.0 Hz, 3 H), 2.38 (s, 3 H), 4.21 (br s, 1 H), 5.65 (s, 1 H), 5.91 (dq, *J* = 3.1, 1.0 Hz, 1 H), 6.14 (dq, *J* = 3.6, 0.9 Hz, 1 H), 6.25 (d, *J* = 3.1 Hz, 1 H), 7.12 (d, *J* = 3.6 Hz, 1 H).

1,2-Bis(5-methylfuran-2-yl)ethan-1,2-dione (7a)

Furoin **2a** (1.41 g, 6.43 mmol) was dissolved in CH_2Cl_2 (60 mL). After cooling to 0 °C, DMP (3.00 g, 7.07 mmol) was added and the reaction mixture was stirred for 2 h at r.t. and for 2 h at reflux temperature. After the addition of distilled H_2O (20 mL) and Et_2O (50 mL), the phases were separated and the organic phase was washed with H_2O (2 × 30 mL) and sat. brine (30 mL). After drying the organic phase with $MgSO_4$ and filtration, the solvent was removed in vacuo. Column chromatography on silica (PE–EtOAc, 2:1) afforded **7a** (1.09 g, 5.02 mmol, 78%) as a colorless solid.[17] R_f (PE–EtOAc, 4:1) = 0.17.

^1H NMR ($CDCl_3$, 300 MHz): δ = 2.46 (s, 6 H), 6.26 (dd, ^3J = 3.6 Hz, ^4J = 0.9 Hz, 2 H), 7.53 (d, ^3J = 3.6 Hz, 2 H).

1,2-Bis(5-ethylfuran-2-yl)ethane-1,2-dione (7b)

Obtained from 5-ethylfuran-2-carbaldehyde (**1b**, 1.00 g, 8.06 mmol), THF (15 mL), triazole catalyst (133 mg, 202 μmol), and K_2CO_3 (5.57 g, 4.03 mmol) at 70 °C (2 d). The crude product was purified by column chromatography (silica gel, PE–Et_2O, 10:1) to give **7b** (786 mg, 79%) as an orange oil; mp 106 °C; R_f = 0.15 (PE–Et_2O, 10:1).

IR (film): 3154, 3139, 3126, 2939, 2878, 1815, 1643, 1500, 1454, 1370 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.31 (t, *J* = 7.5 Hz, 6 H), 2.79 (q, *J* = 7.7 Hz, 4 H), 6.26 (d, *J* = 3.7 Hz, 2 H), 7.54 (d, *J* = 3.7 Hz, 2 H).

^{13}C NMR (76 MHz, $CDCl_3$): δ = 11.64 (q, 2 C), 21.93 (t, 2 C), 77.21 (s, 2 C), 108.57 (d, 2 C), 126.67 (d, 2 C), 151.15 (s, 2 C), 166.66 (s, 2 C).

MS (EI^+, 70 eV): *m*/*z* (%) = 246 (21) $[M]^+$, 213 (5), 201 (6), 182 (3), 151 (12), 123 (100).

HRMS (EI^+, 70 eV): *m*/*z* $[M]^+$ calcd for $C_{14}H_{14}O_4$: 246.0893; found: 246.0893.

Anal. Calcd for $C_{14}H_{14}O_4$ (246.09): C, 68.28; H, 5.73. Found: C, 68.27; H, 5.78.

1,2-Bis(5-butylfuran-2-yl)ethane-1,2-dione (7c)

Obtained from 5-butylfuran-2-carbaldehyde (**1c**, 546 g, 3.59 mmol), EtOH (10 mL), thiazolium salt (28.2 mg, 90.0 μmol), and Et_3N (1.49 g, 10.8 mmol) at 80 °C for 1 d. The crude product was purified by column chromatography (silica gel, PE–Et_2O–CH_2Cl_2, 12:2:1) to give **7c** (200 mg, 36%) as a yellow oil; R_f = 0.35 (PE–Et_2O, 5:1).

IR (film): 3433, 2960, 2928, 2873, 1736, 1499 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.87 (m, 6 H), 1.26 (m, 4 H), 1.64 (m, 4 H), 2.69 (t, *J* = 7.6 Hz, 4 H), 6.07 (d, *J* = 3.8 Hz, 2 H), 6.18 (d, *J* = 3.6 Hz, 2 H).

^{13}C NMR (76 MHz, $CDCl_3$): δ = 13.71 (q, 2 C), 22.27 (t, 2 C), 28.25 (t, 2 C), 29.72 (t, 2 C), 77.20 (s, 2 C), 108.30 (d, 2 C), 109.27 (d, 2 C), 146.17 (s, 2 C), 165.65 (s, 2 C).

MS (EI^+, 70 eV): *m*/*z* (%) = 302 (4), 204 (4), 139 (13), 91 (100) $[M]^+$.

HRMS (EI$^+$, 70 eV): *m/z* [M]$^+$ calcd for $C_{18}H_{22}O_4$: 302.1518; found: 302.1510.

1,2-Bis(5-phenylfuran-2-yl)ethane-1,2-dione (7g)

Obtained from 5-phenylfuran-2-carbaldehyde (**1g**, 2.00 g, 11.6 mmol), thiazolium salt (182 mg, 581 μmol, 5 mol%), Et_3N (391 mg, 3.87 mmol), and EtOH (20 mL) at reflux for 2 h. Stirring was continued under an atmosphere of O_2 at 60 °C for 72 h. Filtration of the crude product (silica gel) gave **7g** (1.83 g, 5.35 mmol, 92%) as a yellow solid; mp 189–192 °C; R_f = 0.57 (PE–Et_2O, 2:1).

IR (film): 1644, 1469, 1256, 1029, 972, 753, 677 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.88 (d, *J* = 3.8 Hz, 2 H), 7.40–7.48 (m, 6 H), 7.75 (d, *J* = 3.8 Hz, 2 H), 7.86–7.89 (m, 4 H).

^{13}C NMR (126 MHz, CD_2Cl_2): δ = 108.31 (d, 2 C), 125.62 (d, 4 C), 127.18 (d, 2 C), 128.79 (s, 2 C), 128.99 (d, 4 C), 130.02 (d, 2 C), 148.86 (s, 2 C), 160.66 (s, 2 C), 176.55 (s, 2 C).

MS (ESI$^+$): *m/z* (%) = 365 (100) [M + Na]$^+$.

HRMS (ESI-EM): *m/z* [M + Na]$^+$ calcd for $C_{22}H_{14}NaO_4$: 365.0784; found: 365.0772.

Anal. Calcd for $C_{22}H_{14}O_4$ (342.34): C, 77.18; H, 4.12. Found: C, 76.93; H, 4.26.

1,2-Bis[5-(4-bromophenyl)furan-2-yl]ethane-1,2-dione (7h)

Obtained from 5-(4-bromophenyl)furan-2-carbaldehyde (**1h**, 350 mg, 1.40 mmol), Et_3N (27.6 mg, 140 μmol), thiazolium catalyst (23.0 mg, 70 μmol, 5 mol%), and EtOH (10 mL). Column chromatography of the crude product (silica gel, PE–EtOAc, 3:1) gave **7h** (271 mg, 1.09 μmol, 78%) as a yellow oil. R_f = 0.20 (PE–Et_2O, 6:1). The product still contained some starting material which could not be separated, thus it was not converted in the next step.

1,2-Bis{5-[3-(trifluoromethyl)phenyl]furan-2-yl}ethane-1,2-dione (7i)

Obtained from 5-[3-(trifluoromethyl)phenyl]furan-2-carbaldehyde (**1i**, 500 mg, 2.08 mmol), Et_3N (63.1 mg, 624 μmol), thiazolium catalyst (32.7 mg, 104 μmol, 5 mol%), and EtOH (10 mL). Column chromatography of the crude product (silica gel, PE–Et_2O, 6:1) gave **7i** (458 mg, 1.91 mmol, 92%) as a yellow solid; mp 177–178 °C; R_f = 0.29 (PE–Et_2O, 4:1).

IR (film): 1646, 1504, 1447, 1327, 1271, 1248, 1159, 1110, 1094, 1068, 1028, 974, 796, 770, 689, 650 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.97 (d, ^3J = 4.0 Hz, 2 H), 7.60 (dd, ^3J = 8.0 Hz, ^3J = 7.5 Hz, 2 H), 7.65 (d, ^3J = 8.0 Hz, 2 H), 7.78 (d, ^3J = 4.0 Hz, 2 H), 8.04 (d, ^3J = 7.5 Hz, 2 H), 8.08 (s, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 109.36 (d, 2 C), 122.31 [d, 2 C (q, $^3J_{C\text{-}F}$ = 3.6 Hz)], 124.91 [s, 2 C (q, $^1J_{C\text{-}F}$ = 273.8 Hz)], 126.43 [d, 2 C (q, $^3J_{C\text{-}F}$ = 3.7 Hz)], 127.05 (d, 2 C), 128.61 (d, 2 C), 129.36 (d, 2 C), 129.65 (d, 2 C), 131.69 [s, 2 C (q, $^2J_{C\text{-}F}$ = 32.6 Hz)], 149.20 (s, 2 C), 158.79 (s, 2 C), 176.20 (s, 2 C).

MS (EI$^+$, 70 eV): *m/z* (%) = 478 (12) [M]$^+$, 239 (100), 183 (23).

Anal. Calcd for $C_{24}H_{12}F_6O_4$ (478.38): C, 60.26; H, 2.53. Found: C, 60.04; H, 2.42.

1,2-Bis[5-(2-methoxyphenyl)furan-2-yl]ethane-1,2-dione (7j)

Obtained from 5-(2-methoxyphenyl)furan-2-carbaldehyde (**1j**, 4.08 g, 20.2 mmol), THF (55 mL), triazolium salt (282 mg, 1.01 mmol), and K_2CO_3 (13.9 g 101 mmol) at 70 °C for 2 d. Column chromatography of the crude product (silica gel, PE–Et_2O–CH_2Cl_2, 10:2:1) gave **7j** (2.55 g, 63%) as a yellow solid; mp 165 °C; R_f = 0.20 (PE–Et_2O–CH_2Cl_2, 12:2:1).

IR (film): 3797, 3758, 3680, 3051, 2964, 1636, 1602, 1505, 1485, 1447 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.90 (s, 6 H), 6.92 (d, *J* = 3.2 Hz, 2 H), 7.00 (d, *J* = 7.5 Hz, 2 H), 7.09 (d, *J* = 3.8 Hz, 2 H), 7.72 (t, *J* = 7.1 Hz, 2 H), 7.31 (t, *J* = 7.1 Hz, 2 H), 8.04 (t, *J* = 7.7 Hz, 2 H).

^{13}C NMR (76 MHz, $CDCl_3$): δ = 55.51 (q, 2 C), 111.19 (d, 2 C), 113.13 (d, 2 C), 117.92 (s, 2 C), 121.00 (d, 2 C), 127.23 (d, 2 C), 127.83 (d, 2 C), 130.92 (d, 2 C), 147.80 (s, 2 C), 157.00 (s, 2 C), 157.53 (s, 2 C), 176.91 (s, 2 C).

MS (EI$^+$, 70 eV): *m/z* (%) = 402 (27) [M]$^+$, 396 (16), 376 (13), 341 (16), 313 (45), 285 (9), 269 (67), 253 (18), 224 (20), 201 (100), 189 (90).

HRMS (EI$^+$, 70 eV): *m/z* [M]$^+$ calcd for $C_{24}H_{18}O_6$: 402.3961; found: 402.1110.

1,2-Bis[5-(3-methoxyphenyl)furan-2-yl]ethane-1,2-dione (7k)

Obtained from 5-(3-methoxyphenyl)furan-2-carbaldehyde (**1k**, 2.00 g, 9.89 mmol), THF (60 mL), triazolium salt (141 mg, 500 μmol), and K_2CO_3 (4.19 g 29.7 mmol) at 70 °C for 2 d. Column chromatography of the crude product (silica gel, PE–Et_2O–CH_2Cl_2, 12:2:1) gave **7k** (1.35 g, 68%) as a yellow solid; mp 128–136 °C; R_f = 0.20 (PE–Et_2O–CH_2Cl_2, 12:2:1).

IR (film): 3440, 3165, 1637, 1603, 1510 cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.81 (s, 6 H), 6.79 (d, *J* = 3.8 Hz, 2 H), 6.89 (d, *J* = 6.5 Hz, 2 H), 7.25–7.39 (m, 6 H), 7.66 (d, *J* = 3.8 Hz, 2 H).

^{13}C NMR (76 MHz, $CDCl_3$): δ = 55.49 (q, 2 C), 108.61 (d, 2 C), 110.59 (d, 2 C), 116.11 (d, 2 C), 118.24 (d, 2 C), 127.18 (d, 2 C), 130.09 (d, 2 C), 148.83 (s, 2 C), 160.05 (s, 2 C), 160.54 (s, 2 C), 176.52 (s, 2 C).

MS (ESI$^+$): *m/z* (%) = 403 (100) [M + H]$^+$.

HRMS (ESI$^+$): *m/z* [M + H]$^+$ calcd for $C_{24}H_{19}O_6$: 403.4041; found: 403.1176.

1,2-Bis(4,5-dimethylfuran-2-yl)ethane-1,2-dione (7l)

Obtained from 2,5-dimethylfuran-2-carbaldehyde (**1l**, 2.00 g, 16.1 mmol), THF (20 mL), triazolium salt (133 mg, 810 μmol), and K_2CO_3 (6.68 g 48.3 mmol) at 70 °C for 2 d. Column chromatography of the crude product (silica gel, PE–Et_2O, 10:1) gave **7l** (1.80 g, 91%) as an orange solid; mp 135 °C; R_f = 0.10 (PE–Et_2O, 10:1).

IR (film): 1633, 1498, 1294, 1163, 1127, 950, 810, 696 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.00 (s, 6 H), 2.35 (s, 6 H), 7.38 (2 H).

^{13}C NMR (76 MHz, $CDCl_3$): δ = 9.66 (q, 2 C), 12.25 (q, 2 C), 77.21 (s, 2 C), 118.91 (d, 2 C), 147.27 (s, 2 C), 157.60 (s, 2 C), 176.91 (s, 2 C).

MS (EI$^+$, 70 eV): *m/z* (%) = 246 (17) [M]$^+$, 201 (3), 182 (2), 151 (8), 123 (100), 111 (11).

HRMS (EI$^+$, 70 eV): *m/z* [M]$^+$ calcd for $C_{14}H_{14}O_4$: 246.0893; found: 246.0883.

PEPPSI-Catalyzed Cross-Coupling for the Synthesis of Substituted Furfurals 1

5-Butylfuran-2-carbaldehyde (1c)

5-Bromofuran-2-carbaldehyde (4.81 g, 27.4 mmol), butylboronic acid (3.34 g, 32.8 mmol), K_2CO_3 (11.4 g, 82.4 mmol), and PEPPSI (465 mg, 685 μmol) were dissolved in dioxane (50 mL) and H_2O (10 mL). The mixture was stirred overnight at 95 °C, then filtered through Celite and the solvent was removed in vacuo. Column chromatography (silica gel, PE–Et_2O, 3:1) gave **1c** (546 mg, 9%) as an orange oil.

R_f = 0.46 (PE–Et_2O, 3:1).

IR (film): 3122, 2961, 2934, 2874, 1728, 1680, 1581, 1518, 1466, 1433 cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.79 (t, *J* = 9.0 Hz, 2 H), 1.13–1.28 (m, 2 H), 1.47–1.57 (m, 2 H), 2.56 (t, *J* = 9.0 Hz, 3 H), 6.11 (d, *J* = 3.0 Hz, 1 H), 7.06 (d, *J* = 3.0 Hz, 1 H), 9.35 (s, 1 H).

^{13}C NMR (76 MHz, $CDCl_3$): δ = 13.31 (q), 21.72 (t), 27.71 (t), 29.26 (t), 108.39 (d), 151.42 (s), 167.83 (s), 176.63 (d).

MS (EI$^+$, 70 eV): *m*/*z* (%) = 152 (74) [M]$^+$, 123 (17), 109 (100), 81 (29), 67 (3), 53 (14), 38 (9), 26 (9).

HRMS (EI$^+$, 70 eV): *m*/*z* [M]$^+$ calcd for $C_9H_{12}O_2$: 152.0837; found: 152.0845.

5-(2-Methoxyphenyl)furan-2-carbaldehyde (1j)

5-Bromofuran-2-carbaldehyde (4.81 g, 27.4 mmol), 2-methoxyphenylboronic acid (5.00 g, 32.9 mmol), K_2CO_3 (11.4 g, 82.4 mmol), and PEPPSI (280 mg, 412 μmol) were dissolved in dioxane (20 mL) and H_2O (4 mL). The mixture was stirred at 95 °C overnight then filtered through Celite and the solvent was removed in vacuo. Column chromatography of the crude product (silica gel, PE–Et_2O–CH_2Cl_2, 10:2:1) gave **1j** (4.64 g, 84%) as an orange oil.

R_f = 0.25 (PE–Et_2O–CH_2Cl_2, 10:2:1).

IR (film): 3075, 2950, 2825, 2750, 1717, 1671, 1602, 1515, 1489, 1433 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.98 (s, 3 H), 7.01 (d, *J* = 8.4 Hz, 1 H), 7.08 (t, *J* = 7.6 Hz, 1 H), 7.15 (d, *J* = 3.7 Hz, 1 H), 7.34 (d, *J* = 3.7 Hz, 1 H), 7.36–7.41 (m, 1 H), 8.07 (d, *J* = 7.8 Hz, 1 H), 9.66 (s, 1 H).

^{13}C NMR (76 MHz, $CDCl_3$): δ = 55.48 (q), 111.18 (d), 112.57 (d), 120.94 (d), 127.43 (d), 130.65 (d), 150.89 (s), 156.20 (s), 156.82 (s), 177.20 (d).

MS (EI$^+$, 70 eV): *m*/*z* (%) = 202 (100) [M]$^+$, 201 (3), 158 (6), 145 (11), 131 (20), 115 (9), 102 (6), 77 (4).

HRMS (EI$^+$, 70 eV): *m*/*z* [M]$^+$ calcd for $C_{12}H_{10}O_3$: 202.0630; found: 202.0636.

5-(3-Methoxyphenyl)furan-2-carbaldehyde (1k)

5-Bromfuran-2-carbaldehyde (4.81 g, 27.4 mmol), 3-methoxyphenylboronic acid (5.00 g, 32.9 mmol), K_2CO_3 (11.4 g, 82.4 mmol), and PEPPSI (486 mg, 715 μmol) were dissolved in dioxane (20 mL) and H_2O (4 mL). The mixture was heated to 95 °C overnight then filtered through Celite and the solvent was removed in vacuo. Purification of the crude product by column chromatography (silica gel, PE–Et_2O–CH_2Cl_2, 10:2:1) gave **1k** (2.92 g, 53%) as an orange oil; R_f = 0.25 (PE–Et_2O–CH_2Cl_2, 10:2:1).

IR (film): 3075, 2950, 2825, 2750, 1675, 1589, 1569, 1519 cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.78 (s, 3 H), 6.75 (d, *J* = 6.0 Hz, 1 H), 6.86 (d, *J* = 12.0 Hz, 1 H), 7.23–7.33 (m, 4 H), 9.56 (s, 1 H).

^{13}C NMR (76 MHz, $CDCl_3$): δ = 55.42 (q), 108.03 (d), 110.34 (d), 115.71 (d), 117.89 (d), 130.05 (d), 177.29 (d), 157.70 (s), 159.30 (s), 160.03 (s).

MS (EI$^+$, 70 eV): *m*/*z* (%) = 202 (100) [M]$^+$, 201 (17), 174 (3), 145 (20), 131 (3), 115 (6), 102 (6).

HRMS (EI$^+$, 70 eV): *m*/*z* [M]$^+$ calcd for $C_{12}H_{10}O_3$: 202.0630; found: 202.0643.

Grignard Addition to the Furoins 7 To Give Bis-furyl-diynes 8

General Workup

After addition of sat. aq NH_4Cl soln (10 mL), the aqueous layer was extracted with Et_2O (3 × 10 mL). The combined organic layers were dried ($MgSO_4$) and filtered and the solvent was removed in vacuo. The conditions of the chromatographic workup are mentioned in the individual experiments.

4,5-Bis(5-methylfuran-2-yl)octa-1,7-diyne-4,5-diol (8a)

To **7a** (200 mg, 917 μmol) at –50 °C was added slowly 1.96 M propargylmagnesium bromide in Et_2O (1.87 mL, 3.67 mmol) in THF (20 mL). The crude product was purified by column chromatography (silica gel, PE–Et_2O, 4:1) to provide **8a** (184 mg, 616 μmol, 67%) as a yellow solid; ratio of diastereomers *anti*-**8a**/*syn*-**8a** 75:25. A second chromatographic separation (silica gel, PE–Et_2O, 6:1) gave pure fractions of both diastereomers. Single crystals of the *anti*-diastereomer were characterized by a single crystal structure analysis; this crystal was then redissolved and a ^{1}H NMR spectrum was measured in order to confirm the assignment of the structure to the ^{1}H NMR of the major diastereomer.

***anti*-8a**

Mp 74–76 °C; R_f = 0.26 (PE–Et_2O; 4:1).

IR (film): 3514, 3292, 2929, 1732, 1556, 1328, 1194, 1022, 955, 777, 664, 627 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.91 (t, *J* = 2.6 Hz, 2 H), 2.28 (d, *J* = 1.0 Hz, 6 H), 2.75 (dd, *J* = 17.0, 2.6 Hz, 2 H), 3.05 (br s, 2 H), 3.09 (*J* = 17.0, 2.6 Hz, 2 H), 5.95 (dq, *J* = 3.2, 1.0 Hz, 2 H), 6.23 (d, *J* = 3.2 Hz, 2 H).

MS (EI$^+$, 70 eV): *m*/*z* (%) = 298 (3) [M]$^+$, 241 (1), 149 (48), 109 (100).

HRMS (EI, 70 eV): *m*/*z* [M]$^+$ calcd for $C_{18}H_{18}O_4$: 298.1205; found: 298.1202.

***syn*-8b**

R_f = 0.21 (PE–Et_2O; 4:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.89 (t, *J* = 2.6 Hz, 2 H), 2.25 (d, *J* = 1.0 Hz, 6 H), 2.72 (dd, *J* = 16.8, 2.6 Hz, 2 H), 3.07 (*J* = 16.8, 2.6 Hz, 2 H), 3.25 (br s, 2 H), 5.92 (dq, *J* = 3.2, 1.0 Hz, 2 H), 6.21 (d, *J* = 3.2 Hz, 2 H).

^{13}C NMR: ($CDCl_3$, 75.5 MHz): δ = 13.69 (q, 2 C), 26.74 (t, 2 C), 71.48 (d, 2 C), 77.28 (s, 2 C), 79.61 (s, 2 C), 106. 54 (d, 2 C), 109.60 (d, 2 C), 151.93 (s, 2 C), 151.95 (s, 2 C).

4,5-Bis(5-ethylfuran-2-yl)octa-1,7-diyne-4,5-diol (8b)

To **7b** (450 mg, 1.83 mmol) in Et_2O (15 mL) at –10 °C was slowly added 1.09 M propargylmagnesium bromide (6.7 mL, 7.31 mmol); stirring was continued at r.t. for 4 h. Column chromatography (silica gel, PE–Et_2O, 3:1) gave *anti*-**8b** (151 mg, 37%) and *syn*-**8b** (132 mg, 28%) as yellow oils.

***anti*-8b**

R_f = 0.38 (PE–Et_2O, 3:1).

IR (film): 3529, 3292, 2973, 2940, 2123, 1692, 1556, 1324, 1203, 1094 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.16 (t, *J* = 7.6 Hz, 6 H), 1.87 (t, *J* = 2.4 Hz, 4 H), 2.60 (q, *J* = 7.7 Hz, 2 H), 2.72 (dd, *J* = 16.8, 2.7 Hz, 2 H), 3.05 (br s, 2 H), 3.03 (dd, *J* = 16.8, 2.7 Hz, 2 H), 5.90 (d, *J* = 3.2 Hz, 2 H), 6.18 (d, *J* = 3.2 Hz, 2 H).

^{13}C NMR (76 MHz, $CDCl_3$): δ = 12.04 (q, 2 C), 21.32 (t, 2 C), 26.61 (t, 2 C), 71.29 (d, 2 C), 77.22 (s, 2 C), 79.48 (s, 2 C), 104.80 (d, 2 C), 109.14 (d, 2 C), 151.72 (s, 2 C), 157.54 (s, 2 C).

MS (EI$^+$, 70 eV): *m*/*z* (%) = 326 (3) [M]$^+$, 269 (4), 213 (3), 163 (86), 123 (100).

HRMS (EI$^+$, 70 eV): *m*/*z* [M]$^+$ calcd for $C_{20}H_{22}O_4$: 326.1518; found: 326.1523.

***syn*-8b**

R_f = 0.34 (PE–Et_2O, 3:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.13 (t, *J* = 7.4 Hz, 6 H), 1.89 (t, *J* = 2.4 Hz, 2 H), 2.52 (q, *J* = 7.1 Hz, 4 H), 2.74 (dd, *J* = 16.9, 2.7

Hz, 2 H), 2.98 (dd, *J* = 17.1, 2.8 Hz, 2 H), 3.21 (br s, 2 H), 5.88 (d, *J* = 3.0 Hz, 2 H), 6.15 (d, *J* = 3.0 Hz, 2 H).

^{13}C NMR (76 MHz, $CDCl_3$): δ = 12.03 (q, 2 C), 21.93 (d, 2 C), 26.28 (t, 2 C), 71.29 (d, 2 C), 77.21 (s, 2 C), 80.12 (s, 2 C), 104.73 (d, 2 C), 109.33 (d, 2 C), 151.09 (s, 2 c), 157.48 (s, 2 C).

4,5-Bis(5-phenylfuran-2-yl)octa-1,7-diyne-4,5-diol (8g)

To **7g** (600 mg, 1.75 mmol) in THF (20 mL) at –20 °C was slowly added 1.96 M propargylmagnesium bromide in Et_2O (1.79 mL, 3.50 mmol). Column chromatography (silica gel, PE–Et_2O, 8:1) gave *anti*-**8g** (263 mg, 624 μmol, 36%) as a yellow solid and *syn*-**8g** (194 mg, 459 μmol, 26%). The assignment of the diastereomers is based on the direct comparison with the ^{1}H NMR spectra of the diastereomers **8a**.

***anti*-8g**

Mp 170–173 °C; R_f = 0.47 (PE–Et_2O, 2:1).

IR (film): 3539, 3269, 1483, 1332, 1086, 1025, 971, 760, 686, 650 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.94 (t, *J* = 2.6 Hz, 2 H), 2.96 (dd, *J* = 16.8, 2.6 Hz, 2 H), 3.27 (br s, 2 OH), 3.27 (dd, *J* = 16.8, 2.6 Hz, 2 H), 6.45 (d, *J* = 3.4 Hz, 2 H), 6.60 (d, *J* = 3.4 Hz, 2 H), 7.22–7.26 (m, 2 H), 7.32–7.35 (m, 4 H), 7.57–7.59 (m, 4 H).

^{13}C NMR (126 MHz, CD_2Cl_2): δ = 26.74 (t, 2 C), 72.02 (d, 2 C), 77.34 (s, 2 C), 78.99 (s, 2 C), 105.84 (d, 2 C), 110.95 (d, 2 C), 123.70 (d, 4 C), 127.41 (d, 2 C), 128.64 (d, 4 C), 130.54 (s, 2 C), 153.30 (s, 2 C), 153.71 (s, 2 C).

MS (EI$^+$, 70 eV): *m*/*z* (%) = 422 (2) [M]$^+$, 211 (100), 171 (98), 115 (26).

Anal. Calcd for $C_{28}H_{22}O_4$ (422.47): C, 79.60; H, 5.25. Found: C, 79.39; H, 5.36.

***syn*-8g**

R_f = 0.44 (PE–Et_2O, 2:1).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.97 (t, *J* = 2.6 Hz, 2 H), 2.93 (dd, *J* = 17.0, 2.6 Hz, 2 H), 3.19 (dd, *J* = 16.8, 2.6 Hz, 2 H), 3.39 (br s, 2 OH), 6.50 (d, *J* = 3.4 Hz, 2 H), 6.63 (d, *J* = 3.4 Hz, 2 H), 7.13–7.21 (m, 6 H), 7.44–7.46 (m, 4 H).

^{13}C NMR (126 MHz, CD_2Cl_2): δ = 26.48 (t, 2 C), 71.85 (d, 2 C), 77.27 (s, 2 C), 79.72 (s, 2 C), 105.65 (d, 2 C), 111.19 (d, 2 C), 123.67 (d, 4 C), 127.31 (d, 2 C), 128.44 (d, 4 C), 130.32 (s, 2 C), 152.53 (s, 2 C), 153.86 (s, 2 C).

4,5-Bis{5-[3-(trifluoromethyl)phenyl]furan-2-yl}octa-1,7-diyne-4,5-diol (8i)

To **7i** (400 mg, 836 μmol) in THF (20 mL) at –20 °C was slowly added 1.96 M propargylmagnesium bromide in Et_2O (1.71 mL, 3.35 mmol). Column chromatography (silica gel, PE–Et_2O, 2:1) gave **8i** (381 mg, 682 mmol, 82%) as a yellow solid; mixture of diastereomers, ratio 57:43, which could not be separated; R_f = 0.30 (PE–Et_2O, 2:1).

IR (film): 3517, 3303, 1332, 1263, 1165, 1120, 794, 698, 649, 617 cm^{-1}.

^{1}H NMR* (500 MHz, $CDCl_3$): δ = 1.97/1.97 (t, *J* = 2.6 Hz, 2 H/2 H), 2.97/2.99 (dd, *J* = 16.9, 2.6 Hz, 2 H/2 H), 3.23/3.23 (dd, *J* = 16.9, 2.6 Hz, 2 H/2 H), 3.31/3.33 (br s, 2 OH/2 OH), 6.52/6.60 (d, *J* = 3.4 Hz, 2 H/2 H), 6.70/6.73 (d, *J* = 3.4 Hz, 2 H/2 H), 7.22 (t, *J* = 7.7 Hz, 2 H), 7.30 (t, *J* = 7.9 Hz, 2 H), 7.39 (t, *J* = 7.8 Hz, 2 H), 7.44 (d, *J* = 8.1 Hz, 2 H), 7.49 (d, *J* = 7.9 Hz, 2 H), 7.51–7.52 (m, 2 H), 7.66 (d, *J* = 7.9 Hz, 2 H), 7.69–7.70 (m, 2 H).

^{13}C NMR* (126 MHz, CD_2Cl_2): δ = 26.11/26.53 (t, 2 C/2 C), 72.10/72.26 (d, 2 C/2 C), 77.32/77.37 (s, 2 C/2 C), 78.73/79.47 (s, 2 C/2 C), 106.93/107.18 (d, 2 C/2 C), 111.30/111.51 (d, 2 C/2 C), 119.95/120.21 (d, J_{C-F} = 4 Hz, 2 C/2 C), 123.68/123.83 (d, J_{C-F} = 4 Hz, 2 C/2 C), 123.85/123.96 (s, J_{C-F} = 272 Hz, 2 C/2 C), 126.35/126.59 (d, 2 C/2 C), 128.81/129.07 (d, 2 C/2 C), 130.72/131.04 (s, 2 C/2 C), 130.81/131.09 (s, J_{C-F} = 33 Hz, 2 C/2 C), 152.25/152.26 (s, 2 C/2 C), 153.39/154.02 (s, 2 C/2 C). * In the diastereomeric mixture the signals of both diastereomers could not be assigned.

MS (EI$^+$, 70 eV): *m*/*z* (%) = 279 (59), 239 (100).

MS (ESI-EM): *m*/*z* [M + Na]$^+$ calcd for $C_{30}H_{20}F_6NaO_4$: 581.1158, found 581.1156.

4,5-Bis[5-(2-methoxyphenyl)furan-2-yl]octa-1,7-diyne-4,5-diol (8j)

To **7j** (1.55 g, 6.30 mmol) in Et_2O (60 mL) at –10 °C was slowly added 1.33 M propargylmagnesium bromide in Et_2O (18.9 mL, 25.1 mmol); the mixture was stirred at r.t. for 4 h. Column chromatography (silica gel, PE–Et_2O–CH_2Cl_2, 12:2:1) provided *anti*-**8j** (974 mg, 32%) and *syn*-**8j** (887 mg, 29%) as yellow solids.

***anti*-8j**

Mp 42 °C; R_f = 0.14 (PE–Et_2O–CH_2Cl_2, 12:2:1).

IR (film): 3590, 3452, 3265, 2940, 2837, 1674, 1602, 1489, 1466, 1434 cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.76 (t, *J* = 2.4 Hz, 2 H), 2.74 (dd, *J* = 2.5, 16.8 Hz, 2 H), 2.90 (dd, *J* = 2.5, 16.8 Hz, 2 H), 3.12 (s, 2 H), 3.72 (s, 6 H), 6.29 (d, *J* = 5.0 Hz, 2 H), 6.54–7.07 (m, 8 H), 7.33 (d, *J* = 2.5 Hz, 2 H).

^{13}C NMR (76 MHz, $CDCl_3$): δ = 26.83 (t, 2 C), 55.36 (q, 2 C), 71.82 (d, 2 C), 79.76 (s, 2 C), 110.99 (d, 2 C), 111.22 (d, 2 C), 119.62 (d, 2 C), 120.67 (d, 2 C), 126.04 (d, 2 C), 128.11 (d, 2 C), 150.28 (s, 2 C), 151.55 (s, 2 C), 152.37 (s, 2 C), 155.38 (s, 2 C); one s, 2 C not detected.

MS (ESI$^+$, 70 eV): *m*/*z* (%) = 428 (11) [M]$^+$, 464 (11), 269 (100), 241 (51).

HRMS (ESI$^+$, 70 eV): *m*/*z* [M]$^+$ calcd for $C_{30}H_{26}O_6$: 482.1729; found: 482.1694.

***syn*-8j**

R_f = 0.10 (PE–Et_2O–CH_2Cl_2, 12:2:1).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.75 (t, *J* = 2.5 Hz, 2 H), 2.75 (dd, *J* = 2.5, 17.5 Hz, 2 H), 3.95 (dd, *J* = 2.4, 16.8 Hz, 2 H), 3.11 (dd, *J* = 2.5, 16.8 Hz, 2 H), 3.15 (s, 2 H), 3.76 (s, 6 H), 6.31 (d, *J* = 3.3 Hz, 2 H), 6.71 (d, *J* = 3.3 Hz, 2 H), 6.74–7.10 (m, 6 H).

^{13}C NMR (76 MHz, $CDCl_3$): δ = 26.76 (t, 2 C), 55.31 (q, 2 C), 71.75 (d, 2 C), 79.20 (s, 2 C), 110.60 (d, 2 C), 111.94 (d, 2 C), 119.62 (s, 2 C), 120.61 (d, 2 C), 125.96 (d, 2 C), 128.06 (d, 2 C), 150.16 (s, 2 C), 152.28 (s, 2 C), 152.37 (s, 2 C), 155.31 (s, 2 C); one s, 2 C not detected.

4,5-Bis[5-(3-methoxyphenyl)furan-2-yl]octa-1,7-diyne-4,5-diol (8k)

To **7k** (313 mg, 1.27 mmol) in Et_2O (30 mL) at –10 °C was slowly added 1.33 M propargylmagnesium bromide (3.82 mL, 5.08 mmol); the mixture was stirred at r.t. for 4 h. Column chromatography (silica gel, PE–Et_2O–CH_2Cl_2, 12:2:1) gave *anti*-**8k** (275 mg, 45%) and *syn*-**8k** (146 mg, 24%) as yellow solids.

***anti*-8k**

Mp 42 °C; R_f = 0.14 (PE–Et_2O–CH_2Cl_2, 12:2:1).

IR (film): 3297, 1612, 1598 1488, 1431, 1289, 1220, 1180, 1093, 1041 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.74 (t, *J* = 2.4 Hz, 2 H), 2.74 (dd, *J* = 2.5, 16.7 Hz, 2 H), 3.05 (dd, *J* = 2.5, 16.7 Hz, 2 H), 3.26 (br s, 2

H), 3.59 (s, 6 H), 6.24 (d, *J* = 3.3 Hz, 2 H), 6.59 (d, *J* = 3.3 Hz, 2 H), 6.90 (s, 2 H), 7.02–7.08 (m, 6 H).

^{13}C NMR (76 MHz, $CDCl_3$): δ = 26.71 (t, 2 C), 55.10 (q, 2 C), 72.02 (d, 2 C), 106.19 (d, 2 C), 109.29 (d, 2 C), 110.96 (d, 2 C), 112.99 (d, 2 C), 116.37 (d, 2 C), 129.72 (d, 2 C), 131.83 (s, 2 C), 153.52 (s, 2 C), 153.52 (s, 2 C), 159.87 (s, 2 C); two s, 2 C not detected.

MS (EI$^+$, 70 eV): *m*/*z* (%) = 482 (49) [M]$^+$, 464 (36), 425 (100), 397 (36), 347 (11), 312 (22), 291 (61), 281 (27).

HRMS (EI$^+$, 70 eV): *m*/*z* [M]$^+$ calcd for $C_{30}H_{26}O_6$: 482.1729; found: 482.1701.

***syn*-8k**

R_f = 0.10 (PE–Et_2O–CH_2Cl_2, 12:2:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.77 (t, *J* = 2.5 Hz, 2 H), 2.77 (d, *J* = 16.7 Hz, 2 H), 3.07 (d, *J* = 16.7 Hz, 2 H), 3.26 (br s, 2 H), 3.59 (s, 6 H), 6.29 (d, *J* = 3.3 Hz, 2 H), 6.42 (d, *J* = 3.5 Hz, 2 H), 6.50 (d, *J* = 8.1 Hz, 2 H), 6.93–7.02 (m, 6 H).

^{13}C NMR (76 MHz, $CDCl_3$): δ = 26.47 (t, 2 C), 55.25 (q, 2 C), 71.87 (d, 2 C), 79.71 (s, 2 C), 105.95 (d, 2 C), 109.00 (d, 2 C), 111.19 (d, 2 C), 113.17 (d, 2 C), 116.30 (d, 2 C), 129.51 (d, 2 C), 131.57 (s, 2 C), 153.59 (s, 2 C), 153.70 (s, 2 C), 159.70 (s, 2 C); one s, 2 C not detected.

4,5-Bis(5-dimethylfuran-2-yl)octa-1,7-diyne-4,5-diol (8l)

To **7l** (200 mg, 812 μmol) in Et_2O (10 mL) at –10 °C was slowly added 1.09 M propargylmagnesium bromide (2.98 mL, 3.25 mmol); the mixture was stirred at r.t. for 4 h. Column chromatography (silica gel, PE–Et_2O, 3:1) gave *anti*-**8l** (107 mg, 40%) and *syn*-**8l** (50 mg, 19%) as yellow oils.

***anti*-8l**

R_f = 0.40 (PE–Et_2O, 3:1).

IR (film): 3287, 1699, 1670, 1559, 1540, 1520, 1421, 1377 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.95 (s, 6 H), 2.03 (t, *J* = 2.7 Hz, 2 H), 2.20 (s, 6 H), 2.71 (d, *J* = 16.7 Hz, 2 H), 3.02 (s, 2 H), 3.08 (d, *J* = 16.7 Hz, 2 H), 6.17 (s, 2 H).

^{13}C NMR (76 MHz, $CDCl_3$): δ = 10.34 (q, 2 C), 11.77 (q, 2 C), 26.58 (t, 2 C), 71.60 (d, 2 C), 80.64 (s, 2 C), 112.44 (d, 2 C), 115.08 (s, 2 C), 147.43 (s, 2 C), 150.20 (s, 2 C); one s, 2 C not detected.

MS (EI$^+$, 70 eV): *m*/*z* (%) = 326 (3) [M]$^+$, 267 (35), 229 (6), 108 (100).

HRMS (EI$^+$, 70 eV): *m*/*z* [M]$^+$ calcd for $C_{20}H_{22}O_4$: 326.1518; found: 326.1488.

***syn*-8l**

R_f = 0.23 (PE–Et_2O, 3:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.85 (s, 6 H), 1.87 (t, *J* = 2.7 Hz, 2 H), 2.06 (s, 6 H), 2.67 (dd, *J* = 2.7, 16.7 Hz, 2 H), 2.89 (dd, *J* = 2.7, 16.7 Hz, 2 H), 3.12 (s, 2 H), 6.02 (s, 2 H).

^{13}C NMR (76 MHz, $CDCl_3$): δ = 9.96 (q, 2 C), 11.39 (q, 2 C), 26.77 (t, 2 C), 71.22 (d, 2 C), 80.24 (s, 2 C), 112.05 (d, 2 C), 114.13 (s, 2 C), 147.04 (s, 2 C), 149.78 (s, 2 C); one s, 2 C not detected.

Gold-Catalyzed 5-*exo*-*dig*-Cyclization To Give Indene Derivatives 10

1-[1,4-Dihydroxy-5-methyl-2-(5-methylfuran-2-yl)-1*H*-inden-1-yl]propan-2-one (10a)

To *anti*-**8a** (53.3 mg, 179 μmol) in CD_2Cl_2 (0.7 mL) was added 10 wt% $AuCl_3$ in CD_3CN soln (27.1 mg, 8.94 μmol, 5 mol%). The reaction progress was monitored by ^{1}H NMR and after complete conversion (see Table 2) the solvent was removed in vacuo; purification by column chromatography (silica gel, PE–Et_2O, 2:1) gave **10a** (49.2 mg, 165 μmol, 92%) as a light brown solid; mp 76–78 °C; R_f = 0.23 (PE–Et_2O, 2:1).

IR (film): 3380, 2920, 1693, 1592, 1430, 1357, 1221, 1018, 786 cm^{-1}.

^{1}H NMR (300 MHz, acetone-d_6): δ = 2.05 (s, 3 H), 2.31 (d, *J* = 0.6 Hz, 3 H), 2.43 (s, 3 H), 2.90 (d, *J* = 14.3 Hz, 1 H), 3.06 (br s, 1 OH), 3.42 (d, *J* = 14.3 Hz, 1 H), 4.83 (br s, 1 OH), 6.23 (dq, *J* = 3.3, 1.0 Hz, 1 H), 6.70 (d, *J* = 3.3 Hz, 1 H), 6.95 (d, *J* = 7.5 Hz, 1 H), 7.01 (d, *J* = 7.5 Hz, 1 H), 7.16 (s, 1 H).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.10 (s, 3 H), 2.21 (s, 3 H), 2.34 (s, 3 H), 2.68 (d, *J* = 16.5 Hz, 1 H), 3.25 (d, *J* = 16.5 Hz, 1 H), 4.50 (br s, 1 OH), 4.99 (br s, 1 OH), 6.06 (d, *J* = 3.2 Hz, 1 H), 6.56 (d, *J* = 3.2 Hz, 1 H), 6.87 (d, *J* = 7.8 Hz, 1 H), 6.91 (d, *J* = 3.2 Hz, 1 H), 6.92 (s, 1 H).

^{13}C NMR (75 MHz, acetone-d_6): δ = 13.60 (q), 16.22 (q), 31.58 (q), 52.58 (t), 83.25 (s), 108.61 (d), 110.34 (d), 115.37 (d), 119.52 (d), 126.05 (s), 128.44 (s), 129.04 (d), 140.17 (s), 148.95 (s), 149.38 (s), 149.48 (s), 152.74 (s), 207.20 (s).

MS (CI$^+$, CH_4): *m*/*z* (%) = 298 (100) [M]$^+$, 281 (27), 255 (23), 240 (39), 43 (41).

HRMS (EI$^+$, 70 eV): *m*/*z* [M]$^+$ calcd for $C_{18}H_{18}O_4$: 298.1205; found: 298.1176.

1-[5-Ethyl-2-(5-ethylfuran-2-yl)-1,4-dihydroxy-1*H*-inden-1-yl]propan-2-one (10b)

To *anti*-**8b** (30.0 mg, 91.9 μmol) in CD_3CN (500 μL) was added 10 wt% $AuCl_3$ in CD_3CN soln [13.9 mg, $AuCl_3$ (1.39 mg, 4.60 μmol, 5 mol%)]. After 24 h the solvent was removed in vacuo. Column chromatography (silica gel, PE–Et_2O, 3:1) gave **10b** (28.5 mg, 95%) as a colorless oil; R_f = 0.28 (PE–Et_2O, 3:1).

A similar conversion of an *anti*/*syn* mixture gave 67% yield of **10b**.

IR (film): 2969, 2936, 1700, 1543, 1435, 1361, 909, 731 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.24 (t, *J* = 7.6 Hz, 3 H), 1.28 (t, *J* = 7.3 Hz, 3 H), 2.12 (s, 3 H), 2.62 (d, *J* = 7.3 Hz, 2 H), 2.70 (q, *J* = 7.7 Hz, 2 H), 3.23 (s, 1 H), 4.50 (br s, 1 H), 4.79 (br s, 1 H), 5.30 (s, 1 H), 6.08 (d, *J* = 3.4 Hz, 1 H), 6.59 (d, *J* = 3.2 Hz, 1 H), 6.93 (d, *J* = 6.2 Hz, 2 H), 6.59 (d, *J* = 3.2 Hz, 1 H).

^{13}C NMR (76 MHz, $CDCl_3$): δ = 12.14 (q), 14.10 (q), 22.77 (t), 31.95 (q), 50.43 (t), 77.21 (s), 83.01 (s), 106.30 (d), 109.91 (d), 115.34 (d), 118.21 (d), 126.90 (d), 127.52 (s), 130.68 (s), 139.28 (s), 147.00 (s), 147.76 (s), 158.32 (s), 210.70 (s).

MS (EI$^+$, 70 eV): *m*/*z* (%) = 326 (77) [M]$^+$, 268 (100), 253 (63), 283 (9), 213 (11), 162 (10), 151 (14).

HRMS (EI$^+$, 70 eV): *m*/*z* [M]$^+$ calcd for $C_{20}H_{22}O_4$: 326.1518; found: 326.1491.

1-[1,4-Dihydroxy-5-phenyl-2-(5-phenylfuran-2-yl)-1*H*-inden-1-yl]propan-2-one (10g)

To *anti*-**8g** (90.0 mg, 213 μmol) in anhyd CH_2Cl_2 (5 mL) was added 10 wt% $AuCl_3$ in MeCN soln (32.2 mg, 10.7 μmol, 5 mol%). After consumption of the starting material (TLC) column chromatography gave **10g** (95% yield); R_f = 0.14 (PE–Et_2O, 4:1).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.19 (s, 3 H), 2.79 (d, *J* = 16.9 Hz, 1 H), 3.35 (d, *J* = 16.9 Hz, 1 H), 4.75 (br s, 1 OH), 5.37 (br s, 1 OH), 6.77 (d, *J* = 3.5 Hz, 1 H), 6.81 (d, *J* = 3.5 Hz, 1 H), 7.05 (d, *J* = 7.6 Hz, 1 H), 7.10 (d, *J* = 7.6 Hz, 1 H), 7.25–7.55 (m, 9 H), 7.74–7.78 (m, 2 H).

1-(1,4-Dihydroxy-5-[3-(trifluoromethyl)phenyl]-2-{5-[3-(trifluoromethyl)phenyl]furan-2-yl}-1*H*-inden-1-yl)propan-2-one (10i)

To a mixture of both diastereomers of **8i** (24.5 mg, 43.8 μmol) in CD_2Cl_2 (0.7 mL) was added 10 wt% $AuCl_3$ in CD_3CN (6.6 mg, 2.19 μmol, 5 mol%). An in situ ^1H NMR taken after 10 min showed complete conversion of the substrate; R_f = 0.30 (PE–Et_2O, 2:1).

^1H NMR (300 MHz, $CDCl_3$): δ = 2.19 (s, 3 H), 2.76 (d, *J* = 16.9 Hz, 1 H), 3.33 (d, *J* = 16.9 Hz, 1 H), 6.40 (d, *J* = 3.5 Hz, 1 H), 6.49 (d, *J* = 3.5 Hz, 1 H), 6.85 (s, 1 H), 7.06 (d, *J* = 7.6 Hz, 1 H), 7.12 (d, *J* = 7.6 Hz, 1 H), 7.22–7.98 (m, 8 H), OH-signals could not be assigned.

1-{1,4-Dihydroxy-5-(2-methoxyphenyl)-2-[5-(2-methoxyphenyl)furan-2-yl]-1*H*-inden-1-yl}propan-2-one (10j)

To *anti*-**8j** (171 mg, 354 μmol) in CD_3CN (700 μL) was added 10 wt% $AuCl_3$ in CD_3CN soln [53.7 mg, $AuCl_3$ (5.37 mg, 17.7 μmol, 5 mol%)]. After 24 h the solvent was removed and column chromatography (silica gel; PE–Et_2O–CH_2Cl_2, 5:2:1) to give **10j** (60.0 mg, 36%) as a yellow oil; R_f = 0.28 (PE–Et_2O, 3:1).

IR (film): 3464, 2924, 2852, 1717, 1671, 1598, 1487 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.10 (s, 3 H), 3.26 (d, *J* = 16.7 Hz, 1 H), 3.71 (d, *J* = 16.7 Hz, 1 H), 3.86 (s, 6 H), 6.35 (s, 1 H), 6.73 (d, *J* = 3.5 Hz, 1 H), 6.88 (m, 6 H), 7.34 (m, 5 H), 7.90 (d, *J* = 6.0 Hz, 2 H).

^{13}C NMR (76 MHz, $CDCl_3$): δ = 14.21 (q), 21.07 (q), 26.56 (t), 2972 (q), 32.01 (q), 50.30 (t), 60.42 (t), 77.25 (s), 110.37 (d), 115.65 (d), 121.13 (d), 126.09 (d), 138.84 (s), 147.60 (s), 149.94 (s), 151.23 (s), 155.65 (s), 210.94 (s).

MS (ESI$^+$, 70 eV): *m*/*z* (%) = 482 (6) $[M]^+$, 470 (65), 461 (13), 445 (25).

HRMS (ESI$^+$, 70 eV): *m*/*z* $[M + Na]^+$ calcd for $C_{30}H_{26}NaO_6$: 505.1549; found: 505.1632.

1-{1,4-Dihydroxy-5-(3-methoxyphenyl)-2-[5-(3-methoxyphenyl)furan-2-yl]-1*H*-inden-1-yl}propan-2-one (10k)

To *anti*-**8k** (16.0 mg, 32.2 μmol) in CD_3CN (500 μL) was added 10 wt% $AuCl_3$ in CD_3CN soln [50 mg, $AuCl_3$ (500 μg 1.66 μmol, 5 mol%)]. After 24 h the solvent was removed in vacuo, column chromatography (silica gel, PE–Et_2O, 3:1) gave **10k** (12.6 mg, 76%) as a yellow oil; R_f = 0.16 (PE–Et_2O, 3:1).

IR (film): 2923, 2852, 1717, 1598, 1584 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.21 (s, 3 H), 2.80 (d, *J* = 16.8 Hz, 1 H), 3.65 (d, *J* = 17.0 Hz, 1 H), 3.89 (s, 3 H), 3.92 (s, 3 H), 4.76 (s, 1 H), 5.53 (s, 1 H), 6.80 (m, 6 H), 7.68 (m, 7 H).

^{13}C NMR (76 MHz, $CDCl_3$): δ = 26.92 (q), 29.70 (q), 31.25 (q), 77.23 (d), 108.50 (d), 110.02 (d), 113.55 (s), 114.01 (d), 116.49 (d), 117.12 (d), 119.97 (d), 120.04 (s), 121.04 (s), 129.82 (s), 129.93 (d), 130.63 (s), 131.11 (s), 155.81 (s), 159.94 (s), 176.05 (s), 188.62 (s), 196.31 (s).

MS (EI$^+$, 70 eV): *m*/*z* (%) = 482 (77) $[M]^+$.

HRMS (EI$^+$, 70 eV): *m*/*z* $[M]^+$ calcd for $C_{30}H_{26}O_4$: 482.1729; found: 482.1688.

1-[2-(4,5-Dimethylfuran-2-yl)-1,4-dihydroxy-5,6-dimethyl-1*H*-inden-1-yl]propan-2-one (10l)

To *anti*-**8l** (100 mg, 306 μmol) in CD_3CN (500 μL) was added 10 wt% $AuCl_3$ in CD_3CN soln [46.5 mg, $AuCl_3$ (4.65 mg, 15.3 μmol, 5 mol%)]. After 24 h the solvent was removed in vacuo and column chromatography (silica gel, PE–Et_2O, 3:1) gave **10l** (72 mg, 72%) as a colorless oil; R_f = 0.20 (PE–Et_2O, 3:1).

IR (film): 3439, 2983, 2922, 1678, 1438 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.08 (s, 3 H), 2.18 (s, 3 H), 2.20 (s, 3 H), 2.28 (s, 3 H), 2.32 (s, 3 H), 2.99 (d, *J* = 17.1 Hz, 1 H), 3.72 (d, *J* = 17.2 Hz, 1 H), 4.66 (s, 2 H), 6.03 (s, 1 H), 6.80 (s, 1 H), 6.96 (s, 1 H).

^{13}C NMR (76 MHz, $CDCl_3$): δ = 11.60 (q), 19.09 (q), 20.41 (q), 53.43 (t), 70.97 (d), 97.67 (s), 106.96 (s), 118.57 (d), 124.46 (d), 137.92 (s), 140.13 (s), 140.27 (s), 150.04 (s), 162.09 (s), 204.92 (s).

MS (FAB$^+$): *m*/*z* (%) = 326 (25) $[M]^+$, 325 (100), 324 (58), 285 (48), 261 (50), 259 (55).

HRMS (FAB$^+$): *m*/*z* $[M]^+$ calcd for $C_{20}H_{22}O_4$: 326.1518; found: 326.1475.

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