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Intramolecular Nicholas Reactions in the Synthesis of Dibenzocycloheptanes. Synthesis of Allocolchicine NSC 51046 and Analogues and the Formal Synthesis of (−)-Allocolchicine

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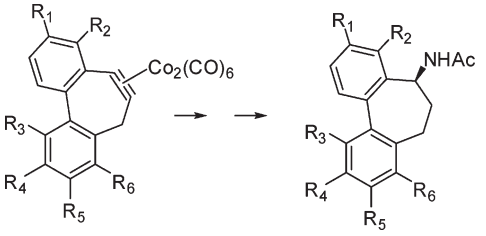

The preparation of dibenzocycloheptyne-$Co_2(CO)_6$ complexes by intramolecular Nicholas reactions of biaryl-2-propargyl alcohol-$Co_2(CO)_6$ derivatives is described. Reductive decomplexation of the dibenzocycloheptyne-$Co_2(CO)_6$ complexes affords the corresponding dibenzocycloheptenes, individual members of which have been employed in a formal total synthesis of (−)-allocolchicine, the preparation of 6,7-dihydro-3,4,9,10,11-pentamethoxy-5*H*-dibenzo[*a*,*c*]cyclohepten-5-one, and the enantioselective total syntheses of NSC 51046 and its 3,8,9,10-tetramethoxy regioisomer.

Introduction

The allocolchicines are a group of compounds containing a tricyclic 6,7,6-system with a highly oxygen-substituted A ring. Individual members of this group, including (−)-allocolchcine (**1**), *N*-acetylcolchicinol methyl ether (NSC 51046, **2**), *N*-acetylcolchicinol (**3**), and its dihydrogenphosphate (ZD 6126, **4**) have gained considerable attention by virtue of having been found to be active against a number of cancer cell lines.[1] These act by inhibiting tubulin assembly and polymerization, therefore arresting cell mitosis. A number of additional naturally occurring allocolchicines, including (−)-androbiphenyline (**4**), (−)-colchibiphenyline (**5**), (−)-jerusalemine (**6**), (−)-salimine (**7**), and (−)-suhailamine, have also been isolated;[2] the latter two of these have undergone structural revision or are structurally in question (Figure 1).[3]

Synthetic access to the allocolchicines historically has been based on oxidation of colchicine itself,[4] although racemic syntheses or those involving resolution are known.[3,5] More recently, the activity of these compounds has stimulated an interest in the enantioselective synthesis of allocolchicines. Initiated by Wulff's Diels−Alder based synthesis of (−)-allocolchicine itself,[6] members of this class of compounds

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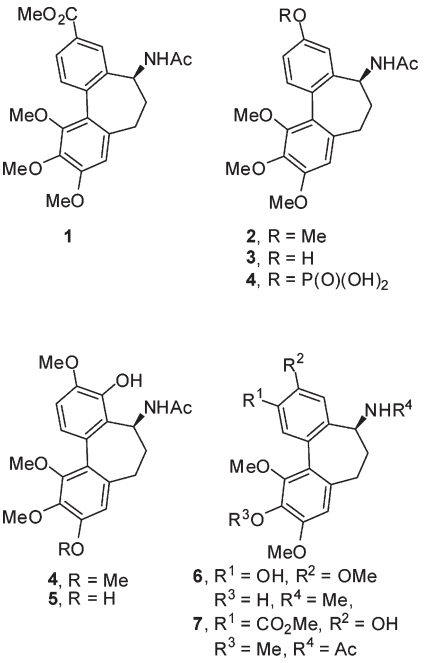


FIGURE 1. Common allocolchicines.

have seen synthesis by way of enyne metathesis/Diels–Alder reactions ((−)-*N*-acetylcolchicine analogues),[7] oxidative coupling and copper-mediated cross-coupling ((−)-*N*-acetylallocolchicinol),[8] C–H activation reactions ((−)-allocolchicine formal synthesis),[9] and aldol condensation chemistry ((−)-*N*-acetylallocolchicinol).[8b,10] In addition, a recent siloxane coupling/ring expansion reaction chemistry approach to (±)-NSC 51046 has been reported.[11]

The application of alkyne-$Co_2(CO)_6$ complexes in the synthesis of seven-membered ring compounds has been demonstrated by our group[12] and by other groups,[13] most often based on Nicholas reaction chemistry. The reactions are suited to seven-membered ring synthesis because complexation of alkynes to $Co_2(CO)_6$ induces a change in bond angle to ca. 140°,[14] in that S_N1' reactivity on the cationic propargyldicobalt complex to give a five-membered ring system does not occur, and since the electrophilicity of these cations is such that arenes substituted with electron-donating groups are sufficiently nucleophilic for facile reaction.[15] In particular, given the propensity of propargyldicobalt cations for reaction with electron-rich arenes and the demonstrated ability of (Z)-arylalkene substituted propargyl acetate complexes to react to form benzocycloheptyne-$Co_2(CO)_6$ complexes,[12d] we considered the potential applicability of intramolecular Nicholas reaction chemistry to dibenzocycloheptanes and consequently allocolchicines to be highly promising. We have reported on the viability of this approach in preliminary form and now describe this chemistry in complete fashion.[16]

Results and Discussion

The general outline of the access to the 6,7,6-system was envisioned to occur by construction of the $Co_2(CO)_6$ complexes of biaryl-2-propargyl alcohol derivatives (**8**), which would deliver dibenzocycloheptyne-$Co_2(CO)_6$ complexes (**9**) in the presence of a Lewis acid. The former were prepared in most instances by Suzuki–Miyaura coupling reactions of arylboronic acids (**10**) with bromobenzaldehydes (**11**) according the conditions employed by Fürstner,[17] giving biaryl-2-carboxaldehydes (**12a–f**) in good yield (Scheme 1, Table 1). These aldehydes were subjected to the Corey–Fuchs protocol, with trapping of the resulting acetylide by paraformaldehyde (Scheme 2). The resultant propargyl alcohols (**13a–f**) were formed in fair to good yields (56–80%) except in the case of thienyl substituted **13d** (40% yield); in this case a significant amount of carbene insertion product **14** (53%) was formed competitively. Acetylation of **13a–f** under standard conditions and complexation with $Co_2(CO)_8$ then afforded **8a–f** in good to excellent yields.

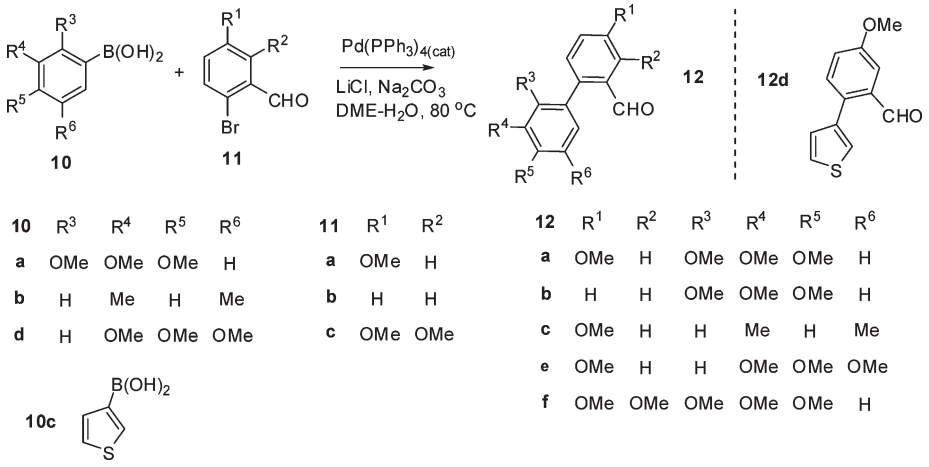
Two additional substrates were prepared by procedures other than the standard one. Unsubstituted **8g** was obtained by way of Sonogashira reaction between 2-iodobiphenyl and

TABLE 1. Preparation of 8a–g[a]

10	11	12	13	8
10a	**11a**	**12a** (85)	**13a** (80)	**8a** (86)
10a	**11b**	**12b** (92)	**13b** (78)	**8b** (84)
10b	**11a**	**12c** (79)	**13c** (57)	**8c** (91)
10c	**11a**	**12d** (81)	**13d** (40)	**8d** (77)
10d	**11a**	**12e** (76)	**13e** (61)	**8e** (84)
10a	**11c**	**12f** (81)	**13f** (56)	**8f** (98)

[a]Yields are in parentheses.

SCHEME 1. Suzuki–Miyaura Coupling Reactions

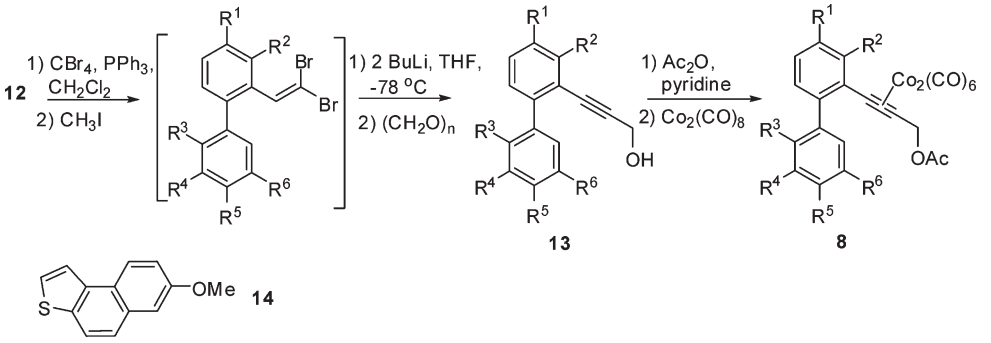


10	R^3	R^4	R^5	R^6
a	OMe	OMe	OMe	H
b	H	Me	H	Me
d	H	OMe	OMe	OMe

11	R^1	R^2
a	OMe	H
b	H	H
c	OMe	OMe

12	R^1	R^2	R^3	R^4	R^5	R^6
a	OMe	H	OMe	OMe	OMe	H
b	H	H	OMe	OMe	OMe	H
c	OMe	H	H	Me	H	Me
e	OMe	H	H	OMe	OMe	OMe
f	OMe	OMe	OMe	OMe	OMe	H

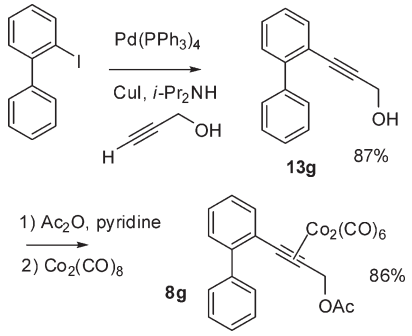
SCHEME 2. Preparation of Biaryl-2-propargyl Acetate-$Co_2(CO)_6$ Complexes (8)



propargyl alcohol to give **13g** (87% yield) (Scheme 3), which was in turn subjected to acetylation and complexation with $Co_2(CO)_8$ under conditions analogous to **13a**−**f**, affording **8g** in 86% yield.

Carbomethoxy-substituted **8h**, the propargyl ether-$Co_2(CO)_6$ complex envisioned as the precursor to allocolchicine itself, required a modified approach for its preparation. In this case, methyl 4-bromo-3-iodobenzoate, prepared by conventional esterification of the corresponding acid,[18] was subjected to Sonogashira reaction with propargyl methyl ether to afford **15** in 92% yield (Scheme 4). The Suzuki−Miyaura reaction of this halide with 2,3,4-trimethoxyboronic acid was somewhat problematic, as conventional conditions resulted in predominant boronic acid hydrolysis and recovery of substantial **15**, with only a small amount of **16** isolated (27% yield). Use of $Pd_2(dba)_3$ with PCy_3, however, gave **16** in acceptable yield (53%, 77% based on recovered starting material [brsm]), with recovery of **15** (31%). While most of the material was carried forward using this protocol, it was found ultimately that use of the PEPPSI-iPr catalyst enabled formation of **16** in 79% yield.[19] Formation of **8h** was accomplished from **16** in a straightforward manner (83% yield) with $Co_2(CO)_8$.

SCHEME 3. Formation of 8g



SCHEME 4. Preparation of 8h

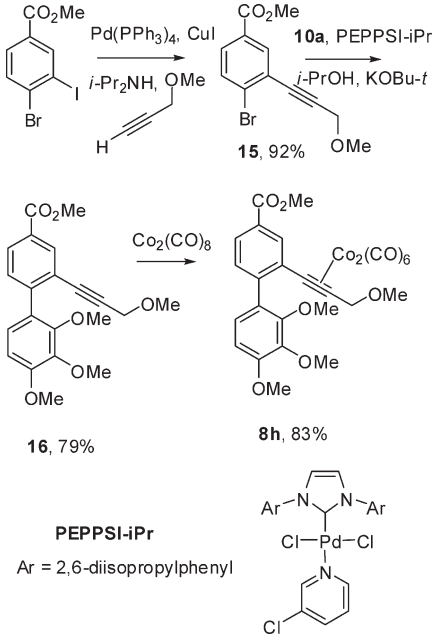


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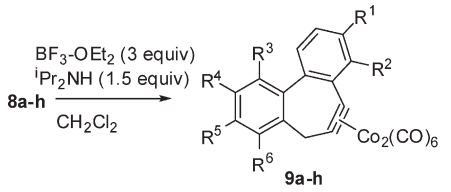
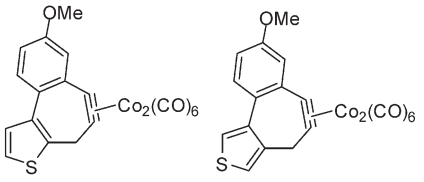
TABLE 2. Intramolecular Nicholas Reactions of 8



9a-h

9	R^1	R^2	R^3	R^4	R^5	R^6
a	OMe	H	OMe	OMe	OMe	H
b	H	H	OMe	OMe	OMe	H
c	OMe	H	H	Me	H	Me
e	OMe	H	H	OMe	OMe	OMe
f	OMe	OMe	OMe	OMe	OMe	H
g	H	H	H	H	H	H
h	CO_2Me	H	OMe	OMe	OMe	H



9d

9d'

entry	8	time (h)	9	yield (%)
1	**8a**	2.5	**9a**	56[a]
2	**8a**	6	**9a**	71
3	**8b**	16	**9b**	59 (66)[b]
4	**8c**	6	**9c**	85
5	**8d**	5	**9d**	82[c]
6	**8e**	4.5	**9e**	91
7	**8f**	4.5	**9f**	83
8	**8g**	16	**9g**	58
9	**8h**	5	**9h**	84

[a]No *i*-Pr_2NEt added. [b]Yields in parentheses based on recovered starting material. [c]Isolated as a 45:55 **9d**:**9d′** mixture.

With the Nicholas reaction precursors in hand, attention was turned to investigation of the cyclizations. Under conditions developed previously for benzocycloheptyne ring-closure reactions, **8a** (0.005 M in CH_2Cl_2) underwent reaction in the presence of BF_3-OEt_2 (3 equiv), giving dibenzocycloheptyne **9a** over 2.5 h (56% yield) (Table 2, entry 1). As a small amount of decomposition was evident chromatographically during this process, and with the belief that this could be due to the acid liberated during the substitution process, the reaction was conducted with the addition of 1.5 equiv of *i*-Pr_2NEt. Although the reaction occurred somewhat more slowly (6 h) (entry 2), **9a** could be isolated in improved yield (71%). These conditions (3 equiv of BF_3-OEt_2, 1.5 equiv of *i*-Pr_2NEt, 0.005−0.01 M) were applied to **8b**−**8h** (Table 2) and afforded fair to excellent yields of **9b**−**h**. While there was some variation in required reaction time (4.5−16 h) and substrate, there was no particular correlation between reaction time and substitution pattern of the arene behaving as nucleophile. In the case of trimethoxy-substituted **8b**, TLC analysis suggested the onset of some decomposition without complete conversion at 16 h, so that the reaction was terminated at this point and small amount of **8b** (10%) could be recovered in addition to the isolated **9b** (59% yield) (entry 3). 3-Thienyl-substituted **8d** underwent competitive cyclization at C-2′ and C-4′, affording **9d** and **9d′** as a regioisomeric mixture (82%, 45:55 **9d**:**9d′**) (entry 5). It is also worthy of note that **8c** → **9c** (entry 4) and **8g** → **9g** (entry 8) proceeded uneventfully, as the less electron-rich arene nucleophiles would be of borderline reactivity and insufficient reactivity, respectively, for participation in intermolecular Nicholas reactions.[15] Evidence of restricted rotation about the aryl−aryl bond was present for several of the cyclization products, as all dibenzocycloheptyne-$Co_2(CO)_6$ complexes bearing an additional substituent ortho to the biaryl gave diastereotopic CH_2's for the propargylic hydrogen atoms in the ^1H NMR spectra (**9a**,**b**,**f**,**g**). In addition, those bearing substitutents ortho to the cycloheptyne either gave a diastereotopic CH_2 (**9c**) or one right at coalescence (**9h**).

Removal of the $Co_2(CO)_6$ fragment for use in synthesis requires concomitant conversion of the alkyne function into one compatible with the seven-membered ring.[20,21] The most commonly employed reagent for this purpose, Bu_3SnH, has caused some isomerization in related benzocycloheptyne cases;[12c] consequently we chose to apply a modification of Isobe's hydrosilylation protocol[20] that would afford the alkene. Addition of triethylsilane to the dibenzocycloheptyne complexes **9** in the presence of bis(trimethylsilylacetylene) (BTMSE) gave a regioisomeric mixture of silylated cycloheptenes, which were not isolated but subjected to in situ desilylation with trifluoroacetic acid (TFA) to give the dibenzocycloheptenes **17**. These dibenzocycloheptenes (**17a**,**e**,**f**,**h**) were isolated in good to excellent yields and with no evidence of double bond isomerization during the reductive decomplexation process (Table 3).

Formal Synthesis of (−)-Allocolchicine. Since several of the existing syntheses of allocolchicines employ the dibenzocycloheptanones (**18**) as critical intermediates, conversion of dibenzocycloheptenes **17** to **18** was considered to be the most prudent approach toward their synthesis. Hydroboration−oxidation of **17h** with BH_3-THF/H_2O_2, with further oxidation of the intermediate alcohol using PDC, afforded ketone **18h** in good yield (81%). Dibenzocycloheptanone **18h** has been converted to (−)-allocolchine by Wulff,[6] and as such this represents a formal synthesis of this natural product.

Similarly, treatment of **17f** by BH_3-THF/H_2O_2 followed by oxidation with PDC afforded **18f** (67% yield). Dibenzocycloheptanone **18f** is a degradation product of (−)-androbiphenyline that has been prepared previously by Seitz,[22] and found to be equally potent as (−)-androbiphenyline in inhibition of tubulin assembly.

Synthesis of (−)-*N*-Acetylcolchicine *O*-Methyl Ether (NSC 51046) and Analogue. Conversion of **17a** to ketone **18a** was accomplished by hydroboration−oxidation with further

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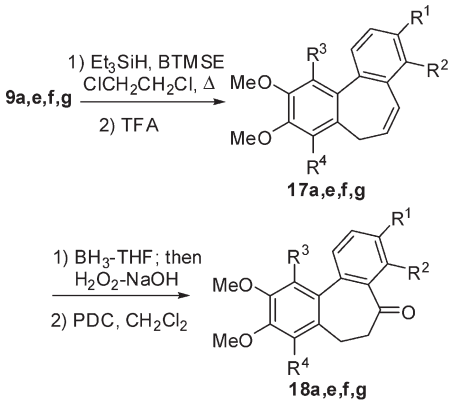
TABLE 3. Conversion of 9 to Dibenzocycloheptanones 18



17a, 18a R^1 = OMe, R^2 = H, R^3 = OMe, R^4 = H
17e, 18e R^1 = OMe, R^2 = H, R^3 = H, R^4 = OMe
17f, 18f R^1 = OMe, R^2 = OMe, R^3 = OMe, R^4 = H
17g, 18g, R^1 = CO_2Me, R^2 = H, R^3 = OMe, R^4 = H

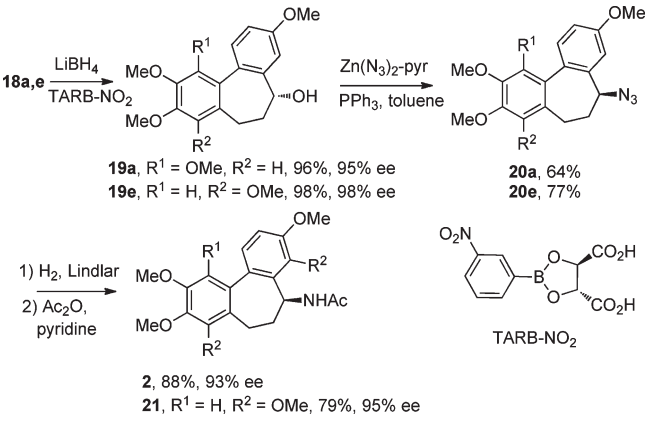
9	17	yield (%)	18	yield (%)
9a	**17a**	97	**18a**	80[a]
9e	**17e**	94	**18e**	68
9f	**17f**	90	**18f**	67
9h	**17h**	79	**18h**	81

[a]Oxidation under Swern conditions (oxalyl chloride-DMSO, Et_3N).

oxidation under Swern conditions (DMSO-oxalyl chloride, Et_3N), giving the ketone in 80% yield. Adopting the approach of Wulff's group toward (−)-allocolchicine, the reduction of ketone **18a** using the $LiBH_4$/tartrate derived boronate ester (TARB-NO_2) protocol of Singaram[23] gave alcohol **19a** in excellent yield and enantioselectivity (96% yield, 95% ee) (Scheme 5). Substitution of azide for the alcohol function by way of zinc azide/diisoproyl azodicarboxylate (DIAD)[24] afforded **20a** (64%), while azide reduction (H_2, Lindlar catalyst) of **20a** and acetylation gave NSC 51046 (**2**) in 88% (93% ee), which was spectroscopically identical to literature report.[11] Recrystallization of **2** gave this compound in >99% ee. To our knowledge this is the first asymmetric synthesis of **2**.

Similarly, dibenzocycloheptene **17e** was converted to an isomeric 3,8,9,10-tetramethoxyallocolchicine (**21**). Hydroboration−oxidation of **17e** and further oxidation with PDC afforded dibenzocycloheptanone **18e** in 68% yield. $LiBH_4$/TARB-NO_2 based reduction afforded the highly enantiomerically enriched alcohol **19e** (98% yield, 98% ee) provided an extended period of substrate/TARB-NO_2 mixing and slow $LiBH_4$ addition protocol was followed.[25] Zinc azide based substitution of the alcohol afforded **20e** without incident (77% yield), while reduction and acetylation gave **21** in 79% yield (95% ee); once again, a single recrystallization enriched this compound to >99% ee. To our knowledge, this is the first example of an allocolchicine with an 8,9,10-oxygenated A ring.

SCHEME 5. Completion of Enantioselective Synthesis of NSC 51046 and Its 3,8,9,10-Tetramethoxy Isomer



In summary, intramolecular Nicholas reactions have proven to be effective in the synthesis of dibenzocycloheptyne-$Co_2(CO)_6$ complexes. Ready decomplexation to the dibenzocycloheptenes allows application of this methodology to the synthesis of allocolchicines or their derivatives, including tubulin-inhibiting ketone 6,7-dihydro-3,4,9,10,11-pentamethoxy-5*H*-dibenzo[*a*,*c*]cyclohepten-5-one (**18f**), a formal total synthesis of (−)-allocolchicine (**1**), the enantioselective total synthesis of *N*-acetylallocolchinol *O*-methyl ether (NSC 51046, **2**), and of the 3,8,9,10- tetramethoxy isomer of NSC 51046 (**21**).

Experimental Section

General Methods. All reaction solvents were used after passage through a solvent purification system. Commercial BF_3-OEt_2 was distilled and stored under nitrogen. All reactions were conducted under a nitrogen atmosphere unless otherwise noted. Flash chromatography was performed as described by Still using silica gel 60 (230−400 mesh).[26] 2-Bromo-5-methoxybenzaldehyde[27] and 6-bromo-2,3-dimethoxybenzaldehyde[28] were prepared by literature methods and were >95% purity as determined by ^{1}H and ^{13}C NMR spectroscopy. All new compounds were >95% purity as determined by ^{1}H and ^{13}C NMR spectroscopy. NMR spectra were run at 500 or 300 MHz for ^{1}H and 125 or 75 MHz for ^{13}C in $CDCl_3$; chemical shifts are given in ppm and coupling constants (*J*) are given in Hz. High resolution mass spectra were run by time-of-flight mass spectroscopy, in EI mode, at 70 eV.

2′,3′,4,4′-Tetramethoxy[1,1′-biphenyl]-2-carboxaldehyde (12a). Prepared according to the method of Fürstner,[17] **11a** (0.3517 g, 1.16 mmol) afforded **7a** (0.4202, 85%): mp 102−3 °C (hexanes); lit.[17] 102−3 °C. This compound was >95% purity as determined by ^{1}H and ^{13}C NMR spectroscopy.

2′,3′,4′-Trimethoxy[1,1′-biphenyl]-2-carboxaldehyde (12b). Prepared according to the method of Fürstner,[17] **11b** (0.2278 g, 1.23 mmol) affording **12b** (0.3706 g, 92%): mp 105−5.5 °C (hexanes); lit.[17] 98−99 °C. This compound was >95% purity as determined by ^{1}H and ^{13}C NMR spectroscopy.

4-Methoxy-3′,5′-dimethyl[1,1′-biphenyl]-2-carboxaldehyde (12c). Prepared as adapted from the method of Fürstner,[17] employing **11a** (0.9593 g, 4.46 mmol) and (3,5-dimethylphenyl)boronic acid (**6b**)

(23) (a) Suri, J. T.; Vu, T.; Hernandez, A.; Congdon, J.; Singaram, B. *Tetrahedron Lett*. **2002**, *43*, 3649–3652. (b) Cordes, D. B.; Nguyen, T. M.; Kwong, T. J.; Suri, J. T.; Luibrand, R. T.; Singaram, B. *Eur. J. Org. Chem*. **2005**, 5289–5295.
(24) Viaud, M. C.; Rollin, P. *Synthesis* **1990**, 130–132.
(25) Rapid addition of $LiBH_4$ afforded **19b** in ca. 50% ee.
(26) Still, W. C.; M. Kahn, M.; Mitra, A. *J. Org. Chem*. **1978**, *43*, 2923–2925.
(27) Bianchi, D. A.; Cipulli, M. A.; Kaufman, T. S. *Eur. J. Org. Chem*. **2003**, 4731–4736.
(28) Kessar, S. V.; Gupta, V. P.; Balakrishnan, P.; Sawal, K. K.; Mohammad, T.; Dutt, M. *J. Org. Chem*. **2003**, *53*, 1708–1713.

(1.3423 g, 8.96 mmol) to give **12c** (0.8472 g, 79% yield), following flash chromatographic purification (15:1 petroleum ether/Et_2O), as a colorless viscous oil which solidified upon standing: mp 71−2 °C; IR (KBr) ν_{max} 3006, 2917, 1688, 1604 cm^{-1}; ^{1}H NMR δ 9.97 (s, 1H), 7.52 (d, J = 2.8, 1H), 7.37 (d, J = 8.5, 1H), 7.19 (dd, J = 8.5, 2.8, 1H), 7.06 (br s, 1H), 6.97 (br s, 2H), 3.90 (s, 3H), 2.39 (s, 6H); ^{13}C NMR 192.4, 159.0, 139.4, 137.9, 137.4, 134.5, 131.9, 129.3, 128.1, 121.2, 109.7, 55.5, 21.2; MS m/e 240 (M^+); HRMS m/e for $C_{16}H_{16}O_2$ calcd 240.1150 (M^+), found 240.1140.

5-Methoxy-2-(3-thienyl)benzaldehyde (12d). Prepared as adapted from the method of Fürstner,[17] employing **11a** (0.2301 g, 1.07 mmol) and 3-thienylboronic acid (**10c**) (0.2003 g, 1.56 mmol) to give **12d** (0.1900 g, 81% yield) following flash chromatographic purification (15:1 petroleum ether/Et_2O): mp 68−69 °C (CH_2Cl_2); IR (KBr) ν_{max} 3100, 2845, 1684 cm^{-1}; ^{1}H NMR δ 10.08 (s, 1H), 7.50 (d, J = 2.7, 1H), 7.44 (dd, J = 4.8, 3.0, 1H), 7.41 (d, J = 8.5, 1H), 7.24 (dd, J = 3.0, 0.9, 1H), 7.19 (dd, J =8.5, 2.7, 1H), 7.17 (dd, J = 4.8, 0.9, 1H), 3.90 (s, 3H); ^{13}C NMR 192.2, 159.0, 137.9, 134.7, 133.5, 131.8, 129.4, 126.1, 124.5, 121.5, 109.7, 55.5; MS m/e 218 (M^+); HRMS m/e for $C_{12}H_{10}O_2S$ calcd 218.0402 (M^+), found 218.0399.

3′,4,4′,5′-Tetramethoxy[1,1′-biphenyl]-2-carboxaldehyde (12e). Prepared according to the method of Fürstner[17] employing **11a** (0.7000 g, 3.26 mmol) and 3,4,5-trimethoxyphenylboronic acid (**10d**) (1.0877 g, 4.89 mmol) to give **12e** (0.7472 g, 76% yield) following flash chromatographic purification (3:1 petroleum ether/Et_2O), as a colorless solid: mp 134−136 °C; IR (KBr) 2931, 1687, 1604 cm^{-1}; ^{1}H NMR δ 9.96 (s, 1H), 7.47 (d, J = 2.8, 1H), 7.37 (d, J = 8.5, 1H), 7.17 (dd, J = 8.5, 2.8, 1H), 6.52 (s, 2H), 3.89 (s, 3H), 3.88 (s, 3H), 3.87 (s, 6H); ^{13}C NMR 192.2, 159.1, 152.9, 139.0, 137.7, 134.5, 133.1, 131.7, 121.2, 109.8, 107.5, 60.9, 56.2, 55.5; MS m/e (M^+) 302; HRMS m/e for $C_{17}H_{18}O_5$ calcd 302.1154, found 302.1139.

2′,3,3′,4,4′-Pentamethoxy[1,1′-biphenyl]-2-carboxaldehyde (12f). Prepared according to the method of Fürstner[17] employing **11c** (0.7937 g, 3.24 mmol) and 2,3,4-trimethoxyphenylboronic acid (**10a**) (1.0993 g, 5.18 mmol) to give **12f** (0.8712 g, 81% yield) following flash chromatographic purification (4:1 petroleum ether/EtOAc): mp 117−119 °C; IR (KBr) ν_{max} 2938, 1699, 1593 cm^{-1}; ^{1}H NMR δ 10.15 (s, 1H), 7.12 (d, J = 8.4, 1H), 7.01 (d, J = 8.4, 1H), 6.87 (d, J = 8.5, 1H), 6.71 (d, J = 8.5, 1H), 3.96 (s, 3H), 3.93 (s, 3H), 3.890 (s, 3H), 3.887 (s, 3H), 3.58 (s, 3H); ^{13}C NMR 191.1, 153.2, 152.0, 150.5, 149.9, 141.7, 131.7, 129.0, 126.6, 125.7, 124.5, 115.9, 106.9, 61.7, 60.7, 60.3, 55.74, 55.68; MS m/e 332 (M^+); HRMS for $C_{18}H_{20}O_6$ (M^+) calcd 332.1260, found 332.1275.

3-(2′,3′,4,4′-Tetramethoxybiphenyl-2-yl)-2-propyn-1-ol (13a). General Procedure A. To a solution of **12a** (0.3378 g, 1.12 mmol) in CH_2Cl_2 (10 mL) were added CBr_4 (0.556 g, 1.68 mmol) and PPh_3 (1.172 g, 4.47 mmol). After 4 h of stirring, petroleum ether (10 mL) and iodomethane (0.4 mL) were added, and the mixture was allowed to stir for 8 h. The volatiles were removed under reduced pressure, and the residue filtered through silica gel, using 1:1 petroleum ether/Et_2O as solvent). The filtrate was concentrated under reduced pressure to give the crude dibromide, which was used without further purification. The dibromide was dissolved in THF (20 mL) and cooled to −78 °C. Butyllithium (1.08 mL of a 2.58 M solution in hexanes, 2.79 mmol) was added, and stirring was continued for 5 h. A suspension of paraformaldehyde (0.4 g, excess) in THF (5 mL) was added, and the reaction was stirred for 8 h as the mixture gradually warmed to room temperature. A conventional extractive workup followed by flash chromatography (1:2 petroleum ether/Et_2O) gave **13a** (0.2919 g, 80%), as a viscous oil: IR (KBr) ν_{max} 3455 br, 2937, 2229 cm^{-1}; ^{1}H NMR δ 7.22 (d, J = 8.6, 1H), 7.05 (d, J = 2.7, 1H), 6.96 (d, J = 8.5, 1H), 6.91 (dd, J = 8.6, 2.7, 1H), 6.68 (dd, J = 8.5, 1H), 4.29 (s, 2H), 3.90 (s, 3H), 3.88 (s, 3H), 3.82 (s, 3H), 3.61 (s, 3H), 2.30 (br, 1H) ; ^{13}C NMR 158.2, 153.1, 151.6, 142.0, 133.3, 131.3, 127.1, 125.6, 123.2, 116.8, 114.8, 106.7, 89.6, 85.2, 61.0, 60.9, 55.9, 55.3, 51.4; MS m/e 328 (M^+); HRMS m/e for $C_{19}H_{20}O_5$ calcd 328.1311 (M^+), found 328.1311 .

3-(2′,3′,4′-Trimethoxybiphenyl-2-yl)-2-propyn-1-ol (13b). Reaction of aldehyde **12b** (0.1514 g, 0.554 mmol) according to General Procedure A afforded **13b** (0.1293 g, 78% yield) following preparative TLC (1:2 hexanes/Et_2O), as a viscous oil: IR (KBr) ν_{max} 3379 br, 2933, 2227 cm^{-1}; ^{1}H NMR δ 7.52 (dd, J = 7.7, 1.0, 1H), 7.25−7.37 (m, 3H), 6.98 (d, J = 8.5, 1H), 6.71 (d, J = 8.6, 1H), 4.29 (s, 2H), 3.91 (s, 3H), 3.91 (s, 3H), 3.63 (s, 3H), 2.07 (br, 1H); ^{13}C NMR 153.3, 151.5, 142.0, 140.8, 132.3, 130.2, 128.0, 127.5, 126.9, 125.3, 122.4, 106.8, 89.9, 85.2, 61.0, 60.9, 56.0, 51.4; MS m/e 298 (M^+); HRMS m/e for $C_{18}H_{18}O_4$ calcd 298.1205 (M^+), found 298.1201.

(3-Methoxy-3′,5′-dimethylbiphenyl-2-yl)-2-propyn-1-ol (13c). Reaction of aldehyde **12c** (0.8472 g, 3.53 mmol) according to General Procedure A afforded **13c** (0.5389 g, 57% yield) following flash chromatography (2:1 petroleum ether/Et_2O) as a viscous oil: IR (KBr) ν_{max} 3400 br, 2917, 1603 cm^{-1}; ^{1}H NMR δ 7.31 (d, J = 8.5, 1H), 7.20 (s, 2H), 7.08 (d, J = 2.8, 1H), 7.00 (s, 1H), 6.96 (dd, J = 8.5, 2.7, 1H), 4.37 (s, 2H), 3.84 (s, 3H), 2.38 (s, 6H), 1.55 (br, 1H) ; ^{13}C NMR 158.3, 140.0, 137.3, 136.9, 130.6, 128.7, 127.1, 121.6, 117.4, 115.4, 89.8, 85.6, 55.4, 51.6, 21.3; MS m/e 266 (M^+); HRMS m/e for $C_{18}H_{18}O_2$ calcd 266.1307 (M^+), found 266.1294.

3-(5-Methoxy-2-(3-thienyl)phenyl)-2-propyn-1-ol (13d) and 7-Methoxynaphtho[2,1-*b*]thiophene (14). Reaction of aldehyde **12d** (0.0876 g, 0.401 mmol) according to General Procedure A gave, in order of elution, **14** (0.0452 g, 53% yield) and **13d** (0.0389 g, 40% yield), following preparative TLC (1:1 petroleum ether/Et_2O). **14** as a colorless solid: mp 118−120 °C; IR (KBr) ν_{max} 2956, 1621 cm^{-1}; ^{1}H NMR δ 8.26 (d, J = 8.8, 1H), 7.92 (d, J = 5.4, 1H), 7.87 (d, J = 8.7, 1H), 7.67 (d, J = 8.7, 1H), 7.58 (d, J = 5.4, 1H), 72.6−7.31 (m, 2H), 3.97 (s, 3H); ^{13}C NMR 157.2, 136.1, 135.4, 132.2, 125.9, 125.1, 124.5, 124.3, 121.7, 121.2, 118.0, 107.6, 55.4; MS m/e 214 (M^+); HRMS for $C_{13}H_{10}O_2S$ (M^+) calcd 214.0452, found 214.0454. **13d** as a viscous oil: IR (KBr) ν_{max} 3384 br, 2928, 2228 cm^{-1}; ^{1}H NMR δ 7.54 (dd, J = 3.0, 1.4, 1H), 7.42 (dd, J = 5.0, 1.4, 1H), 7.34 (d, J = 8.6, 1H), 7.34 (dd, J = 5.0, 3.0, 1H), 7.06 (d, J = 2.7, 1H), 6.93 (dd, J = 8.6, 2.7,1H) 4.46 (d, J = 4.2, 2H), 3.84 (s, 3H), 1.61 (br, 1H); ^{13}C NMR 158.2, 140.5, 131.2, 130.2, 128.5, 124.7, 122.6, 121.2, 117.7, 115.6, 90.2, 85.7, 55.4, 51.8; MS m/e 244 (M^+); HRMS m/e for $C_{14}H_{12}O_2S$ calcd 244.0558 (M^+), found 244.0550.

3-(3′,4,4′,5′-Tetramethoxybiphenyl-2-yl)-2-propyn-1-ol (13e). Reaction of aldehyde **12e** (0.4674 g, 1.55 mmol) according to General Procedure A gave **13e** (0.3115 g, 61% yield), following flash chromatography (1:1 petroleum ether/Et_2O), as a viscous oil: IR (KBr) 3500 br, 2935, 2224, 1602 cm^{-1}; ^{1}H NMR δ 7.29 (d, J = 8.6, 1H), 7.06 (d, J = 2.7, 1H), 6.92 (dd, J = 8.6, 2.7, 1H), 6.79 (s, 2H), 4.38 (s, 2H), 3.88 (s, 3H), 3.87 (s, 6H), 3.81 (s, 3H), 2.33 (br s, 1H); ^{13}C NMR 158.1, 152.5, 137.0, 136.1, 135.4, 130.3, 121.3, 117.6, 115.2, 106.4, 90.3, 84.8, 60.7, 56.0, 55.2, 51.2; MS m/e (M^+) 328; HRMS m/e for $C_{19}H_{20}O_5$ calcd 328.1311, found 328.1308.

3-(2′3,3′,4,4′-Pentamethoxybiphenyl-2-yl)-2-propyn-1-ol (13f). Reaction of aldehyde **12f** (0.8629 g, 2.60 mmol) according to General Procedure A gave **13f** (0.5257 g, 56% yield), flash chromatography (1:1 hexanes/Et_2O), as a viscous oil: IR (KBr) 3509 br, 2936, 2227, 1591 cm^{-1}; ^{1}H NMR δ 6.96 (d, J = 8.5, 1H), 6.91 (d, J = 8.6, 1H), 6.88 (d, J = 8.5, 1H), 6.64 (d, J = 8.6, 1H), 4.28 (br d, J = 4.8, 2H), 3.89 (s, 3H), 3.85 (s, 3H), 3.84 (s, 3H), 3.83 (s, 3H), 3.61 (s, 3H), 2.88 (br, 1H); ^{13}C NMR 152.8, 151.24, 151.17, 149.9, 141.6, 133.9, 126.7, 125.4, 125.3, 117.4, 112.0, 106.4, 94.3, 80.3, 60.7, 60.61, 60.57, 55.6, 51.0; MS m/e 358 (M^+); HRMS m/e for $C_{20}H_{22}O_6$ calcd 358.1416, found 358.1404.

3-Biphenyl-2-yl-2-propyn-1-ol (13g). To a solution of 2′-iodobiphenyl (0.10 mL, 0.57 mmol), $Pd(PPh_3)_4$ (10 mg), and CuI (20 mg) in degassed diisopropylamine (5 mL) was added propargyl alcohol (0.15 mL, 2.6 mmol). After 20 h of stirring, the volatiles were removed under reduced pressure, the residue was filtered

through silica with Et_2O, and the volatiles were again removed in vacuo. Preparative TLC in 2:1 hexanes/Et_2O gave 0.1025 g of **13g** (87% yield): bp 135−140 °C (0.15 Torr) (bulb-to-bulb); IR (KBr) ν_{max} 3054, 3061, 2925, 2235 cm^{-1}; ^{1}H NMR δ 7.58 (d, J= 7.3, 2H), 7.57 (d, J = 7.9, 1H), 7.44 (apparent t, J_{ave} = 7.5, 2H), 7.35−7.41 (m, 3H), 7,31 (m, 1H), 4.35 (s, 2H), 1.63 (br s, 1H); ^{13}C NMR (40 °C) 144.0, 140.5, 133.1, 129.5, 129.2, 128.6, 127.9, 127.4, 127.0, 121.0, 90.2, 85.4, 51.5; MS m/e 208 (M^+); HRMS m/e for $C_{15}H_{12}O$ calcd 208.0888 (M^+), found 208.0890.

Methyl 4-Bromo-3-iodobenzoate. To a solution of 4-bromo-3-iodobenzoic acid (1.3227 g, 3.68 mmol) in methanol (40 mL) was added H_2SO_4 (10 drops). The mixture was heated to reflux for 12 h. Following a conventional extractive workup (Et_2O) and extraction of the Et_2O layers with $NaOH_{(aq)}$, the Et_2O layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Flash chromatography (8:1 petroleum ether/Et_2O) afforded methyl 4-bromo-3-iodobenzoate (1.2550 g, 91% yield) as a colorless solid: mp 70−71 °C; IR (KBr) ν_{max} 3087, 1726 cm^{-1}; ^{1}H NMR δ 8.46 (s, 1H), 7.81 (d, J=8.2, 1H), 7.66 (d, J=8.2, 1H), 3.90 (s, 3H); ^{13}C NMR 164.8, 141.1, 135.2, 132.5, 130.12, 130.08, 101.0, 52.5; MS m/e (M^+) 340/342; HRMS m/e for $C_8H_6BrIO_2$ calcd 339.8596, found 339.8603.

Methyl 4-Bromo-3-(3-methoxyprop-1-ynyl)benzoate (15). To a solution of methyl 4-bromo-3-iodobenzoate (1.255 g, 3.21 mmol) and propargyl methyl ether (0.47 mL, 5.9 mmol) in diisopropylamine (5 mL) were added CuI (0.0404 g, 0.212 mmol) and Pd(PPh_3)$_4$ (0.070 g, 0.061 mmol). After 12 h of stirring, the mixture was subjected to a conventional extractive workup. Flash chromatography (5:1 petroleum ether/Et_2O) afforded **15** (0.9599 g, 92% yield) as yellow crystals: mp 42−43 °C; IR (KBr) ν_{max} 3033, 2953, 1739, 1593 cm^{-1}; ^{1}H NMR δ 8.10 (d, J= 2.0, 1H), 7.78 (dd, J=8.4, 2.0, 1H), 7.64 (d, J=8.4, 1H), 4.37 (s, 2H), 3.89 (s, 3H), 3.48 (s, 3H); ^{13}C NMR 165.6, 134.4, 132.5, 130.6, 130.1, 129.2, 125.2, 90.7, 84.0, 60.2, 57.7, 52.3; MS m/e 282/284 (M^+); HRMS for $C_{12}H_{11}BrO_3$ calcd 283.9891, found 283.9900.

Methyl 2′,3′,4′-Trimethoxy-2-(3-methoxyprop-1-ynyl)biphenyl-4-carboxylate (16). A mixture of methyl 4-bromo-3-(3-methoxyprop-1-ynyl)benzoate (**15**) (0.0712 g, 0.251 mmol), 2,3,4-trimethoxyphenylboronic acid (**10a**) (0.1333 g, 0.629 mmol), K_3PO_4 (0.1590 g, 0.750 mmol), $Pd_2(dba)_3$ (0.0046 g, 0.0050 mmol), and PCy_3 (0.0035 g, 0.012 mmol) in toluene (10 mL) was heated to 100 °C for 37 h. Following an extractive workup, radial chromatography (5:1 petroleum ether/Et_2O) afforded, in order of elution, recovered **15** (0.0218 g, 31% recovery), and **16** (0.0493 g, 53% yield) as a viscous oil: IR (KBr) ν_{max} 2936, 1730, 1605 cm^{-1}; ^{1}H NMR δ 8.22 (d, J = 1.8, 1H), 8.00 (dd, J = 8.1, 1.8, 1H), 7.41 (d, J = 8.1, 1H), 7.01 (d, J = 8.5, 1H), 6.72 (d, J = 8.5, 1H), 4.20 (s, 2H), 3.94 (s, 3H), 3.92 (s, 3H), 3.91 (s, 3H), 3.66 (s, 3H), 3.23 (s, 3H); ^{13}C NMR 166.4, 153.8. 151.4, 145.3, 142.1, 133.7, 130.6, 128.9, 126.6, 125.2, 122.9, 106.7, 88.2, 85.2, 61.2, 61.0, 60.2, 57.2, 56.1, 52.2; MS m/e 370 (M^+); HRMS for $C_{21}H_{22}O_6$ (M^+) calcd 370.1416, found 370.1416.

A solution of potassium *tert*-butoxide (0.0351 g, 0.314 mmol) and (1,3-diisopropylimiazol-2-ylidene)(3-chloropyridyl)palladium-(II) dichloride (0.0014 g, 1 mol %) in isopropanol (1 mL) was stirred for 10 min. To this solution was added 2,3,4-trimethoxyphenylboronic acid (**10a**) (0.0975 g, 0.460 mmol) and **15** (0.0590 g, 0.209 mmol). After stirring for 12 h, diethyl ether was added, and reaction was subjected to a conventional extractive workup (Et_2O). Preparative TLC (5:1 petroleum ether/Et_2O) afforded **16** (0.0612 g, 79% yield).

Hexacarbonyl[μ-η^4-(3-acetoxy-(2′,3′,4,4′-tetramethoxybiphenyl-2-yl)-1-propyne)]dicobalt (8a). General Procedure B. To alcohol **13a** (0.2875 g, 0.876 mmol) at 0 °C were added acetic anhydride (1 mL) and pyridine (1 mL). The solution was stirred 4 h, as the solution came to room temperature. The volatiles were removed under reduced pressure, and the residue was dissolved in CH_2Cl_2 (25 mL). An unweighed amount of octacarbonyldicobalt (excess) was added, and the mixture was stirred 4 h. After concentration under reduced pressure, flash chromatography (100% petroleum ether → 5:1 petroleum ether/Et_2O) gave acetate complex **8a** (0.4952 g, 86% yield) as a red-brown solid: mp 122−124 °C ; IR (KBr) ν_{max} 2919, 2090, 2050, 2018, 1743 cm^{-1}; ^{1}H NMR δ 7.30 (d, J=2.5, 1H), 7.00 (d, J = 8.5, 1H), 6.88 (dd, J = 8.5, 2.5, 1H), 6.80 (d, J=8.5, 1H), 6.73 (d, J = 8.5, 1H), 4.58 (d, J = 15.0, 1H), 3.97 (d, J = 15.0, 1H), 3.96 (s, 3H), 3.93 (s, 3H), 3.86 (s, 3H), 3.59 (s, 3H), 2.02 (s, 3H); ^{13}C NMR 199.4, 199.3, 170.3, 159.2, 153.9, 151.2, 142.4, 137.6, 131.8, 129.4, 128.2, 125.4, 118.0, 114.5, 107.3, 92.5, 88.7, 64.4, 60.7, 60.4, 56.2, 55.0, 20.2 ; MS m/e 600 (M^+ − 2CO), 572 (M^+ − 3CO), 488 (M^+ − 6CO). Anal. Calcd for $C_{27}H_{22}Co_2O_{12}$ C, 49.41; H, 3.38. Found: C, 49.68; H, 3.38.

Hexacarbonyl[μ-η^4-(3-acetoxy-(2′,3′,4′-trimethoxybiphenyl-2-yl)-1-propyne]dicobalt (8b). Subjecting **13b** (0.1214 g, 0.407 mmol) to General Procedure B afforded **18b** (0.2140 g, 84% yield) following flash chromatographic purification (10:1 → 4:1 petroleum ether/Et_2O), as a red-brown solid: mp 108−110 °C; IR (KBr) ν_{max} 2938, 2090, 2052, 2022, 1745 cm^{-1}; ^{1}H NMR δ 7.76 (d, J=7.8, 1H), 7.40 (apparent t, J=7.4, 1H), 7.31 (apparent t, J=7.3, 1H), 7.11 (d, J = 7.5, 1H), 6.82 (d, J = 8.4, 1H), 6.75 (d, J=8.4, 1H), 4.59 (d, J=14.5, 1H), 3.98 (d, J=14.5, 1H), 3.98 (s, 3H), 3.94 (s, 3H), 3.60 (s, 3H), 2.03 (s, 3H); ^{13}C NMR 199.3, 170.4, 154.1, 151.5, 142.6, 137.1, 136.6, 134.3, 130.9, 128.6, 128.1, 127.4, 125.0, 107.5, 92.6, 88.6, 64.6, 60.8, 60.5, 56.4. 20.2 ; MS m/e 570 (M^+ − 2CO), 542 (M^+ − 3CO), 458 (M^+ − 6CO); HRMS for $C_{26}H_{20}Co_2O_{11}$ calcd 597.9720 (M^+ − CO), found 597.9741.

Hexacarbonyl[μ-η^4-(3-acetoxy-(3-methoxy-3′,5′-dimethylbiphenyl-2-yl)-1-propyne]dicobalt (8c). Subjecting **13c** (0.0608 g, 0.228 mmol) to General Procedure B afforded acetate complex **8c** (0.1232 g, 91% yield) of acetate complex (91% yield) following flash chromatography (10:1 petroleum ether/Et_2O), as a red-brown solid: mp 250 °C (dec); IR (KBr) ν_{max} 2961, 2090, 2058, 1998, 1748 cm^{-1}; ^{1}H NMR δ 7.28 (d, J = 2.7, 1H), 7.08 (s, 1H), 7.04 (d, J = 8.4, 1H), 6.89 (dd, J = 8.4, 2.7, 1H), 6.86 (s, 2H), 4.02 (s, 2H), 3.87 (s, 3H), 2.37 (s, 6H), 2.04 (s, 3H); ^{13}C NMR 199.4, 170.4, 159.2, 141.6, 138.2, 136.4, 134.2, 131.1, 129.2, 127.4, 118.0, 114.6, 93.3, 88.9, 64.2, 55.2, 21.1, 20.3; MS m/e 566 (M^+ − CO), 510 (M^+ − 3CO), 426 (M^+ − 6CO); HRMS m/e for $C_{26}H_{20}Co_2O_9$ calcd 565.9822 (M^+ − CO), found 565.9811.

Hexacarbonyl[μ-η^4-(3-acetoxy-1-(5-methoxy-2-(3-thienyl)phenyl)-1-propyne]dicobalt (8d). Subjecting **13d** (0.0418 g, 0.171 mmol) to General Procedure B gave acetate complex **8d** (0.0756, 77% yield) following flash chromatography (10:1 petroleum ether/Et_2O), as a red-brown solid: mp 104−105 °C; IR (KBr) ν_{max} 2941, 2090, 2055, 2021, 1745 cm^{-1}; ^{1}H NMR δ 7.46 (dd, J = 4.7, 3.1, 1H), 7.28 (d, J = 2.6, 1H), 7.15 (m, 1H), 7.06 (d, J = 8.4, 1H), 7.02 (d, J = 4.7, 1H), 6.88 (dd, J = 8.4, 2.6, 1H), 4.30 (s, 2H), 3.87 (s, 3H), 2.05 (s, 3H); ^{13}C NMR 199.3, 170.5, 159.6, 141.9, 137.2, 131.8, 130.1, 128.3, 126.1, 123.8, 118.3, 114.7, 93.1, 88.4, 63.9, 55.2, 20.3; MS m/e 544 (M^+ − CO), 488 (M^+ − 3CO), 404 (M^+ − 6CO); HRMS m/e for $C_{22}H_{14}Co_2O_9S$ calcd 543.9073 (M^+ −CO), found 543.9078.

Hexacarbonyl[μ-η^4-(3-acetoxy-(,3′,4,4′,5′-tetramethoxybiphenyl-2-yl)-1-propyne)]dicobalt (8e). Subjecting **13e** (0.2809 g, 0.855 mmol) to General Procedure B afforded **8e** (0.4722 g, 84% yield) following flash chromatographic purification (3:1 petroleum ether/Et_2O), as a red-brown solid: mp 126−128 °C; IR (KBr) ν_{max} 2938, 2090, 2010, 1974, 1748 cm^{-1}; 1H NMR δ 7.27 (d, J = 2.6, 1H), 7.05 (d, J = 8.4, 1H), 6.89 (dd, J = 8.4, 2.6, 1H), 6.42 (s, 2H), 4.22 (s, 2H), 3.93 (s, 3H), 3.86 (s, 3H), 3.82 (s, 6H), 2.02 (s, 3H); ^{13}C NMR 199.3, 170.3, 159.4, 153.2, 137.7, 137.3, 136.4, 133.6, 131.2, 117.7, 114.7, 106.9, 93.1, 88.3, 63.9, 61.1, 56.1, 55.1, 20.2; MS m/e 628 (M^+ − CO), 600 (M^+ − 2CO), 572 (M^+ − 3CO), 544 (M^+ − 4CO), 516 (M^+ − 5CO),

488 ($M^+ - 6CO$); HRMS for $C_{27}H_{22}Co_2O_{12}$ calcd ($M^+ - CO$) 627.9826, found 627.9802.

Hexacarbonyl[μ-η^4-(3-acetoxy-(2′,3,3′,4,4′-pentamethoxybiphenyl-2-yl)-1-propyne)]dicobalt (8f). Subjecting **13f** (0.5231 g, 1.46 mmol) to General Procedure B afforded **8f** (0.9818 g, 98% yield) following flash chromatographic purification (4:1 petroleum ether/Et_2O), as a red-brown solid: mp 120−121 °C; IR (KBr) ν_{max} 3002, 2939, 2088, 2009, 1743 cm^{-1}; ^1H NMR δ 6.95 (d, J = 8.4, 1H), 6.80 (d, J = 8.4, 1H), 6.73 (d, J = 8.4, 1H), 6.71 (d, J = 8.4, 1H), 4.53 (d, J = 14.5, 1H), 4.07 (s, 3H), 3.95 (s, 3H), 3.92 (s, 3H), 3.90 (s, 3H), 3.83 (d, J = 14.5, 1H), 3.61 (s, 3H), 2.00 (s, 3H); ^{13}C NMR 199.8, 170.4, 153.9, 151.6, 151.4, 149.5, 142.4, 131.3, 128.84, 128.79, 125.6, 125.4, 112.2, 107.2, 94.3, 81.0, 65.4, 60.6, 60.3, 59.9, 56.2, 55.7, 20.2; MS m/e 630 (M^+-2CO), 602 ($M^+ - 3CO$), 518 ($M^+ - 6CO$), 400 ($M^+ - Co_2(CO)_6$); HRMS for $C_{28}H_{24}Co_2O_{13}$ ($M^+ - 2CO$) calcd 629.9997, found 629.9995.

Hexacarbonyl[μ-η^4-(3-acetoxy-1-biphenyl-2-yl)-1-propyne]dicobalt (8g). Subjecting **13g** (0.0799 g, 0.384 mmol) to General Procedure B gave acetate complex **8g** (0.1763 g, 86% yield) following flash chromatography (50:1 petroleum ether/Et_2O), as a red-brown oil which gradually solidified: mp 99−101 °C; IR (KBr) ν_{max} 3073, 2977, 2087, 2055, 2006, 1749 cm^{-1}; ^{1} H NMR δ 7.77 (d, J = 7.8, 1H), 7.45−7.52 (m, 3H), 7.42 (apparent t, J_{ave} = 7.6, 1H), 7.34 (apparent t, J_{ave} = 7.3, 1H), 7.26−7.30 (m, 2H), 7.14 (d, J = 7.8, 1H), 4.02 (s, 2H), 2.02 (s, 3H); ^{13}C NMR 199.3, 170.4, 142.2, 141.2, 135.3, 134.3, 130.2, 129.3, 128.6, 128.3, 128.0, 127.6, 93.1, 88.4, 64.1, 20.3; MS m/e 480 ($M^+ - 2CO$), 452 ($M^+ - 3CO$), 396 ($M^+ - 5CO$), 368 ($M^+ - 6CO$). Anal. Calcd for $C_{23}H_{14}Co_2O_8$ C, 51.52; H, 2.63. Found C, 51.75; H, 2.51.

Hexacarbonyl[μ-η^4-(3-methoxy-(4-carbomethoxy-2′,3′,4′-trimethoxybiphenyl-2-yl)-1-propyne)]dicobalt (8h). To a solution of **16** (0.1223 g, 0.330 mmol) in CH_2Cl_2 at 0 °C was added octacarbonyldicobalt (excess). The cooling bath was removed, and the mixture was allowed to stir for 2 h. After concentration under reduced pressure, flash chromatography (3:1 petroleum ether/Et_2O) afforded **8h** (0.1797 g, 83% yield) as a red-brown solid: mp 143−144 °C; IR (KBr) ν_{max} 2956, 2091, 2039, 2009, 1726 cm^{-1}; ^1H NMR δ 8.45 (d, J = 1.7, 1H), 7.93 (dd, J = 7.9, 1.7, 1H), 7.18 (d, J = 7.9, 1H), 6.80 (1/2 AB quartet, J = 8.5, 1H), 6.74 (1/2 AB quartet, J = 8.5, 1H), 3.97 (s, 3H), 3.96 (s, 3H), 3.94 (s, 3H), 3.87 (d, J = 13.4, 1H), 3.59 (s, 3H), 3.30 (s, 3H), 3.25 (d, J = 13.4, 1H); ^{13}C NMR 199.4, 166.6, 154.0, 151.3, 142.4, 141.3, 137.8, 135.7, 131.2, 130.1, 128.1, 127.8, 124.9, 107.1, 95.7, 86.0, 71.7, 60.8, 60.6, 58.6, 56.3, 52.3; MS m/e 572 ($M^+ - 3CO$), 516 ($M^+ - 5CO$); HRMS for $C_{27}H_{22}Co_2O_{12}$ calcd ($M^+ - 3CO$) 571.9928, found 571.9924.

Hexacarbonyl[μ-η^4-(1,2,3,9-tetramethoxy-5*H*-dibenzo[*a*,*c*]cycloheptyne]dicobalt (9a). General Procedure C. To a solution of **8a** (0.1193 g, 0.182 mmol) in CH_2Cl_2 (35 mL) at 0 °C was added diisopropylethylamine (48 μL, 1.5 equiv) and BF_3-OEt_2 (69 μL, 3.0 equiv). The cooling bath was removed, and the reaction was allowed to stir for 6 h, at which time consumption of starting material was complete. Following an extractive workup, flash chromatography (5:1 petroleum ether/Et_2O) afforded **9a** (0.0766 g, 71% yield), as a red-brown oil which gradually solidified: mp 117−119 °C; IR (KBr) ν_{max} 2939, 2090, 2020 cm^{-1}; ^{1} H NMR δ 7.57 (d, J = 8.5, 1H), 7.21 (d, J = 3.0, 1H), 6.92 (dd, J = 8.5, 2.5, 1H), 6.65 (s, 1H), 4.01 (d, J = 14.0, 1H), 3.91 (s, 3H), 3.90 (s, 3H), 3.82 (s, 3H), 3.63 (d, J = 14.0, 1H) 3.38 (s, 3H); ^{13}C NMR 199.3, 198.7, 158.9, 152.9, 152.2, 142.3, 138.9, 137.2, 133.7, 126.1, 124.8, 116.5, 112.0, 107.7, 105.4, 93.0, 60.9, 60.2, 56.0, 55.1, 39.8; MS m/e 596 (M^+), 540 ($M^+ - 2CO$), 512 ($M^+ - 3CO$), 484 ($M^+ - 4CO$); HRMS m/e for $C_{25}H_{18}Co_2O_{10}$ calcd 539.9666 ($M^+ - 2CO$), found 539.9642.

Hexacarbonyl[μ-η^4-(1,2,3-Trimethoxy-5*H*-dibenzo[*a*,*c*]cycloheptyne]dicobalt (9b). Subjecting acetate complex **8b** (0.0848 g, 0.135 mmol) to General Procedure C (16 h), followed by flash chromatography (5:1 petroleum ether/Et_2O) afforded **9b** (0.0452 g, 59% yield, 66% yield based on recovered starting material) followed by recovered **8b** (0.0085 g, 10% recovery). **9b**: red-brown solid, mp 116−118 °C; IR (KBr) ν_{max} 3057, 2934, 2090, 2051 cm^{-1}; ^{1} H NMR δ 7.69 (dd, J = 7.4, 1.3, 1H), 7.63 (dd, J = 7.6, 1.3, 1H), 7.38 (apparent dt, J = 1.3, 7.4, 1H), 7.35 (apparent dt, J = 1.3, 7.6, 1H), 6.67 (s, 1H), 4.03 (d, J = 14.0, 1H), 3.94 (s, 3H), 3.84 (s, 3H), 3.66 (d, J = 14.0, 1H), 3.39 (s, 3H); ^{13}C NMR 198.9 (br), 153.1, 152.7, 142.5, 137.7, 137.5, 132.6, 132.4, 132.0, 127.8, 126.4, 126.2, 107.9, 105.7, 92.9, 61.0, 60.4, 56.1, 40.0; MS m/e 538 ($M^+ - 1CO$), 510 ($M^+ - 2CO$), 482 ($M^+ - 3CO$), 454 ($M^+ - 4CO$), 426 ($M^+ - 5CO$), 398 ($M^+ - 6CO$); HRMS m/e for $C_{24}H_{16}Co_2O_9$ calcd 537.9509 ($M^+ - CO$), found 537.9492 .

Hexacarbonyl[μ-η^4-(9-methoxy-2,4-dimethyl-5*H*-dibenzo[*a*,*c*]cycloheptyne]dicobalt (9c). Subjecting acetate complex **8c** (0.1232 g, 0.207 mmol) to General Procedure C (6 h) gave **9c** (0.0938 g, 85% yield), following flash chromatography (50:1 petroleum ether/Et_2O), as a brown solid: mp 142−144 °C; IR (KBr) ν_{max} 2924, 2090, 2055, 2025 cm^{-1}; ^{1} H NMR (−30 °C) δ 7.54 (d, J = 8.5, 1H), 7.21 (d, J = 3.0, 1H), 6.97 - 7.01 (m, 3H), 4.49 (d, J = 14.0, 1H), 3.93 (s, 3H), 3.34 (d, J = 14.0, 1H), 2.50 (s, 3H), 2.29 (s, 3H) ; ^{13}C NMR 199.1, 159.4, 140.6, 139.0, 136.20, 136.15, 134.1, 132.2, 132.0, 131.7, 130.0, 116.7, 113.5, 105.2, 92.7, 55.4, 32.9, 21.0, 20.9; MS m/e 534 (M^+), 450 ($M^+ - 3CO$), 394 ($M^+ - 5CO$); HRMS m/e for $C_{24}H_{16}Co_2O_7$ calcd 533.9560 (M^+), found 533.9569.

Hexacarbonyl[μ-η^4-(8-methoxy-4*H*-benzo[3,4]cycloheptyne-[1,2-*b*]thiophene]dicobalt (9d) and Hexacarbonyl[μ-η^4-(8-methoxy-4*H*-benzo[3,4]cycloheptyne[1,2-*c*]thiophene]dicobalt (9d′). Subjecting **8d** (0.0654 g, 0.114 mmol) to General Procedure C (5 h) afforded **9d/9d′** (0.0494 g, 82% yield) following flash chromatography, as an inseparable 45:55 mixture, as a red-brown viscous oil: IR (KBr) ν_{max} 2937, 2091, 2067, 2045, 1603 cm^{-1}. ^{1} H NMR: for **9d** δ 7.53 (d, J = 8.5, 1H), 7.24 (d, J = 2.8, 1H), 7.18 (d, J = 5.3, 1H), 7.13 (d, J = 5.3, 1H), 6.95 (dd, J = 8.3, 2.8, 1H), 4.25 (s, 2H), 3.900 (s, 3H); for **9d′** δ 7.55 (d, J = 8.5, 1H), 7.28 (d, J = 3.1, 1H), 7.19 (d, J = 2.8, 1H), 7.14 (obscured d, 1H), 6.93 (dd, J = 8.3, 2.8 1H), 4.17 (s, 2H), 3.897 (s, 3H); ^{13}C NMR 199.0, 159.6, 159.1, 141.3, 139.5, 138.0, 137.2, 136.9, 135.7, 131.1, 130.2, 129.9, 127.1, 127.0, 125.4, 121.9, 121.5, 117.3, 117.1, 114.0, 113.8, 100.9, 100.4, 92.5, 55.4, 34.8, 33.3; MS m/e 512 (M^+), 455 ($M^+ - 2CO$), 399 ($M^+ - 4CO$); HRMS m/e for $C_{20}H_{10}Co_2O_7S$ calcd 511.8811 (M^+), found 511.8808.

Hexacarbonyl[μ-η^4-(2,3,4,9-tetramethoxy-5*H*-dibenzo[*a*,*c*]cycloheptyne]dicobalt (9e). Subjecting (**8e**) (0.6621 g, 1.01 mmol) to General Procedure C (4.5 h) afforded **9e** (0.5457 g, 91% yield) following flash chromatography (7:1 petroleum ether/Et_2O), as a red-brown solid: mp 138−140 °C; IR (KBr) ν_{max} 2938, 2091, 2051, 2023, 1601 cm^{-1}; ^1H NMR δ 7.47 (d, J = 8.7, 1H), 7.22 (d, J = 2.7, 1H), 6.98 (dd, J = 8.7, 2.7, 1H), 6.67 (s, 1H), 4.03 (v br, 2H), 3.95 (s, 3H), 3.91 (s, 6H), 3.84 (s, 3H); ^{13}C NMR 199.1, 159.5, 152.0, 150.1, 141.7, 138.9, 136.1, 131.35, 131.29, 127.1, 116.8, 113.6, 112.7, 105.6, 92.6, 61.4, 60.9, 56.2, 55.4, 29.4; MS m/e 596 (M^+), 568 ($M^+ - CO$), 540 ($M^+ - 2CO$), 512 ($M^+ - 3CO$), 484 ($M^+ - 4CO$), 456 ($M^+ - 5CO$); HRMS for $C_{25}H_{18}Co_2O_{10}$ (M^+) calcd 595.9564, found 595.9548.

Hexacarbonyl[μ-η^4-(1,2,3,8,9-pentamethoxy-5*H*-dibenzo[*a*,*c*]cycloheptyne]dicobalt (9f). Subjecting (**8f**) (0.9250 g, 1.35 mmol) to General Procedure C (4.5 h) afforded **9f** (0.7021 g, 83% yield) following flash chromatography (5:1 hexanes/Et_2O), as a dark brown solid: mp 115−117 °C; IR (KBr) ν_{max} 2939, 2090, 2054, 1593 cm^{-1}; ^1H NMR δ 7.30 (d, J = 8.7, 1H), 6.97 (d, J = 8.7, 1H), 6.63 (s, 1H), 3.99 (d, J = 14.0, 1H), 3.99 (s, 3H), 3.95 (s, 3H), 3.92 (s, 3H), 3.81 (s, 3H), 3.67 (d, J = 14.0, 1H), 3.40 (s, 3H); ^{13}C NMR 199.5, 153.1, 152.3, 152.0, 148.4, 142.3, 137.3, 132.2, 128.3, 126.3, 125.9, 110.6, 107.5, 107.3, 85.8, 61.0, 60.7,

60.4, 56.1, 55.8, 40.3; MS *m*/*e* 626 (M^+), 598 ($M^+ - CO$), 570 ($M^+ - 2CO$), 542 ($M^+ - 3CO$), 514 ($M^+ - 4CO$), 486 ($M^+ - 5CO$), 458 ($M^+ - 6CO$); HRMS for $C_{26}H_{20}Co_2O_{11}$ (M^+) calcd 625.9670, found 625.9673.

Hexacarbonyl[μ-η^4-(5*H*-dibenzo[*a*,*c*]cycloheptyne]dicobalt (9g). Subjecting **8g** (0.0604 g, 0.127 mmol) to General Procedure C (16 h) afforded **9g** (0.0311, 58% yield) following flash chromatography (100% petroleum ether), as a dark brown solid: mp 130−132 °C; IR (KBr) ν_{max} 3059, 2959, 1688, 2091, 2052, 2022 cm^{-1}; ^{1}H NMR δ 7.71 (m, 1H), 7.59 (s, 1H), 7.40−7.47 (m, 3H), 7.28−7.36 (m, 3H), 4.05 (s, 2H); ^{13}C NMR 199.0, 140.4, 140.2, 138.5, 137.3, 133.2, 132.1, 130.4, 128.6, 128.3, 127.92, 127.86, 127.5, 104.2, 92.0, 39.9; MS *m*/*e* 420 ($M^+ - 2CO$), 336 ($M^+ - 5CO$), 308 ($M^+ - 6CO$); HRMS *m*/*e* for $C_{21}H_{10}Co_2O_6$ calcd 447.9192 ($M^+ - CO$), found 447.9214.

Hexacarbonyl[μ-η^4-(9-carbomethoxy-1,2,3-trimethoxy-5*H*-dibenzo[*a*,*c*]cycloheptyne]dicobalt (9h). Subjecting (**8h**) (0.2304 g, 0.351 mmol) to General Procedure C (5 h) afforded **9h** (0.1831 g, 84% yield) following flash chromatography (5:1 petroleum ether/Et_2O), as a dark brown viscous oil: IR (KBr) ν_{max} 2952, 2092, 2055, 2023, 1730 cm^{-1}; ^{1}H NMR δ 8.30 (d, *J*= 1.9, 1H), 7.98 (dd, *J* = 8.2, 1.9, 1H), 7.69 (d, *J* = 8.2, 1H), 6.67 (s, 1H), 4.05 (d, *J* = 14.1, 1H), 3.98 (s, 3H), 3.95 (s, 3H), 3.84 (s, 3H), 3.65 (d, *J* = 14.1, 1H), 3.39 (s, 3H); ^{13}C NMR 198.7, 166.7, 153.24, 153.15, 142.4, 138.3, 137.9, 137.0, 132.9, 129.4, 126.8, 125.5, 107.9, 105.4, 91.4, 61.1, 60.6, 56.1, 52.3, 39.9; MS *m*/*e* 596 (M^+-1CO), 568 (M^+-2CO), 540 ($M^+ - 3CO$), 512 (M^+-4CO), 484 (M^+-5CO);); HRMS for $C_{26}H_{18}Co_2O_{11}$ ($M^+ - 3CO$) calcd 539.9666, found 539.9683.

1,2,3,9-Tetramethoxy-5*H*-dibenzo[*a*,*c*]cycloheptene (17a). To a solution of **9a** (0.0782 g, 0.131 mmol) in degassed 1,2-dichloroethane (2 mL) was added bis(trimethylsilyl)acetylene (62 μL, 0.274 mmol) and triethylsilane (0.10 mL, 0.63 mmol). The mixture was heated to 65 °C for 6 h and cooled to room temperature, at which point trifluoroacetic acid (0.5 mL) was added. After stirring for an additional 12 h, the mixture was subjected to a conventional extractive workup. Preparative TLC (4:1 hexanes/Et_2O) afforded **17a** (0.0396 g, 97% yield) as a colorless solid: mp 102−3 °C (MeOH), lit.[29] 102−3 °C (MeOH).

2,3,4,9-Tetramethoxy-5*H*-dibenzo[*a*,*c*]cycloheptene (17e). To a solution of **9e** (0.3492 g, 0.586 mmol) in degassed 1,2-dichloroethane (20 mL) were added bis(trimethylsilyl)acetylene (0.27 mL, 1.2 mmol) and triethylsilane (0.47 mL, 2.9 mmol). The mixture was heated to 65 °C for 6 h and cooled to room temperature, at which point trifluoroacetic acid (1.0 mL) was added. After stirring for an additional 12 h, the mixture was subjected to a conventional extractive workup. Preparative TLC (10:1 petroleum ether/Et_2O) afforded **17e** (0.1718 g, 94% yield) as a colorless viscous oil: IR (KBr) ν_{max} 2936, 1604 cm^{-1}; ^{1}H NMR δ 7.61 (d, *J* = 8.7, 1H), 6.95 (dd, *J* = 8.7, 2.6, 1H), 6.85 (d, *J* = 2.6, 1H), 6.82 (s, 1H), 6.57 (d, *J* = 10.0, 1H), 6.26 (m, 1H), 3.94 (s, 3H), 3.93 (s, 3H), 3.90 (s, 3H), 3.89 (s, 3H), 2.47 (v br, 2H); ^{13}C NMR 158.2, 151.1, 148.9, 141.9, 137.4, 134.3, 132.8, 132.3, 130.7, 129.6, 128.3, 113.4, 112.9, 109.1, 61.5, 60.9, 56.2, 55.3, 24.0; MS *m*/*e* 312 (M^+); HRMS for $C_{19}H_{20}O_4$ (M^+) calcd 312.1362, found 312.1356.

1,2,3,8,9-Pentamethoxy-5*H*-dibenzo[*a*,*c*]cycloheptene (17f). To a solution of **9f** (0.0945 g, 0.151 mmol) in degassed 1,2-dichloroethane (2 mL) were added bis(trimethylsilyl)acetylene (62 μL, 0.32 mmol) and triethylsilane (0.12 mL, 0.76 mmol). The mixture was heated to 65 °C for 6 h and cooled to room temperature, at which point trifluoroacetic acid (0.5 mL) was added. After stirring for an additional 12 h, the mixture was subjected to a conventional extractive workup. Preparative TLC (7:1 petroleum ether/Et_2O) afforded **17f** (0.0465 g, 90% yield) as a colorless solid: mp 163−165 °C; IR (KBr) ν_{max} 3036, 2926, 1573 cm^{-1}; ^{1}H NMR δ 7.55 (d, *J* = 8.7, 1H), 6.94 (d, *J* = 8.7, 1H), 6.78 (d, *J* = 10.1, 1H), 6.58 (s, 1H), 6.29 (m, 1H), 3.95 (s, 3H), 3.91 (s, 3H), 3.90 (s, 3H), 3.85 (s, 3H), 3.48 (s, 3H), 3.06 (dd, *J* = 12.9, 7.9, 1H), 2.80 (ddd, *J* = 12.9, 5.9, 1.8, 1H); ^{13}C NMR 152.3, 150.4, 145.2, 140.7, 140.1, 132.2, 131.1, 128.3, 127.5, 124.0, 123.8, 109.9, 105.6, 61.0, 60.6, 60.4, 55.9, 55.8, 33.5; MS *m*/*e* 342 (M^+); HRMS for $C_{20}H_{22}O_5$ calcd 342.1467, found 342.1475.

9-Carbomethoxy-1,2,3-trimethoxy-5*H*-dibenzo[*a*,*c*]cycloheptene (17h). To a solution of **9h** (0.1831 g, 0.293 mmol) in degassed 1, 2-dichloroethane (7 mL) was added bis(trimethylsilyl)acetylene (0.14 mL, 0.59 mmol) and triethylsilane (0.23 mL, 0.14 mmol). The mixture was heated to 65 °C for 6 h and cooled to room temperature, at which point trifluoroacetic acid (3.0 mL) was added. After stirring for an additional 12 h, the mixture was subjected to a conventional extractive workup. Preparative TLC (5:1 hexanes/Et_2O) afforded **17h** (0.0789 g, 79% yield) as a colorless solid: mp 85−86 °C; IR (KBr) ν_{max} 2950, 1722, 1594 cm^{-1}; ^{1}H NMR δ 8.03 (s, 1H), 7.91 (1/2 AB quartet, *J* = 8.3, 1H), 7.89 (1/2 AB quartet, *J* = 8.3, 1H), 6.62 (d, *J* = 10.0, 1H), 6.59 (s, 1H), 6.29 (m, 1H), 3.96 (s, 3H), 3.92 (s, 3H), 3.90 (s, 3H), 3.46 (s, 3H), 3.08 (m, 1H), 2.75 (m, 1H); ^{13}C NMR 167.0, 153.3, 152.3, 140.8, 140.5, 139.4, 136.5, 133.2, 132.0, 130.1, 128.8, 127.6, 125.4, 123.3, 105.8, 61.1, 60.7, 55.9, 52.1, 33.3; MS *m*/*e* 340 (M^+); HRMS for $C_{20}H_{20}O_5$ (M^+) calcd 340.1311, found 340.1306.

6,7-Dihydro-3,9,10,11-tetramethoxy-5*H*-dibenzo[*a*,*c*]cyclohepten-5-one (18a). To a solution of alkene **17a** (0.0521 g, 0.167 mmol) in THF (7 mL) at 0 °C was added BH_3-THF (0.75 mL of a 1 M solution). The cooling bath was removed, and the reaction was stirred at room temperature for 12 h. NaOH (1 mL of a 10% aqueous solution) and H_2O_2 (1 mL of a 33% aqueous solution) were added, and the mixture was stirred for 4 h, followed by warming to 40 °C for 0.5 h. A conventional workup gave a crude alcohol which was added slowly as a solution in CH_2Cl_2 to a −78 °C solution prepared from the addition of DMSO (0.14 mL, 2.0 mmol) to oxalyl chloride (86 μL, 1.0 mmol) in CH_2Cl_2 (10 mL) at −78 °C. Diisopropylethylamine (0.70 mL, 4.0 mmol) was added, and the solution was allowed to come to room temperature over 6 h. A conventional workup gave a residue with a 96:4 mixture of ketone regioisomers (by integration of relevant ^{1}H NMR resonances); preparative TLC (1:1 hexanes/Et_2O) afford **18a** (0.0440, 80% yield) as a colorless solid: mp 141−2 °C (hexanes), lit. 142−3 °C (MeOH),[5a] 140.5−141 °C,[30] 135−6 °C.[11]

6,7-Dihydro-3,8,9,10-tetramethoxy-5*H*-dibenzo[*a*,*c*]cyclohepten-5-one. (18e). To a solution of alkene **17e** (0.1793 g, 0.574 mmol) in THF (20 mL) at 0 °C was added BH_3-THF (2.7 mL of a 1 M solution). The cooling bath was removed, and the reaction was stirred at room temperature for 12 h. NaOH (3 mL of a 10% aqueous solution) and H_2O_2 (3 mL of a 33% aqueous solution) were added, and the mixture was stirred for 4 h, followed by warming to 40 °C for 0.5 h. A conventional workup gave a crude alcohol which was dissolved in CH_2Cl_2 (20 mL). To this solution was added PDC (0.55 g), and the mixture was stirred for 12 h. A conventional workup followed by preparative TLC (3:1 petroleum ether/Et_2O) afforded **18e** (0.1291 g, 68% yield) as a colorless solid: mp 123−125 °C; IR (KBr) ν_{max} 2937, 1681, 1601 cm^{-1}; ^{1}H NMR δ 7.36 (m, 1H), 7.14 (s, 1H), 7.13 (obscured m, 1H), 6.69 (s, 1H), 3.92 (s, 3H), 3.89 (s, 3H), 3.88 (s, 6H), 2.97−3.00 (m, 2H), 2.92−2.94 (m, 2H); ^{13}C NMR 206.3, 158.9, 152.2, 150.1, 141.6, 139.7, 134.4, 131.4, 130.5, 125.4, 118.8, 112.1, 109.0, 61.3, 60.8, 56.0, 55.4, 47.3, 20.4; MS *m*/*e* 328 (M^+); HRMS for $C_{19}H_{20}O_5$ (M^+) calcd 328.1311, found 328.1322.

6,7-Dihydro-3,4,9,10,11-pentamethoxy-5*H*-dibenzo[*a*,*c*]cyclohepten-5-one (18f). To a solution of alkene **17f** (0.2175 g, 0.636 mmol) in THF (25 mL) at 0 °C was added BH_3-THF (3.0 mL of a 1 M

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solution). The cooling bath was removed, and the reaction was stirred at room temperature for 12 h. NaOH (3 mL of a 10% aqueous solution) and H_2O_2 (3 mL of a 33% aqueous solution) were added, and the mixture was stirred for 4 h, followed by warming to 40 °C for 0.5 h. A conventional workup gave a crude alcohol which was dissolved in CH_2Cl_2 (20 mL). To this solution was added PDC (0.55 g), and the mixture was stirred for 12 h. A conventional workup followed by preparative TLC (3:1 petroleum ether/Et_2O) afforded **18f** (0.1505 g, 67% yield) as a colorless solid: mp 164−165 °C, lit. 156−157 °C;[22] IR (KBr) ν_{max} 2939, 1701, 1598 cm^{-1}; ^1H NMR δ 7.26 (d, J = 8.6, 1H), 7.00 (d, J = 8.6, 1H), 6.56 (s, 1H), 3.91 (s, 3H), 3.87 (s, 3H), 3.86 (s, 6H), 3.57 (s, 3H), 2.97−3.05 (m, 2H), 2.85 (m, 1H), 2.59 (m, 1H); ^{13}C NMR 204.8, 152.6, 151.8, 151.7, 144.3, 141.4, 135.24, 135.21, 126.24, 126.16, 123.8, 113.0, 107.5, 62.2, 61.0, 60.8, 55.9, 55.8, 49.6, 30.1; MS m/e 354 (M^+); HRMS for $C_{20}H_{22}O_6$ (M^+) calcd 358.1416, found 358.1402.

6,7-Dihydro-3-carbomethoxy-9,10,11-trimethoxy-5*H*-dibenzo[*a*,*c*]cyclohepten-5-one (18h). To a solution of alkene **17h** (0.0307 g, 0.0902 mmol) in THF (5 mL) at 0 °C was added BH_3-THF (0.45 mL of a 1 M solution). The cooling bath was removed, and the reaction was stirred at room temperature for 12 h. NaOH (1 mL of a 10% aqueous solution) and H_2O_2 (1 mL of a 33% aqueous solution) were added, and the mixture was stirred for 4 h, followed by warming to 40 °C for 0.5 h. A conventional workup gave a crude alcohol which was dissolved in CH_2Cl_2 (10 mL). To this solution was added PDC (0.5 g), and the mixture was stirred for 12 h. A conventional workup followed by preparative TLC (1:1 petroleum ether/Et_2O) afforded **18h** (0.0.0260 g, 81% yield) as a colorless solid: mp 144−145 °C; lit.[6] 144.2−144.8 °C.

(5*R*)-6,7-Dihydro-3,9,10,11-tetramethoxy-5*H*-dibenzo[*a*,*c*]cyclohepten-5-ol (19a). A suspension of 3-nitrophenylboronic acid (0.334 g, 2.0 mmol), L-tartaric acid (0.0300 g, 2.0 mmol), and CaH_2 (0.168 g, 4.0 mmol) in THF (5 mL) was heated to reflux for 1 h. After cooling and the solids were allowed to settle, the supernatant solution (2.5 mL, ca. 1 mmol) was added to ketone **18a** (0.0634 g, 0.193 mmol). Lithium borohydride (0.5 mL of a 2 M solution, 1.0 mmol) was added over a period of 5 min, and the solution was stirred for 0.5 h. NaOH (1 mL of a 10% aqueous solution) and water (2 mL) were added, and the reaction subjected to a conventional extractive workup. Preparative TLC (2:1 petroleum ether/Et_2O) afforded **19a** (0.0610 g, 96%), 95% ee (Chiralcel OD-H, *i*-PrOH/hexanes): mp 137−9 °C (CH_2Cl_2/petroleum ether) $[\alpha]^{22}_D$ 120° (*c* 0.0144); ^{1}H NMR (DMSO-d_6) δ 7.24 (d, J = 8.4, 1H), 7.17 (d, J = 2.8, 1H), 6.85 (dd, J = 84, 2.8, 1H), 6.75 (s, 1H), 5.23 (d, J = 4.7, 1H), 4.27 (m, 1H), 3.82 (s, 3H), 3.80 (s, 3H), 3.75 (s, 3H), 3.48 (s, 3H), 2.32−2.45 (m, 2H), 2.06 (m, 1H), 1.73 (m, 1H); ^{13}C NMR (DMSO-d_6) 158.3, 151.9, 150.2, 144.5, 140.4, 135.2, 130.3, 124.9, 124.0, 111.2, 108.7, 107.9, 68.1, 60.5, 60.4, 55.8, 54.9, 41.3, 29.9; HRMS m/e for $C_{19}H_{22}O_5$ calcd 330.1467 (M^+), found 330.1479.

(5*R*)-6,7-Dihydro-3,8,9,10-tetramethoxy-5*H*-dibenzo[*a*,*c*]cyclohepten-5-ol (19e). A suspension of 3-nitrophenylboronic acid (0.334 g, 2.0 mmol), L-tartaric acid (0.0300 g, 2.0 mmol), and CaH_2 (0.168 g, 4.0 mmol) in THF (5 mL) was heated to reflux for 1 h. After cooling and the solids were allowed to settle, the supernatant solution (2.5 mL, ca. 1 mmol) was added to ketone **18e** (0.0217 g, 0.0661 mmol). Lithium borohydride (0.2 mL of a 2 M solution, 0.4 mmol) was added over a period of 1.5 h, and the solution stirred for 0.5 h. NaOH (1 mL of a 10% aqueous solution) and water (2 mL) were added, and the reaction subjected to a conventional extractive workup. Preparative TLC (1:1 petroleum ether/Et_2O) afforded **19e** (0.0213 g, 98%), 98% ee (Chiralcel AS-H, 10% *i*-PrOH/hexanes) as a viscous oil, $[\alpha]^{22}_D$ 102° (*c* 0.533); IR (KBr) ν_{max} 3500 br, 2936, 1646 cm^{-1}; ^{1}H NMR (DMSO-d_6) 7.30 (d, J = 8.5, 1H), 7.18 (d, J = 2.5, 1H), 6.91 (dd, J = 8.5, 2.5, 1H), 5.25 (d, J = 4.5, 1H), 3.83 (s, 3H), 3.81 (s, 3H), 3.79 (s, 3H), 3.78 (s, 3H), 2.86 (m, 1H), 2.38 (m, 3H), 1.75−1.86 (m, 2H); ^{13}C NMR ($CDCl_3$) 159.4, 151.7, 150.8, 143.2, 141.3, 135.4, 130.3, 129.0, 125.0, 112.5, 108.7 (br), 107.9, 70.7 (br), 61.6, 61.0, 55.1, 55.4, 41.5, 21.5; MS m/e 330 (M^+); HRMS for $C_{19}H_{22}O_5$ (M^+) calcd 330.1467, found 330.1481.

(5*S*)-5-Azido-6,7-dihydro-3,9,10,11-tetramethoxy-5*H*-dibenzo[*a*,*c*]cycloheptene (20a). To a suspension of alcohol **19a** (0.0583 g, 0.176 mmol), $Zn(N_3)_2$-(pyridine)$_2$ (0.0810 g, 0.264 mmol), and triphenylphosphine (0.185 g, 0.704 mmol) in toluene (2 mL) was added diisopropyl azodicarboxylate (0.14 mL, 0.70 mmol) in a dropwise fashion. After stirring for 4 h, the mixture was filtered through a plug of silica gel, and concentrated under reduced pressure. Preparative TLC (4:1 hexanes/Et_2O) afforded **20a** contaminated by 10% of alkene **17a** (0.0440 g, 64% of **20a**, 7% of **17a**). Repeated preparative TLC (10:1 hexanes/EtOAc) afforded pure **20a** as a viscous oil, $[\alpha]^{22}_D$ 110° (*c* 0.0100) (93% ee material as evaluated on **2**); IR (KBr) ν_{max} 2936, 2013 cm^{-1}; ^{1}H NMR (major atropisomer, 91%) δ 7.42 (d, J = 8.5, 1H), 7.13 (d, J = 2.5, 1H), 6.92 (dd, J = 8.5, 2.5, 1H), 6.60 (s, 1H), 4.44 (dd, J = 11.5, 7.0, 1H), 3.92 (s, 6H), 3.90 (s, 3H), 3.65 (s, 3H), 2.45−2.60 (m, 2H), 2.33 (m, 1H), 2.00 (m, 1H); resonances from the minor atropisomer (9%) could be observed at 7.42 (d, J = 8.8, 1H), 6.97 (dd, J = 8.8, 2.6, 1H), 6.81 (d, J = 2.6, 1H), 6.58 (s, 1H), 4.71 (d, J = 6.8, 1H), 3.93 (s, 3H), 3.88 (s, 3H), 3.62 (s, 3H); ^{13}C NMR 159.0, 152.6, 150.9, 141.2, 138.6, 134.7, 131.7, 126.0, 124.3, 112.5, 109.2, 107.6, 61.1, 61.0, 60.8, 56.0, 55.3, 38.9, 30.4; MS m/e 355 (M^+); HRMS m/e for $C_{19}H_{21}N_3O_4$ calcd 355.1532 (M^+), found 355.1541.

(*S*)-*N*-Acetyl-*O*-methyl-colchicinol (NSC 51046) (2). To a solution containing azide **20a** with 10% alkene **17a** (0.0186 g, 48.1 μmol **20a**) in 100% EtOH saturated with H_2 was added Lindlar catalyst (0.0068 g). The mixture was stirred under H_2 for 20 h, filtered through Celite, and concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2 and cooled to 0 °C, and acetic anhydride (0.2 mL) and pyridine (0.2 mL) were added. The mixture was allowed to stir 12 h with gradual warming to room temperature. Concentration under reduced pressure, followed by preparative TLC (19:1 CH_2Cl_2/MeOH) afforded **2** (0.0157 g, 88% yield), which was spectroscopically identical with authentic material,[5,11] 93% ee (Chiralcel OD-H, 10% *i*-PrOH/hexanes). A single recrystallization afforded **2** of >99% ee: mp 203−4 °C (CH_2Cl_2/hexanes); lit.[4b] 204−5 °C (CH_2Cl_2/hexanes); $[\alpha]^{24}_D$ −64° (*c* 0.0056, $CHCl_3$); lit.[4b] $[\alpha]^{20}_D$ −65° (*c* 0.46, $CHCl_3$); lit.[4a] $[\alpha]^{20}_D$ −64.9° (*c* 1.03%, $CHCl_3$); ^{1}H NMR (DMSO-d_6) δ 8.34 (d, J = 8.6, 1H), 7.25 (d, J = 8.4, 1H), 6.91 (d, J = 2.6, 1H), 6.87 (dd, J = 8.4, 2.6, 1H), 6.76 (s, 1H), 4.52 (m, 1H), 3.83 (s, 3H), 3.79 (s, 3H), 3.78 (s, 3H), 3.47 (s, 3H), 2.48 (m, 1H, obscured), 2.15 (m, 1H), 2.07 (m, 1H), 1.88 (s, 3H), 1.85 (m, 1H); ^{13}C NMR (DMSO-d_6) 168.2, 158.3, 152.1, 150.3, 141.8, 140.5, 134.7, 130.5, 126.1, 124.3, 110.7, 109.4, 108.1, 60.50, 60.45, 55.8, 54.9, 48.1, 30.1, 22.6.

(5*S*)-5-Azido-6,7-dihydro-3,8,9,10-tetramethoxy-5*H*-dibenzo-[*a*,*c*]cycloheptene (20e). To a suspension of **19e** (0.0346 g, 0.105 mmol), $Zn(N_3)_2$-(pyridine)$_2$ (0.0484 g, 0.157 mmol), and triphenylphosphine (0.1099 g, 0.419 mmol) in toluene (3 mL) was added diisopropyl azodicarboxylate (81 μL, 0.42 mmol) in a dropwise fashion. After stirring for 4 h, the mixture was filtered through a plug of silica gel and concentrated under reduced pressure. Preparative TLC (4:1 hexanes/EtOAc) afforded **20e** (0.0286 g, 77% yield) as a viscous oil: $[\alpha]^{24}_D$ −126° (*c* 0.663, $CHCl_3$) (95% ee material as evaluated on **21**); IR (KBr) ν_{max} 2937, 2095 cm^{-1}; ^{1}H NMR δ 7.31 (d, J = 8.4, 1H), 7.12 (br s, 1H), 6.94 (dd, J = 8.4, 2.7, 1H), 6.70 (s, 1H), 4.46 (m, 1H), 3.94 (s, 3H), 3.91 (s, 3H), 3.905 (s, 3H), 3.900 (s, 3H), 3.01 (br m, 1H), 2.55 (m, 1H), 2.06 (m, 2H); ^{13}C NMR (DMSO-d_6) 158.8, 151.6, 150.3, 141.0, 138.0, 134.7, 130.7, 129.9, 123.4, 112.8, 110.6 (br), 108.2, 61.4, 61.2, 60.4, 55.8, 55.2, 38.1, 21.3; MS m/e 355 (M^+); HRMS for $C_{19}H_{21}N_3O_4$ (M^+) calcd 355.1532, found 355.1537.

(5*S*)-5-Acetamido-6,7-dihydro-3,8,9,10-tetramethoxy-5*H*-dibenzo-[*a*,*c*]cycloheptene (21). To a solution containing azide **20e** with

(0.0286 g, 80.5 μmol) in 100% EtOH (10 mL) saturated with H_2 was added Lindlar catalyst (0.0109 g). The mixture was stirred under H_2 for 20 h, filtered through Celite, and concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2 (10 mL) and cooled to 0 °C, and acetic anhydride (0.2 mL) and pyridine (0.2 mL) were added. The mixture was allowed to stir for 12 h with gradual warming to room temperature. Concentration under reduced pressure, followed by preparative TLC (19:1 CH_2Cl_2/MeOH) afforded **21** (0.0237 g, 79% yield) in 95% ee (Chiralcel OD-H, 10% *i*-PrOH/hexanes). A single recrystallization afforded **21** of >99% ee, as colorless crystals: mp 186−188 °C (Et_2O/hexanes); $[\alpha]^{22}_D$ −52.4° (*c* 0.783, $CHCl_3$); IR (KBr) ν_{max} 3288 br, 2936, 1664 cm^{-1}; ^1H NMR (DMSO-d_6) 8.41 (d, J = 8.4, 1H), 7.32 (d, J = 8.1, 1H), 6.88−6.94 (m, 2H), 6.79 (s, 1H), 4.51 (m, 1H), 3.85 (s, 3H), 3.79 (s, 6H), 3.78 (s, 3H), 2.91 (dd, J = 13.2, 6.0, 1H), 2.16 (m, 1H), 1.95 (m, 1H), 1.89 (s, 3H), 1.78 (m, 1H); ^{13}C NMR (DMSO-d_6) 168.6, 158.9, 151.6, 150.4, 141.4, 140.9, 135.3, 130.9, 129.3, 123.7, 111.3, 110.1, 108.3, 61.5, 60.4, 55.9, 55.1, 48.4, 22.7, 21.9; (a resonance at 40.0 in $CDCl_3$ is obscured in DMSO-d_6); MS *m*/*e* 371 (M^+); HRMS for $C_{21}H_{25}NO_5$ (M^+) calcd 371.1733, found 371.1740.

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Supporting Information Available: ^1H and ^{13}C spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.