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Efficient Activation of 2-Iminomethylpyridine/Cobalt-Based Alkyne [2+2+2] Cycloaddition Catalyst by Addition of a Silver Salt

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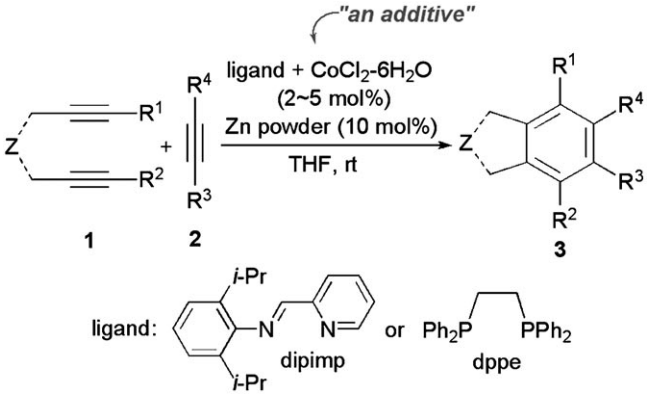
Abstract: The addition of silver triflate (AgOTf) or silver hexafluoroantimonate ($AgSbF_6$) significantly increased the activity of the 2-(arylimino)methylpyridine/cobalt(II) chloride hexahydrate ($CoCl_2 \cdot 6H_2O$)/zinc catalyst in alkyne cyclotrimerizations thereby accelerating the reaction and enabling the use of unactivated, simple internal alkynes as the monoyne substrate: The rate of reaction was found to be highly dependent on the nature of the counter anion (X^-) and the ligand (L) in the postulated cationic cobalt(I) complex $[LCo(I)]^+X^-$.

Keywords: catalytic cycloaddition; cobalt; iminomethylpyridine; silver triflate; substituted benzenes

Introduction

Research in developing the catalytic [2+2+2] cycloaddition of unsaturated compounds, such as alkyne cyclotrimerization and alkyne/nitrile cycloaddition,[1] has demonstrated the importance of cationic metal species as a catalyst. For example, Tanaka and coworkers have reported cationic Rh(I)/diphosphine catalysts for [2+2+2] cycloaddition of alkynes, alkynes/nitriles and alkynes/isocycnates under mild reaction conditions, whereas, use of neutral Rh(I) complexes did not exhibit any catalytic activity.[2] Kirchner et al. documented cationic Ru complexes for [2+2+2] and [2+2+1] cycloaddition reactions of alkynes.[3] Hilt et al. reported the diphosphine, 1,2-diimine or 1,2-disulfide/CoX_2/Zn-catalyzed intermolecular cycloaddition of alkynes where cationic Co species generated by the addition of ZnI_2 have been proposed as an active catalyst.[4] Furthermore, there are many examples of cationic species as catalysts for [2+2] and [4+2] cycloaddition reactions.[5]

We have recently developed a highly practical and user-friendly catalyst for alkyne cycloaddition, which could be generated on demand from the stable, inexpensive cobalt salt and easily available ligand 2-(2,6-diisopropylphenyl)iminomethylpyridine (dipimp) or 1,2-bis(diphenylphosphino)ethane (dppe) by *in situ* reduction with commercial zinc powder (Scheme 1).[6a]



Scheme 1. Ligand/$CoCl_2 \cdot 6H_2O$/Zn-catalyzed reaction of alkynes to benzene derivatives.

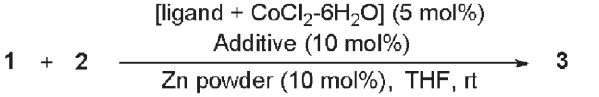
The catalysis cycloadds a variety of alkynes intra- and intermolecularly to the corresponding substituted benzenes; however, the production of sterically demanding benzene derivatives sometimes requires a long reaction time and unactivated simple internal alkynes such as 4-octyne cannot be utilized as the substrate **2**. Inspired by the results described above, we assumed that by addition of a suitable additive, an electron-deficient cationic Co(I) species could be generated, which may be more active and could overcome the aforementioned drawbacks to make the method more general. As a result, we found that a certain silver salt exhibited a unique additive effect specific to the dipimp-Co system.

Results and Discussion

First, the effect of an additive on the reaction of diynes **1a** and **1b** with alkynes **2a** and **2b** was investigated and the results are summarized in Table 1, where the time for consumption of **1** was confirmed by TLC analysis of the reaction mixture.

As revealed from entries 1–9, addition of AgOTf or $AgSbF_6$ significantly increased the activity of the catalyst: The reaction of **1a** and phenylacetylene (**2a**) by dipimp/$CoCl_2{\cdot}6H_2O$/Zn with AgOTf or $AgSbF_6$ proceeded smoothly at room temperature and was complete within 0.5 h to give substituted benzene **3aa** quantitatively (entries 4 and 7), while the reaction without an additive required 4 h (entry 1). Similar results were observed in the reactions with use of anhydrous $CoCl_2$ instead of $CoCl_2{\cdot}6H_2O$ (entries 2 and 5). Addition of AgOTf (4 mol%) to a reduced amount of the catalyst (dipimp/$CoCl_2{\cdot}6H_2O$/Zn = 2/2/10 mol%) was also effective (entry 6). Other silver salts such as $AgBF_4$ and $AgPF_6$ were not effective and, in fact, slowed down the reaction rate (entries 8 and 9). Addition of ZnI_2[4] to a dipimip/$CoCl_2{\cdot}6H_2O$/Zn system resulted in no effect (entry 3).

Table 1. Effect of an additive on the reaction of diyne **1a** and alkyne **2**.[a]



Entry	1	2 (equivs.)	Ligand	Additive	Time	Yield[b]
1	**1a**	**2a** (1.3)	dipimp	-	4 h	98%
2[c]	**1a**	**2a** (1.3)	dipimp	-	4 h	96%
3	**1a**	**2a** (1.3)	dipimp	ZnI_2	4 h	87%
4	**1a**	**2a** (1.3)	dipimp	AgOTf	0.5 h	97% (92%)[d]
5[c]	**1a**	**2a** (1.3)	dipimp	AgOTf	1 h	95%
6[e]	**1a**	**2a** (1.3)	dipimp	AgOTf	1.5 h	94%
7	**1a**	**2a** (1.3)	dipimp	$AgSbF_6$	0.5 h	94%
8	**1a**	**2a** (1.3)	dipimp	$AgBF_4$	12 h	96%
9	**1a**	**2a** (1.3)	dipimp	$AgPF_6$	8 h	98%
10	**1a**	**2a** (1.3)	dppe	-	24 h	89%
11	**1a**	**2a** (1.3)	dppe	AgOTf	24 h	91%
12[f]	**1a**	**2b** (2)	dipimp	-	3 h	Trace[g]
13[f]	**1a**	**2b** (2)	dipimp	AgOTf	3 h	82%
14	**1b**	**2b** (2)	dipimp	-	96 h	Trace[h]
15	**1b**	**2b** (2)	dipimp	AgOTf	3 h	95% (72%)[d]
16	**1b**	**2b** (2)	dppe	-	96 h	Trace[h]
17	**1b**	**2b** (2)	dppe	AgOTf	96 h	Trace[h]

[a] *Reaction conditions:* **1** (0.5 mmol), **2** (0.65 or 1.0 mmol), dipimp (0.03 mmol), $CoCl_2{\cdot}6H_2O$ (0.025 mmol), additive (0 or 10 mol%), Zn powder (0.05 mmol), THF (2.0 mL).
[b] Unless otherwise indicated, ^1H NMR yield confirmed by using an internal standard.
[c] Anhydrous $CoCl_2$ was used instead of $CoCl_2{\cdot}6H_2O$.
[d] Isolated yield.
[e] Dipimp (2 mol%), $CoCl_2{\cdot}6H_2O$ (2 mol%) and AgOTf (4 mol%) were used.
[f] A THF solution of **1a** was added dropwise over 3 h to a mixture of **2b**, dipimp, $CoCl_2{\cdot}6H_2O$, AgOTf and Zn in THF.
[g] A dimer and a trimer of **1a** were formed.
[h] Substrates were recovered quantitatively.

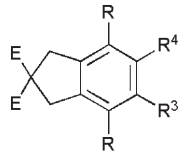
In general, the reaction of a diyne consisting of terminal alkynes with an unactivated aliphatic internal alkyne is difficult because self-dimerization and/or -trimerization of the diyne proceeds predominantly. The cyclotrimerization of terminally unsubstituted diyne and 4 equivs. of 3-hexyne with an Ru catalyst gave only 13% of the desired product.[7] Very recently, Takeuchi and co-workers recommended a slow addition technique for such reactions to minimize the self-addition of the diyne: thus, they employed an [Ir(cod)Cl]$_2$/dppe catalyst for the cyclotrimerization using the procedure of slow addition (7 h) of diyne to the mixture of monoyne (3 equivs.) and catalyst to provide the corresponding benzene derivative in good yield.[8] In our catalytic system, slow addition of **1a** (3 h) to the reaction mixture with **2b** (2 equivs.) in the absence of AgOTf led only to self-dimerization and -trimerization of **1a** (entry 12) while, in striking contrast, under the same reaction conditions, addition of AgOTf enabled the production of **3ab** in 82% yield (entry 13).

Meanwhile, the reaction of **1b** consisting of internal alkynes with an unactivated internal alkyne **2b** in the presence of the dipimp/$CoCl_2{\cdot}6H_2O$/AgOTf/Zn reagent the catalyzed cycloaddition proceeded smoothly to give **3bb** in 72% isolated yield under the standard reaction conditions, while the reaction without AgOTf did not yield the corresponding product at all after 96 h (entries 14 and 15). It is noteworthy that the effect of AgOTf as an additive was specific to the dipimp/$CoCl_2{\cdot}6H_2O$/Zn catalyst. Although the reaction with the use of dppe as a ligand instead of dipimp gave **3aa**, in the absence or presence of AgOTf, the reaction rate was not affected by inclusion of the additive (entries 10 and 11); in addition, the reaction with dppe did not yield **3bb** to any appreciable extent (entries 16 and 17).

Similarly, an addition of AgOTf to a dppe/$CoCl_2{\cdot}6H_2O$/Zn reagent system, which has been proved to be an efficient catalyst for the cycloaddition of diynes and nitriles to the corresponding substituted pyridines,[6b] did not have any advantageous effect on the pyridine formation.

Table 2 summarizes the results of the reaction of other diynes (1.0 equiv.) and alkynes (1.0 equiv.) catalyzed by dipimp/$CoCl_2{\cdot}6H_2O$/Zn in the presence or absence of AgTOf. The data clearly reveal an acceler-

Table 2. Examples for effect of AgOTf as an additive for synthesis of hexa-substituted benzenes.[a]



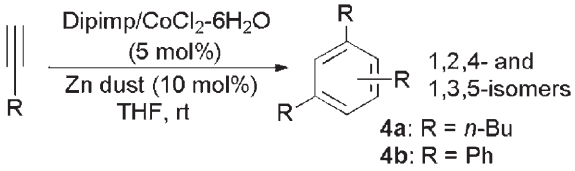
Entry		R	R^3	R^4	AgOTf[b]	Time	Yield[c]
1	**3bc**	*n*-Bu	*n*-Bu	C≡C-*n*-Bu	–	96 h	Trace
2	**3bc**	*n*-Bu	*n*-Bu	C≡C-*n*-Bu	+	2 h	62%
3	**3bd**	*n*-Bu	Et	$(CH_2)_2OH$	–	48 h	76%
4	**3bd**	*n*-Bu	Et	$(CH_2)_2OH$	+	3 h	82%
5	**3ce**	$SiMe_3$	*n*-Bu	CH_2OH	–	96 h	48%
6	**3ce**	$SiMe_3$	*n*-Bu	CH_2OH	+	2.5 h	91%
7	**3df**	Ph	*n*-Bu	CH_2OAc	–	48 h	48%
8	**3df**	Ph	*n*-Bu	CH_2OAc	+	2.5 h	94%

[a] E = CO_2Et. *Reaction conditions (equivs.):* diyne **1** (1.0), alkyne **2** (1.0), dipimp (0.06), $CoCl_2 \cdot 6H_2O$ (0.05), Zn (0.10).
[b] With 10 mol% of AgOTf (+) or without AgOTf (–).
[c] Isolated yield.

ating and/or activating effect of the additive again. The reactions which required several days (entries 3, 5 and 7) or did not proceed (entry 1) with the dipimp/$CoCl_2 \cdot 6H_2O$/Zn reagent were accomplished in a few hours, when they were performed with AgOTf, to provide the corresponding fully substituted benzene in good to excellent yield. Similarly, fully intermolecular reactions were accelerated with AgOTf (Table 3). Interestingly, reactions in the presence of the dipimp/$CoCl_2 \cdot 6H_2O$/Zn reagent and AgOTf produced more 1,3,5-isomer than those without AgOTf.

The catalyst activation by the addition of AgOTf can also be applied to the tandem cycloaddition reactions of tetrayne and monoyne as illustrated in Table 4. The reaction of tetrayne **5** and alkyne **2c** (6 equivs.) catalyzed by the dipimp/$CoCl_2 \cdot 6H_2O$/Zn reagent proceeded in a tandem fashion and gave biaryl **6** in excellent yields, where it was observed again that the reaction in the presence of AgOTf was much faster than that without AgOTf. In contrast, a dppe/$CoCl_2 \cdot 6H_2O$/Zn reagent could not provide **6** even with AgOTf but afforded mono-cyclized compound **7** in good yields. The complementary reactivity of dipimp and dppe ligands in the reaction of **5** and **2c** might be synthetically useful. The known catalysts such as $ClRh(PPh_3)_3$[9] and $X_2Ni(dppe)/Zn$[9] were utilized for the reaction under the appropriate reaction conditions but product **7** instead of **6** was obtained or the reaction gave a complex mixture. These results demonstrate the high reactivity of the dipimp/$CoCl_2 \cdot 6H_2O$/AgOTf/Zn catalyst.

Table 3. Fully intermolecular reactions of 1-alkynes.



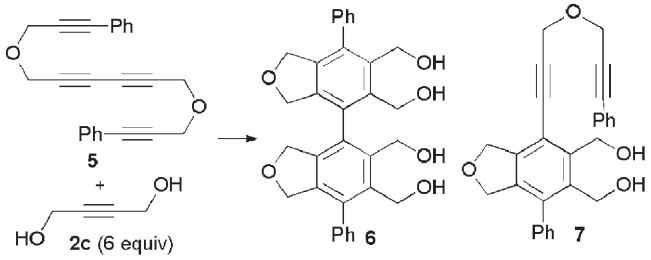
R	AgOTf[a]	Time	1,2,4:1,3,5	Total Yield
n-Bu	–	15 h	63:37	70%
n-Bu	+	0.5 h	23:77	83%
Ph	–	2 h	>99:1	91%
Ph	+	<0.5 h	90:10	94%

[a] (–): in the absence of AgOTf, (+): in the presenece of AgOTf (10 mol%).

The specificity of the additive effect to the dipimp ligand can be explained as follows: it can be assumed that the Co(I) complex such as dipimp-Co(I)Cl (**A**),[6] derived from the reaction of dipimp with $CoCl_2$ and followed by reduction with Zn, may be converted to the corresponding cationic complex of the type **B** by the reaction with AgX. The positive charge present in the complex **B** can be delocalized to the pyridine moiety of the ligand such as in the structure **C** (Scheme 2). The specific additive effect to the dipimp system can be addressed by the contribution of such a resonance stabilization, while such a stabilization is not possible in the case of the dppe-Co complex (**E**). The electron-deficient nature of the cationic complex **B** (or **C**) with a weaker σ-donative dipimp ligand than dppe in complex **E** may facilitate the reaction with unactivated monoalkynes. Such an explanation may be of interest in the research field of alkene oligomerization, polymerization and other synthetic reactions based on 2-iminomethylpyridine-metal complexes as a catalyst.[10]

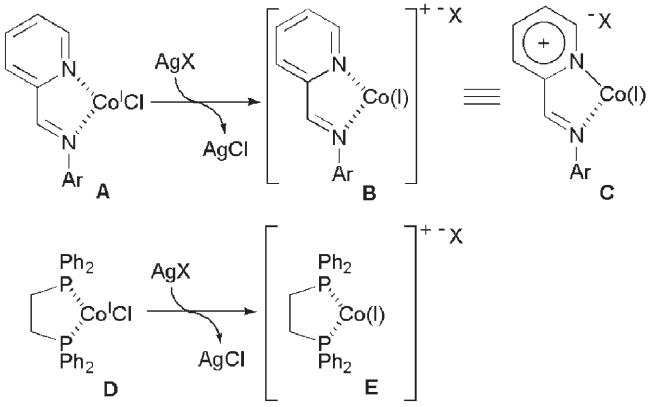
Although there are many examples where a reasonable explanation has been given of counter ion effects on cationic metal complexes and their resulting effect

Table 4. Tandem reaction with various catalyst systems.



Catalyst	Time	Product(s): Yield
dipimp/$CoCl_2 \cdot 6H_2O$/Zn[a]	3 days	**6**: 93 %[b]
dipimp/$CoCl_2 \cdot 6H_2O$/Zn/AgOTf[c]	1.5 h	**6**: 91 %[b]
dppe/$CoCl_2 \cdot 6H_2O$/Zn[d]	3 days	**7**: 72 %[e]
dppe/$CoCl_2 \cdot 6H_2O$/Zn/AgOTf[f]	3 days	**7**: 69 %[e]
$RhCl(PPh_3)_3$[g]	3 days	**7**: 87 %[e]
$RhCl(PPh_3)_3$[h]	2 days	**7**: 42 %[e] + complex mix.
Br_2Ni(dppe)/Zn[i]	4 days	complex mix.

[a] dipimp (0.06)/$CoCl_2 \cdot 6H_2O$ (0.05)/Zn (0.10), THF, room temperature.
[b] ^{1}H NMR yields.
[c] dipimp (0.06)/$CoCl_2 \cdot 6H_2O$ (0.05)/AgOTf (0.10)/Zn (0.010), THF, room temperature.
[d] dppe (0.06)/$CoCl_2 \cdot 6H_2O$ (0.05)/Zn (0.10), THF, room temperature.
[e] Isolated yield.
[f] dppe (0.06)/$CoCl_2 \cdot 6H_2O$(0.05)/AgOTf (0.10)/Zn (0.10), THF, room temperatute.
[g] $RhCl(PPh_3)_3$ (0.05), THF, room temperature.
[h] $RhCl(PPh_3)_3$ (0.05), THF, reflux.
[i] Br_2Ni(dppe) (0.05)/Zn (0.10), THF, room temperature.



Scheme 2. Postulated intermediate.

on reaction efficiency and selectivity,[11] the reason why silver salts other than AgOTf and $AgSbF_6$ were less effective in the present catalysis is unclear at this stage.

Conclusions

We have found a unique additive effect of silver salts in a ligand/$CoCl_2 \cdot 6H_2O$/Zn catalyst system for the [2+2+2] cycloaddition reaction of alkynes. The effect was specific to reactions with the 2-iminomethylpyridine ligand but no effect was observed for the phoshine-based system. The catalysis thus developed introduces a practical and quick route to highly subsituted benzenes from various alkynes. Further investigations of the mechanism as well as work extending this application to other iminopyridine-based metal complexes are underway.

Experimental Section

General Remarks

NMR spectra were recorded in $CDCl_3$ at 600, 500 and 270 MHz for ^{1}H and 150, 125 and 67.5 MHz for ^{13}C, respectively, on JEOL JNM-ECA600, 500 and -EX270 spectrometers. Chemical shifts are reported in parts per million (ppm, δ) relative to Me_4Si (δ = 0.00), residual $CHCl_3$ (δ = 7.26 for ^{1}H NMR), or $CDCl_3$ (δ = 77.0 for ^{13}C NMR). IR spectra were recorded on an FT-IR spectrometer (Shimadzu, IR Prestige-21). All reactions sensitive to oxygen and/or moisture were performed under an argon atmosphere. Dry solvent [tetrahydrofuran (THF)] was purchased from Kanto Chemicals. Other chemicals which are commercially available, unless otherwise indicated, were used as received. Starting materials **1**, **2** and **6** were prepared by conventional reaction procedures. 2-(2,6-Diisopropylphenyl)iminomethylpyridine (dipimp) was prepared according to the reported procedure with a minor modification.[10c] A mixture of 2-pyridinecarboxaldehyde (30.0 mmol), 2,6-diisopropylaniline (30.0 mmol) and anhydrous $MgSO_4$ (*ca.*1–2 g) in dry THF (40 mL) was stirred overnight at room temperature, and then filtered through a pad of Celite. The filtrate was concentrated by rotary evaporation and dried under vacuum for 10 h. The resulting yellow crystalline material, which was analyzed by ^{1}H NMR to confirm the formation of dipimp and complete consumption of the starting materials, was utilized for the Co-catalyzed reactions directly without further purification.

The crystalline ligand was stored in a sealed bottle in the refrigerator. In addition, a catalyst precursor solution of $CoCl_2 \cdot 6H_2O$ and dipimp in THF was prepared and used for the reaction since the solution could be stored in a Schlenk tube under argon for months.

Procedure for the Intermolecular Cyclotrimerization of Diynes 1 and Monoynes 2 to Annulated Benzene Derivatives Catalyzed by a 2-(2,6-Diisopropylphenyl)iminomethylpyridine (dipimp)/$CoCl_2 \cdot 6H_2O$/Zn Reagent in the Presence of an Additive (Tables 1 and 2)

To a stirred mixture of zinc powder (3.5 mg, 0.05 mmol), diyne **1** (0.5 mmol), monoyne **2** (1–2.0 equivs.) and an additive (ZnI_2 or Ag salt; 10 mol %) in THF (0.5 mL) was added

a solution of $CoCl_2 \cdot 6H_2O$ (6 mg, 0.025 mmol) and dipimp (8 mg, 0.03 mmol) in THF (1.5 mL) at room temperature. The reaction progress was checked by TLC analysis. After completion of the reaction, a small portion of Et_2O was added and the mixture was passed through a pad of Celite with ether. The filtrate was concentrated to dryness and the residue was chromatographed on silica gel using hexane/Et_2O (2/1) to give the corresponding annulated benzene **3**. The above-mentioned procedure was also performed without an additive.

Diethyl 5-phenyl-1*H*-indene-2,2(3*H*)-dicarboxylate (3aa): ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.55 (d, 2H, J = 7.2 Hz, Ar), 7.43–7.35 (m, 4H, Ar), 7.32 (t, 1H, J = 7.2 Hz, Ar), 7.25 (d, 1H, J = 7.2 Hz, Ar), 4.22 (q, 4H, J = 7.2 Hz, OCH_2CH_3), 3.65 (s, 2H, $ArCH_2C$), 3.63 (s, 2H, $ArCH_2C$), 1.26 (t, 6H, J = 7.2 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 171.6, 141.3, 140.7, 140.3, 139.1, 128.6, 127.1, 127.0, 126.1, 124.4, 123.0, 61.70, 60.53, 40.43, 40.27, 14.11. Spectroscopic data were identical with those reported.[6]

Diethyl 4,7-dibutyl-5,6-dipropyl-1*H*-indene-2,2(3*H*)-dicarboxylate (3bb): ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 4.20 (q, 4H, J = 7.2 Hz, OCH_2CH_3), 3.52 (s, 4H, $ArCH_2C$), 2.51–2.47 (m, 8H, $ArCH_2$), 1.47–1.42 (m, 12H, methylene), 1.25 (t, 6H, J = 7.2 Hz, OCH_2CH_3), 1.03 (t, 6H, J = 7.4 Hz, $CH_2CH_2CH_3$), 0.96 (t, 6H, J = 6.8 Hz, CH_2 $CH_2CH_2CH_3$); ^{13}C NMR ($CDCl_3$, 67.5 MHz): δ = 171.7, 137.4, 136.0, 134.0, 61.48, 59.70, 39.59, 32.59, 31.61, 30.36, 25.12, 23.36, 15.03, 14.03, 13.93; IR (neat): ν = 2960, 2931, 2872, 1747, 1255, 1097, 1066, 800 cm^{-1}; anal. calcd. for $C_{29}H_{46}O_4$ (458.67): C 75.94, H 10.11; found: C 76.05, H 10.09.

Diethyl 4,5,7-tributyl-6-(hex-1-ynyl)-1*H*-indene-2,2(3*H*)-dicarboxylate (3bc): ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 4.20 (q, 4H, J = 7.1 Hz, OCH_2CH_3), 3.52 (s, 2H, $ArCH_2C$), 3.51 (s, 2H, $ArCH_2C$), 2.74 (t, 2H, J = 8.0 Hz, $ArCH_2$), 2.68 (t, 2H, J = 8.0 Hz, $ArCH_2$), 2.50 (t, 2H, J = 7.9 Hz, $ArCH_2$), 2.46 (t, 2H, J = 7.1 Hz, $C{\equiv}CCH_2$), 1.60–1.38 (m, 16H, methylene), 1.25 (t, 6H, J = 7.1 Hz, OCH_2CH_3), 0.96–0.93 (m, 12H, $CH_2CH_2CH_2CH_3$); ^{13}C NMR ($CDCl_3$, 67.5 MHz): δ = 171.5, 141.7, 137.96, 137.91, 135.3, 133.4, 122.1, 95.90, 78.41, 61.55, 59.82, 39.68, 39.26, 33.03, 32.52, 32.07, 31.78, 31.08, 30.08, 23.34, 23.18, 23.07, 21.97, 19.32, 14.02, 13.93, 13.60 (three carbons were not differentiated); IR (neat): ν = 2956, 2929, 2872, 2858, 1742, 1463, 1246, 1188, 1159, 1068, 1014, 862 cm^{-1}; anal. calcd. for $C_{33}H_{50}O_4$ (510.75): C 77.60, H 9.87; found: C 77.61, H 9.98.

Diethyl 4,7-dibutyl-5-ethyl-6-(2-hydroxyethyl)-1*H*-indene-2,2(3*H*)-dicarboxylate (3bd): mp 91–92 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 4.20 (q, 4H, J = 7.1 Hz, OCH_2CH_3), 3.74 (t, 2H, J = 7.4 Hz, $ArCH_2CH_2OH$), 3.52 (bs, 4H, $ArCH_2C$), 2.92 (t, 2H, J = 7.4 Hz, $ArCH_2CH_2OH$), 2.64 (q, 2H, J = 7.5 Hz, $ArCH_2CH_3$), 2.54 (t, 2H, J = 7.8 Hz, $ArCH_2$), 2.51 (t, 2H, J = 8.0 Hz, $ArCH_2$), 1.46–1.42 (m, 8H, methylene), 1.26 (t, 6H, J = 7.1 Hz, OCH_2CH_3), 1.13 (t, 3H, J = 7.5 Hz, CH_2CH_3), 0.95 (t, 6H, J = 7.6 Hz, $CH_2CH_2CH_2CH_3$); ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 171.9, 139.8, 137.3, 136.5, 135.3, 134.4, 131.9, 63.64, 61.66, 59.75, 39.66, 39.64, 32.71, 32.66, 32.21, 30.54, 30.32, 23.38, 23.36, 22.08, 15.94, 14.05, 14.01, 13.97; IR (KBr): ν = 3433, 2956, 2931, 2870, 1737, 1462, 1249, 1047, 862 cm^{-1}; anal. calcd. for $C_{27}H_{42}O_5$ (446.62): C 72.61, H 9.48; found: C 72.67, H 9.27.

Diethyl 5-butyl-6-(ethanoyloxymethyl)-4,7-diphenyl-1*H*-indene-2,2(3*H*)-dicarboxylate (3df): ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.45–7.35 (m, 6H, Ph), 7.27–7.25 (m, 4H, Ph), 4.91 (s, 2H, CH_2OAc), 4.11 (q, 4H, J = 7.6 Hz, OCH_2CH_3), 3.31 (s, 2H, $ArCH_2C$), 3.27 (s, 2H, $ArCH_2C$), 2.46 (t, 2H, J = 8.1 Hz, $ArCH_2CH_2$), 1.98 (s, 3H, $OCOCH_3$), 1.32–1.29 (m, 2H, $ArCH_2CH_2$), 1.16 (t, 6H, J = 7.6 Hz, OCH_2CH_3), 1.12–1.08 (m, 2H, $ArCH_2CH_2CH_2$), 0.66 (t, 3H, J = 7.8 Hz, $CH_2CH_2CH_3$); ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 171.5, 170.6, 140.4, 139.89, 139.87, 139.82, 139.1, 138.2, 136.5, 129.9, 128.9, 128.38, 128.31, 127.3, 127.0, 61.99, 61.59, 59.66, 40.86, 40.55, 33.87, 29.70, 22.94, 20.94, 13.96, 13.51 (one carbon was not differentiated); IR (neat): ν = 2978, 2958, 2931, 1741, 1730, 1442, 1236, 912 cm^{-1}; anal. calcd. for $C_{34}H_{38}O_6$ (542.66): C 75.25, H 7.06; found: C 75.31, H 6.87.

Diethyl 5-butyl-6-(hydroxymethyl)-4,7-bis(trimethylsilyl)-1*H*-indene-2,2(3*H*)-dicarboxylate (3ce): ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 4.72 (d, 2H, J = 4.6 Hz, $ArCH_2OH$), 4.19 (q, 4H, J = 7.0 Hz, OCH_2CH_3), 3.58 (s, 2H, $ArCH_2C$), 3.57 (s, 2H, $ArCH_2C$), 2.84 (t, 2H, J = 8.0 Hz, $ArCH_2CH_2$), 1.45–1.41 (m, 4H, methylene), 1.24 (t, 6H, J = 7.0 Hz, OCH_2CH_3), 0.94 (t, 3H, J = 7.6 Hz, $CH_2CH_2CH_2CH_3$), 0.43 (s, 9H, $SiMe_3$), 0.41 (s, 9H, $SiMe_3$); ^{13}C NMR ($CDCl_3$, 150 MHz): δ = 171.6, 146.9, 145.8, 143.5, 142.1, 137.7, 136.3, 61.72, 61.67, 60.54, 42.03, 41.88, 36.69, 32.57, 23.15, 14.20, 14.05, 2.97, 2.74; IR (neat): ν = 3531, 2980, 2931, 2902, 1732, 1251, 1070, 1049, 852 cm^{-1}; anal. calcd. for $C_{26}H_{44}O_5Si_2$ (492.80): C 63.37, H 9.00; found: C 63.07, H 8.67.

Procedure with the Slow Addition of Diyne (Table 1, enrty 13)

To a stirred mixture of zinc powder (3.5 mg, 0.05 mmol), 4-octyne (1 mmol) and AgOTf (0.05 mmol) was added a solution of $CoCl_2 \cdot 6H_2O$ (6 mg, 0.025 mmol) and dipimp (8 mg, 0.03 mmol) in THF (0.5 mL). A THF solution (1.5 mL) of **1a** (118 mg, 0.5 mmol) was added dropwise to the reaction mixture over 3 h by a syring pump with stirring at room temperature. After complete addition of diyne **1a**, a small portion of Et_2O was added and the mixture was passed through a pad of Celite with ether. The filtrate was concentrated to dryness and the residue was chromatographed on silica gel using hexane/Et_2O (2/1) to give **3ab** as a pale yellow liquid.

Diethyl 5,6-dipropyl-1*H*-indene-2,2(3*H*)-dicarboxylate (3ab): ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 6.97 (bs, 2H, Ar), 4.19 (q, 4H, J = 7.5 Hz, OCH_2CH_3), 3.54 (s, 4H, $ArCH_2C$), 2.53 (t, 4H, J = 8.0 Hz, $ArCH_2CH_2$), 1.57–1.55 (m, 4H, $CH_2CH_2CH_3$), 1.25 (t, 6H, J = 7.5 Hz, OCH_2CH_3), 0.98 (t, 6H, J = 7.8 Hz, $CH_2CH_2CH_3$); ^{13}C NMR ($CDCl_3$, 67.5 MHz): δ = 171.6, 138.9, 137.2, 124.5, 61.5, 60.4, 40.2, 34.8, 24.5, 14.3, 14.0; IR (neat): ν = 2984, 2937, 2906, 1737, 1251, 1079, 1045, 843 cm^{-1}; anal. calcd. for $C_{21}H_{30}O_4$ (346.46): C 72.80, H 8.73; found: C 72.91, H 8.78.

Procedure for the Intermolecular Cyclotrimerization of 1-Alkynes to Tri-Substituted Benzenes Catalyzed by a 2-(2,6-Diisopropylphenyl)iminomethylpyridine (dipimp)/$CoCl_2.6H_2O$/Zn Reagent in the Presence of AgOTf as an Additive (Table 3)

To a stirred mixture of zinc powder (3.5 mg, 0.05 mmol), 1-alkyne **2** (0.5 mmol) and AgOTf (12.8 mg, 0.05 mmol) in THF (0.5 mL) was added a solution of $CoCl_2 \cdot 6H_2O$ (6 mg,

0.025 mmol) and dipimp (8 mg, 0.03 mmol) in THF (1.5 mL) at room temperature. The dark brown reaction mixture was stirred at ambient temperature and the consumption of **2** was checked by TLC analysis. After completion of the reaction, a small portion of Et_2O was added and the mixture was passed through a pad of Celite with ether. The filtrate was concentrated under vacuum and the crude material was purified by column chromatography on silica gel using hexane/Et_2O (4/1) to afford the corresponding benzene derivatives. The above-mentioned procedure was also performed in the absence of an additive.

Tri-*n*-butylbenzene (4a): Selected peaks for the 1,2,4-isomer: ^{1}H NMR ($CDCl_3$, 600 MHz): $\delta = 7.04$ (d, 1H, $J = 7.2$ Hz, Ar), 6.94 (s, 1H, Ar), 6.93 (d, 1H, Ar); ^{13}C NMR ($CDCl_3$, 150 MHz): $\delta = 140.3$, 140.1, 137.6, 129.2, 128.9, 125.6. Identified spectroscopically by comparison with the literature data.[3,4] Selected peaks for the 1,3,5-isomer: ^{1}H NMR ($CDCl_3$, 500 MHz): $\delta = 6.81$ (s, 3H, Ar); ^{13}C NMR ($CDCl_3$, 125 MHz): $\delta = 142.7$, 125.8, 35.68, 33.78, 22.53, 14.03. Identified spectroscopically by comparison with the literature data.[4b,12] The regioisomeric ratio was determined by ^{1}H NMR analysis using signals at $\delta = 7.04$, 6.94, 6.93, 6.81 ppm.

Triphenylbenzene (4b): Identification and regioisomeric ratio of 1,2,4- and 1,3,5-triphenylbezene were carefully determined by comparison of literature data[12] as well as by checking the ^{1}H NMR spectra of a commercially available authentic sample (1,3,5-triphenylbenzene) using the signal at $\delta = 7.78$ ppm.

Procedure for the Cycloaddition Reactions of Tetrayne 5 and 2-Butyne-1,4-diol to 6 and 7 (Table 4)

To a stirred mixture of zinc powder (3.5 mg, 0.05 mmol, 10 mol%), tetrayne **5** (169 mg, 0.5 mmol) and 2-butyne-1,4-diol (258.3 mg, 3 mmol, 6 equivs.) and AgOTf (12.8 mg, 0.05 mmol, 10 mol%) in THF (0.5 mL) was added a solution of $CoCl_2 \cdot 6H_2O$ (5 mol%) and dipimp or dppe (6 mol%) in THF (1.5 mL) at room temperature. The reaction progress was checked by TLC analysis. A small portion of EtOAc was added and the mixture was passed through a pad of Celite with EtOAc. The solvent was removed under vacuum and the residue was chromatographed on silica gel using hexane/EtOAc (2/1) to afford **6** or **7**.

The compound **6** was contained trace amount of starting diol which it was not possible to separate by column chromatography. Therefore, **6** was converted to the corresponding fully acetylated compound by conventional methods (Ac_2O/Et_3N/cat. DMAP/CH_2Cl_2) and characterized by NMR, IR spectroscopy as well as elemental analysis.

The above-mentioned method for metal-catalyzed cycloaddition reaction was also employed in the presence of Br_2Ni(dppe)/Zn reagent as well as $ClRh(PPh_3)_3$ as a catalyst under the reaction conditions indicated in Table 4.

(7,7′-Diphenyl-1,1′,3,3′-tetrahydro-4,4′-biisobenzofuran-5,5′,6,6′-tetrayl)tetramethanol (6): ^{1}H NMR ($CDCl_3$, 500 MHz): $\delta = 7.43$–7.36 (m, 8H, Ph), 7.23–7.20 (m, 2H, Ph), 5.40 (bs, 2H, ArCH_2O), 5.04 (d, 2H, $J = 8.2$ Hz, ArCH_2O), 4.87 (t, 4H, ArCH_2O), 4.72–4.63 (m, 4H, ArCH_2OH), 5.42 (d, 2H, $J = 8.2$ Hz, ArCH_2OH), 4.21 (d, 2H, $J = 8.2$ Hz, ArCH_2OH); ^{13}C NMR ($CDCl_3$, 125 MHz): $\delta = 138.6$, 138.2, 138.0, 137.4, 136.9, 131.3, 128.9, 128.7, 128.5, 127.8, 74.40, 74.15, 59.85, 58.99; IR (KBr): $\nu = 3402$, 2926, 2854, 1055, 1012, 904 cm^{-1} (measured using a mixture of **6** and 2-butyne-1,4-diol).

(7,7′-Diphenyl-1,1′,3,3′-tetrahydro-4,4′-biisobenzofuran-5,5′,6,6′-tetrayl)tetrakis(methylene) tetraethanoate (tetraacetate of 6): mp 85–86 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): $\delta =$ 7.45–7.42 (m, 6H, Ph), 7.32–7.29 (m, 4H, Ph), 5.40 (bs, 2H, ArCH_2O), 5.01–4.80 (m, 14H, ArCH_2O), 2.00 (s, 6H, $OCOCH_3$), 1.99 (s, 6H, $OCOCH_3$); ^{13}C NMR ($CDCl_3$, 150 MHz): $\delta = 170.3$, 170.2, 140.0, 139.1, 138.5, 137.4, 133.3, 133.0, 132.1, 128.69, 128.61, 128.1, 74.22, 74.14, 61.14, 60.88, 20.82, 20.69; IR (KBr): $\nu = 2960$, 2922, 2852, 1741, 1232, 1026, 962, 908 cm^{-1}; anal. calcd. for $C_{40}H_{38}O_{10}$ (678.72): C 70.78, H 5.64; found C 70.89, H 5.69.

{4-Phenyl-7-[3-(3-phenylprop-2-ynyloxy)prop-1-ynyl]-1,3-dihydroisobenzofuran-5,6-diyl}dimethanol (7): mp 68–69 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): $\delta = 7.47$–7.35 (m, 6H, Ph), 7.33–7.30 (m, 3H, Ph), 7.28–7.27 (m, 1H, Ph), 5.20 (s, 2H, ArCH_2O), 5.07 (s, 2H, ArCH_2O), 4.90 (s, 2H, ArCH_2OH), 4.59 (s, 2H, ArCH_2OH), 4.55 (bs, 4H, C≡CCH_2OCH_2C≡C); ^{13}C NMR ($CDCl_3$, 150 MHz): $\delta = 141.9$, 141.3, 138.6, 137.8, 137.7, 137.4, 131.8, 128.67, 128.62, 128.3, 127.9, 122.3, 115.8, 92.23, 87.15, 83.99, 82.04, 74.57, 74.47, 61.37, 59.75, 57.53, 57.36 (one carbon was not differentiated); IR (KBr): $\nu = 3419$, 3055, 2933, 2848, 1072, 1014, 902, 756 cm^{-1}; anal. calcd. for $C_{28}H_{24}O_4$ (424.49): C 79.22, H 5.70; found: C 79.02, H 5.85.

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