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Transition Metal-Catalyzed [4 + 2 + 2] Cycloadditions of Bicyclo[2.2.1]hepta-2,5-dienes (Norbornadienes) and Bicyclo[2.2.2]octa-2,5-dienes[1]

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The transition-metal-catalyzed [4 + 2 + 2] cycloadditions of norbornadienes, bicyclo[2.2.2]octa-2,5-diene, and benzobarrelene with 1,3-butadienes proceed in excellent yields using cobalt-based catalytic systems. Two key distinctions between these [4 + 2 + 2] cycloadditions and the corresponding transition-metal-catalyzed [2 + 2 +2] reactions of norbornadiene are the requirement of a bimetal catalytic system with a bisphosphine ligand for the former and exclusive regioselectivity in the [4 + 2 + 2] reaction of 2-substituted norbornadienes to produce 1-substituted adducts. These distinctions may indicate two distinct mechanisms for the [4 + 2 + 2] and [2 + 2 + 2] reactions.

Fused carbobicyclic ring systems form the core of numerous natural products, many of which exhibit important biological activities. The synthesis of these bicyclic systems has long been explored by innumerable strategies, with transition-metal-promoted cycloaddition chemistry playing a frequent and prominent role.[2] We have been interested in the synthesis of cis-fused bicyclo[5.3.0]decanes from a [4 + 2 + 2] cycloaddition−fragmentation sequence beginning with a norbornadiene and butadiene as illustrated in Scheme 1. To construct more functionalized bicyclo[5.3.0]decane skeleta embodied in potential synthetic targets such as guaiane, pseudoguaiane, and other sesquiterpenes[3] (Figure 1), we have explored the scope and limitations of the transition-metal-catalyzed [4 + 2 + 2] cycloadditions of norbornadienes and 1,3-butadienes[4] and expanded this work to several bicyclo[2.2.2]octa-2,5-dienes.

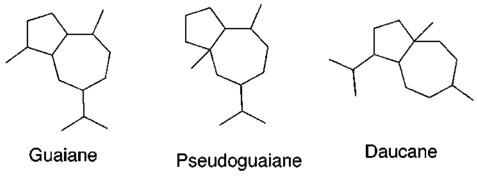
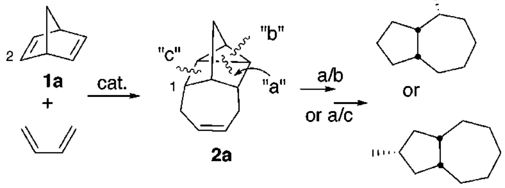


Figure 1. Examples of sesquiterpenoid skeleta embodying the bicyclo[5.3.0]decane ring system.

Scheme 1



In earlier communications,[5] we reported the optimization of the catalytic systems for the [4 + 2 + 2] cycloadditons of norbornadiene, the tolerance of the reaction to different substituents on the norbornadiene, and the opening of the [4 + 2 + 2] cycloadducts **2** to bicyclo[5.3.0]-decanes adapting either Nickon's acid-catalyzed deltacyclane opening[5a,6] or the Zeise's dimer promoted cyclopropane cleavage.[5b,7] The transition-metal-catalyzed [4 + 2 + 2] cycloadditions of norbornadiene were found to differ from the [2 + 2 + 2] cycloadditions in several

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(1) Taken primarily from the PhD Dissertation of Y. Chen, Boston University, 1999.

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10.1021/jo010268o CCC: $20.00

Table 1. Optimization of the Transition Metal Catalyzed [4 + 2 + 2] Cycloaddition of Norbornadiene (1a) with 1,3-Butadiene To Form Cycloadduct 2a[a]

entry	catalyst[b]	mol %[c]	solvent	time (h)	yield of **2a**[d] (%)
1	$Co(acac)_2$/dppe/Et_2AlCl (1:1.5:10)	1	toluene	4	79
2	$Fe(acac)_3$/dppe/Et_2AlCl (1:1.5:10)	1	toluene	8	79
3	$Ni(acac)_2$/dppe/Et_2AlCl (1:1.5:10)	1	toluene	5	0[e]
4	$Co(acac)_2/PPh_3/Et_2AlCl$ (1:3:10)	1	toluene	22	0[e]
5	$Ni(COD)_2/PPh_3$ (1:2)	5	CH_2Cl_2	18	0[e]
6	$CoI_2/PPh_3/Zn$ (1:2:10)	2.5	CH_2Cl_2/rt	19	0[f]
7	$CoI_2/PPh_3/Zn$ (1:2:10)	2.5	CH_2Cl_2	4	28[e]
8	$CoI_2/PPh_3/Zn$ (1:1:10)	2.5	CH_2Cl_2	4	24[e]
9	$CoI_2/P(O^iPr)_3/Zn$ (1:2:10)	2.5	CH_2Cl_2	4	0[f]
10	CoI_2/dppe/Zn (1:2:10)	2.5	CH_2Cl_2	4	76
11	CoI_2/dppe/Zn (1:1:10)	2.5	CH_2Cl_2	4	85
12	CoI_2/dppe/Zn (1:2:10)	2.5	$ClCH_2CH_2Cl$	4	83
13	CoI_2/dppe/ZnI_2 (1:2:5)	2.5	CH_2Cl_2	4	81
14	CoI_2/dppe (1:2)	2.5	CH_2Cl_2	4	0[e]
15	ZnI_2/dppe (1:2)	2.5	CH_2Cl_2	4	0[e]
16[g]	$Co_2(CO)_8$/dppe or PPh_3 (1:2)	1−10	$ClCH_2CH_2Cl$ or CH_2Cl_2	4−22	0[f]
17	$Co_2(CO)_8$/dppe/ZnI_2 (1:2:5)	2.5	CH_2Cl_2	4	30[e]
18	CoI_2 (5 mol %)/dppe/$NaBH_4/ZnI_2$ (1:1:1:3)[h]	5	CH_2Cl_2/rt	10	80
19	CoI_2 (5 mol %)/dppe/$NaBH_4/ZnCl_2$ (1:1:1:3)[h]	5	CH_2Cl_2/rt	10	90
20	$Co(acac)_2$/dppe/Et_2AlCl (1:1.5:10)	1	toluene/rt	4	0[f]
21	CoI_2/dppe/Zn (1:1:10)	2.5	CH_2Cl_2/rt	4	0[f]
22	CoI_2/dppe/ZnI_2 (1:2:5)	2.5	CH_2Cl_2/rt	4	0[f]

[a] All reactions were run at 60 °C, with the exception of entries 6 and 18−22, which were run at rt, in a sealed tube with 1.5 equiv of 1,3-butadiene relative to **1a**, [**1a**] = 0.5 M in toluene, or 1.6 M in CH_2Cl_2 and $ClCH_2CH_2Cl$ unless otherwise noted. [b] Numbers in parentheses indicate the molar ratio of reagents in catalytic system. [c] Mol % of transition metal relative to **1a**. [d] Isolated yields. [e] Considerable polymer formation. [f] No reaction. [g] A variety of conditions were attempted and are summarized in this entry. [h] [**1a**] = 0.5 M.

ways. First, the [4 + 2 + 2] cycloadditions required a bimetal catalytic system, with one of the metals being cobalt or iron and the second metal being a Lewis acidic metal, zinc or aluminum typically serving that role. In contrast, the [2 + 2 + 2] cycloadditions, including norbornadiene dimerizations that produce homo Diels−Alder adducts, are well-known to proceed smoothly with a catalytic system comprised of a single metal,[8,9,10] with nickel[11] and cobalt[12] catalysts serving best. Nickel-based catalysts, however, were not successful in promoting the [4 + 2 + 2] reactions, even in the presence of zinc or aluminum reagents as cocatalysts. Furthermore, the [4 + 2 + 2] cycloadditions of 2-substituted norbornadienes were unique in comparison to those of the transition-metal-catalyzed [2 + 2 + 2] reactions in that the regioselectivity for the latter was quite variable and sensitive to the substituent identity.[11−13] In contrast, the [4 + 2 + 2] cycloadditions gave exclusive regioselectivity with the orignal norbornadiene C2 substituent residing at C1 of the adduct irrespective of its electronic nature.[5b] Good to excellent enantioselectivities have already been reported for both the [2 + 2 + 2][14] and [4 + 2 + 2][15] cycloadditions of norbornadiene using chiral phosphine ligands. In this paper, we present a full account of the work on the transition-metal-catalyzed cycloadditions, and in the following paper, we present the subsequent opening of the norbornadiene adducts to bicyclo[5.3.0]-decane ring systems.

Results

Optimization of the Catalyst. An examination of the reaction between norbornadiene (**1a**) and 1,3-butadiene to produce tetracyclo[5.4.0.0.^{2,4}0^{3,7}]undec-9-ene (**2a**) using cobalt, iron, and nickel catalysts previously known to promote either the [2 + 2 + 2] or [4 + 2 + 2] cycloadditions of **1a** was undertaken (Table 1, Scheme 1). Both Co and Fe catalysts were effective in promoting the desired cycloaddition (Table 1, entries 1, 2, 10−13, 18,

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and 19), but the Ni systems (Table 1, entries 3 and 5) failed in the [4 + 2 + 2] reactions, leading only to polymer formation. The best systems found were cobalt-based: the modified Lyons catalyst,[8f−h,16] Co(acac)$_2$/dppe[17]/Et$_2$AlCl (1:1.5:10), in toluene (79%, Table 1, entry 1), which was previously successful in both [2 + 2 + 2][8f] and [4 + 2 + 2][8h] cycloadditions of **1a**, the modified Duan catalyst,[18] CoI$_2$/dppe/Zn (1:2:10), in CH$_2$Cl$_2$ or ClCH$_2$CH$_2$Cl (76−85%, Table 1, entries 10−12) which was previously reported only for [2 + 2 + 2] cycloadditions of **1a** with alkynes, and the modified Binger catalyst,[19] CoI$_2$/dppe/ZnI$_2$ (1:2:5), in CH$_2$Cl$_2$ (81%, Table 1, entry 13). The recently described Hilt system[8n] was also notable in that it promoted the cycloaddition at room temperature (Table 1, entries 18 and 19), though the use of NaBH$_4$ limits its application to reactants without borohydride reducible groups. No other catalytic system promoted the cycloaddition at room temperature (Table 1, entries 6 and 20−22). Neither the Binger nor the Hilt systems have been previously used in [4 + 2 + 2] cycloadditions. The generation of an active cobalt catalyst was indicated in each system by the appearance of a brown, cloudy solution. In contrast, a poorly active or inactive catalytic system showed a green tinge, which also resulted upon exposure of the active catalyst to air. The Carbonaro catalyst,[20] Fe(acac)$_3$/dppe/Et$_2$AlCl (1:1.5:10), was also quite successful in promoting the cycloaddition (79%, Table 1, entry 2), though as later found, was considerably less successful for substituted norbornadienes. The formation of adduct **2a** was readily apparent from the ^{1}H NMR spectra, which revealed the three cyclopropyl and the two vinyl hydrogens: δ 0.82 (d, J = 5.2 Hz, H2/3), 1.01 (t, J = 5.2 Hz, H4), and 5.45−5.53 (m, H9/10).

Several features were immediately apparent from these results, which also served to distinguish the [4 + 2 + 2] cycloaddition from the related [2 + 2 + 2] reaction. The optimal catalytic systems for the [4 + 2 + 2] reaction all employed a bimetal, bisphosphine ligand system. The use of the monodentate PPh$_3$ invariably resulted in either a complete loss of, or a great reduction in the yield of cycloadduct **2a**, which stands in contrast to the [2 + 2 + 2] cycloadditions of **1a** using cobalt[14e,19] and nickel[8a,b,e,h,11,13,21] catalytic systems, which were very successful with PPh$_3$ as a ligand. For example, the Duan catalyst, CoI$_2$/PPh$_3$/Zn, which had shown excellent activity in the [2 + 2 + 2] cycloadditions of **1a** with alkynes,[18] gave only a 28% yield of **2a** (Table 1, entry 7), but 85% of **2a** was obtained when dppe was used as the ligand in place of PPh$_3$ (Table 1, entry 11). This is somewhat ironic since the use of dppe as a ligand in the Duan catalyst was reported to drastically slow the [2 + 2 + 2] reaction, with only a trace of cycloadduct formed![18] The use of P(O^{i}Pr)$_3$ in place of PPh$_3$ in the Duan catalyst failed to give any reaction (Table 1, entry 9). It is also interesting that the use of 2 equiv of dppe was not detrimental to the reaction (compare entries 10 and 11 of Table 1). More dramatic results were observed when PPh$_3$ was used in place of dppe in the Lyons catalyst, with no cycloadduct **2a** being produced when PPh$_3$ was employed (Table 1, entry 4), while a 79% yield of **2a** was obtained with dppe as the ligand (Table 1, entry 1). Given these observations, the original Binger catalyst was modified in this work to incorporate dppe rather than PPh$_3$ (Table 1, entry 13), resulting in an excellent yield of **2a** (81%). The success of the modified Binger catalyst was significant in that no zero or low valent metal is present in this system, previously considered a requirement for the transition-metal-catalyzed homo-Diels−Alder cycloadditions of norbornadiene. Neither CoI$_2$ nor ZnI$_2$ with dppe promoted the cycloaddition by themselves (Table 1, entries 14 and 15, respectively).

Table 2. Other Bidentate Ligands in the [4 + 2 + 2] Cycloaddition of 1a with 1,3-Butadiene[a]

entry	catalyst[b]	time (h)	yield of **2a** (%)
1	CoI$_2$/dppm/Zn	4	7
2	CoI$_2$/dppm/Zn	24	18
3	CoI$_2$/dppp/Zn	4	18
4	CoI$_2$/dpppZn	24	62
5	CoI$_2$/dpae/Zn	4	32
6	CoI$_2$/dpae/Zn	24	28

[a] All reactions were run in ClCH$_2$CH$_2$Cl in a sealed tube at 60 °C, with 1.5 equiv of 1,3-butadiene, [**1a**] = 1.6 M. [b] 2.5 mol % CoI$_2$ relative to **1a**, 2 equiv of ligand relative to CoI$_2$, 10 equiv of Zn relative to CoI$_2$.

In addition to the failure of the Ni systems, Co$_2$(CO)$_8$ also failed to catalyze the [4 + 2 + 2] cycloaddition in the presence of PPh$_3$ or dppe with or without photolysis (Entry 16), though the modest success of this cobalt carbonyl complex in the catalysis of [2 + 2 + 2] reactions of norbornadiene is long-established.[8b] The catalytic activity was recovered somewhat upon addition of ZnI$_2$ (Entry 17), producing **2a** in yields (30%) comparable to those reported in the [2 + 2 + 2] cycloadditions of norbornadiene promoted by Co$_2$(CO)$_8$ alone (28%).[8b] Thus, all successful catalysts included a second, Lewis acidic metal. Lautens has already reported that both Co(acac)$_2$ and Co(acac)$_3$ can successfully serve as cobalt sources with slightly higher yields for the [2 + 2 + 2] cycloadducts from Co(II),[12] so further examination of a possible distinction between Co(II) and Co(III) in forming the catalytic system was not undertaken in this work.

Other bidentate ligands were also examined in this [4 + 2 + 2] reaction to produce **2a**: dppm,[22] dppp,[23] and dpae[24] using the Duan catalyst (Table 2). All of these ligands proved inferior to dppe in effecting the desired cycloaddition, requiring longer reaction times while producing lower yields of **2a** (compare yields in Table 2 to Table 1, entry 11). Furthermore, considerable polymer formation accompanied the reactions in each case, something not observed with dppe.

In no case was the [2 + 2 + 2] cycloadduct **3** detected in the product mixtures, even those employing catalysts known to promote [2 + 2 + 2] cycloadditions of **1a** but which did not effectively promote the [4 + 2 + 2] reaction, such as the nickel catalysts, though we cannot rule out the production of **3** in very minor amounts. In most of

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[16] The modification employed was the use of Co(acac)$_2$ instead of Co(acac)$_3$. A similar, successful catalytic system for the [4 + 2 + 2] cycloaddition of **1a** with butadiene to give **2a** (68%) had been reported earlier by Carbonaro [CoCl$_2$/dppe/Et$_2$AlCl], Carbonaro, A.; Cambisi, F.; Dall'Asta, G. *J. Org. Chem.* **1971**, *36*, 1443−1445.

[17] dppe = 1,2-bis(diphenylphosphino)ethane.

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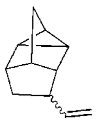
[22] dppm = bis(diphenylphosphino)methane.

[23] dppp = 1,3-bis(diphenylphosphino)propane.

[24] dpae = 1,2-bis(diphenylarsino)ethane.

these cases, the product mixture was dominated by polymeric material produced from the butadiene. (Subjecting 1,3-butadiene to the reaction conditions led to considerable polymer formation.) The appearance of **3** in low yields has been noted in both iron-[20] and possibly cobalt-catalyzed[25] reactions, accompanying the [4 + 2 + 2] cycloadduct **2a**, as well as in nickel-catalyzed[16] reactions between **1a** and 1,3-butadiene.



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[4 + 2 + 2] Cycloadditions of Substituted Norbornadienes. The 7- and 2-substituted and 2,7-disubstituted norbornadienes **1b**−**i** were prepared following or adapting known literature procedures. Though low yielding (23% and 28% respectively, in our hands, 25% and 36% respectively, in the literature), the one-step preparations of 7-substituted derivatives **1b**[26] and **1c**[27] were easy to perform (Scheme 2, eq 1). 2-Substituted derivatives **1d**−**i** were prepared by metalation of **1a** or **1b** with Schlosser's base[28] followed by appropriate electrophilic quench as reported for known compound **1g** (Scheme 2, eqs 2 and 3).[29] Diastereomers **1h** and **1i**, produced in a 8:1 ratio (99+% combined yield) from **1b** with the syn isomer **1h** favored presumably due to the directing effect of the C7 oxygen in the metalation, were readily separated by either distillation or flash chromatography depending upon the quantity being prepared. The assignment of the dominant *syn*-diastereomer was routine from DNOE studies: irradiation of the H7 resonance (δ 3.70, br s) resulted in an enhancement of the H5 (δ 6.63, m) and H6 (δ 6.64, m) vinyl proton resonances, while saturation of the *tert*-butyl singlet (δ 1.11, s, 9H) produced an enhancement in the H3 vinyl proton (δ 5.96, br s) and 2-CH_3 (δ 1.87, d, J = 1.8 Hz, 3H) resonances. Ester **1f** was also prepared equally simply (48% in our hands) from the cycloaddition of cyclopentadiene with methyl propynoate.[30]

Scheme 2

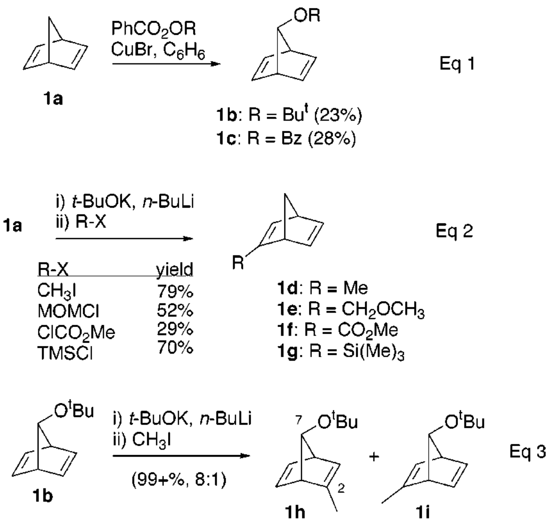
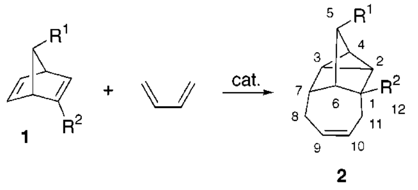


Table 3. Cycloadditions of Substituted Norbornadienes with Butadiene[a]

entry	**1**	cat.[b] (mol %)	T (°C)	time (h)	R^1	R^2	product (% yield)[c]
1	**1b**	A (1)	50	13	*t*-BuO	H	**2b** (84)
2	**1b**	B (5)	70	20	*t*-BuO	H	**2b** (59)
3	**1b**	C (5)	rt	20	*t*-BuO	H	**2b** (75)
4	**1b**	D (5)	rt	20	*t*-BuO	H	**2b** (55)
5	**1b**	E (5)	70	20	*t*-BuO	H	**2b** (69)
6	**1b**	F (5)	70	20	*t*-BuO	H	**2b** (79)
7	**1c**	A (5)	80	24	$PhCO_2$	H	**2c** (24)
8	**1c**	F (5)	80	24	$PhCO_2$	H	**2c** (89)
9	**1d**	A (1)	60	8	H	CH_3	**2d** (82)
10	**1e**	A (2.5)	90	24	H	CH_2OCH_3	**2e** (15)
11	**1e**	E (2.5)	90	24	H	CH_2OCH_3	**2e** (44)
12	**1e**	F (2.5)	80−90	5	H	CH_2OCH_3	**2e** (59)
13	**1f**	A (1)	rt	12	H	CO_2Me	**4** (70)[d]
14	**1f**	B (1)	80	24	H	CO_2Me	NR
15	**1f**	C (1)	rt	24	H	CO_2Me	polymer
16	**1f**	D (1)	rt	24	H	CO_2Me	polymer
17	**1f**	E (1)	80	31	H	CO_2Me	**2f** (60)
18	**1f**	F (1)	80	31	H	CO_2Me	**2f** (76)
19	**1g**	A/F (1)	50/90	18/28	H	TMS	NR
20	**1h**	A (1)	60	9	*t*-BuO	CH_3	**2h** (82)

[a] All reactions were run with 1.5 equiv of 1,3-butadiene relative to **1**. [b] Cat. A: $Co(acac)_2/dppe/Et_2AlCl$ (1:1.5:10), in toluene (0.5 M). Cat. B: $CoI_2/dppe/ZnI_2$ (1:2:5), in CH_2Cl_2 (1.6 M). Cat. C: $CoI_2/dppe/NaBH_4/ZnI_2$ (1:1:1:3) in CH_2Cl_2 (0.5 M). Cat. D: $CoI_2/dppe/NaBH_4/ZnCl_2$ (1:1:1:3) in CH_2Cl_2 (0.5 M). Cat. E: $CoI_2/dppe/Zn$ (1:2:10), in CH_2Cl_2 (1.6 M). Cat. F: $CoI_2/dppe/Zn$ (1:2:10), in $ClCH_2CH_2Cl$ (1.6 M). [c] Isolated yields. [d] [4 + 2] cycloaddition.

Scheme 3



With the substituted norbornadienes in hand, the cycloadditions with 1,3-butadiene were then achieved in good yields using either the modified Lyons or Duan catalysts producing adducts **2** (Scheme 3, Table 3), with the exception of **1g**, which did not participate in the cycloaddition. This also stands in contrast with the [2 + 2 + 2] cycloadditions wherein **1g** was an active participant in both the cobalt-[12] and nickel-catalyzed[11] reactions. As with **2a**, the formation of the desired cycloadducts **2b**−**h** was indicated in the ^1H NMR spectrum by the appearance of three distinct cyclopropyl hydrogens typically between δ 0.6−1.2 depending upon the adduct substituents, along with two vinyl hydrogens between δ 5.5−5.6.

The 7-oxygenated norbornadiene **1b** required only 1 mol % of the modified Lyons catalyst to achieve a good yield of cycloadduct **2b** (84%, Table 3, entry 1), while

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(25) Takahashi, A.; Inukai, T. *J. Chem. Soc., Chem. Commun.* **1970**, 1473. Also, in a preliminary communication, Lautens indicated that [2 + 2 + 2] cycloadducts of norbornadiene with butadienes were formed (ref 15, footnote 21), but later states in the full paper that no such adducts were detected (ref 12).

(26) (a) Story, P. R. *J. Org. Chem.* **1961**, *26*, 287−290. (b) Story, P. R.; Fahrenholtz, S. R. *Org. Synth., Coll. Vol. V*, **1973**, 151−154.

(27) Tanida, H.; Tsuji, T. *J. Org. Chem.* **1964**, *29*, 849−852.

(28) Schlosser, M. *J. Organomet. Chem.* **1967**, *8*, 9−16.

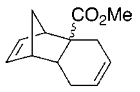
(29) (a) Verkruijsse, H. D.; Brandsma, L. *Recl. Trav. Chim. Pays-Bas* **1986**, *105*, 66−68. (b) Brandsma, L.; Verkrujsse, H. D. *Prepr. Polar Organomet. Chem.* **1987**, *1*, 52−53. For a related preparation of **1d**: (c) Maskornick, M. J. *Tetrahedron Lett.* **1972**, 1797−1800.

(30) (a) Adam, W.; De Lucchi, O.; Pasquato, L.; Will, B. *Chem. Ber.* **1987**, *120*, 531−535. (b) Alder, K.; Wirtz, H.; Koppelberg, H. *Liebigs Ann. Chem.* **1956**, *601*, 138−154. (c) Baumgaertel, O.; Szeimies, G. *Chem. Ber.* **1983**, *116*, 2180−2204. An improved procedure has also been reported by Lautens: ref 11.

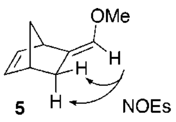
7-benzoyloxynorbornadiene (**1c**) gave only 24% of adduct **2c** with this catalyst, accompanied by significant amounts of a chlorine-containing byproduct in a very messy reaction (Table 3, entry 7). Attempts to increase the quantity of this byproduct, which was never completely purified, by increasing the amount of Et_2AlCl led only to an intractable mixture. A higher yield of **2c** (89%, Table 3, entry 8), however, was achieved using the Duan catalyst, which avoids the relatively harsh Et_2AlCl. The excellent reactivity of **1b** was further demonstrated using either the recently described CoI_2/dppe/$NaBH_4$/ZnI_2 or CoI_2/dppe/$NaBH_4$/$ZnCl_2$ as the catalytic system,[8n] with the former being more effective, which enabled the cycloaddition to be accomplished in acceptable yields at room temperature (75% and 55%, respectively, Table 3, entries 3 and 4). The modified Duan catalyst was also effective for these cycloadditions (Table 3, entries 5 and 6).

The most striking feature of the cycloadditions of the 2-substituted norbornadienes **1d**−**f**,**h** was the high regioselectivity, with the original norbornadiene C2 substituents located exclusively at the C1 position of the cycloadducts. The exclusive regioselectivity, initially indicated by delineation of the scalar coupling spin systems through simple H,H-COSY spectra and the observation of three cyclopropyl hydrogens in the ^1H NMR spectra, was confirmed by the HMQC or H,C-COSY spectra, which revealed the coupling of these relatively high-field cyclopropyl methine hydrogens with the relatively high-field cyclopropyl methine carbons.[31] In all adducts, the H11 hydrogens appeared as the AB part of an ABX multiplet with the endo hydrogen showing sharp, four-lined multiplicity (dd) around δ 2.2−2.3, while the exo hydrogen appeared downfield (δ 2.3−2.5) as a broadened doublet. In contrast, the H8 hydrogens were invariably the unresolved AA′ part of an AA′MX-system around δ 2.2−2.3.[32] Long-range heteronuclear couplings ($^3J_{H,C}$) observed in the HMBC spectra recorded on **2e** and **2h** confirmed the regiochemical assignment: couplings were observed between H10/C1 and $H11_{endo}$/C12.

While the cycloaddition of **1d** was successful with the Lyons catalyst, the successful [4 + 2 + 2] reaction of **1f** required the modified Duan catalyst. Use of the Lyons catalyst [$Co(acac)_2$/dppe/Et_2AlCl] produced only the [4 + 2] adducts **4** as a mixture of endo and exo isomers in 70% yield (Table 3, entry 13). These normal Diels−Alder products were not observed, however, with the modified Duan catalyst (CoI_2/dppe/Zn) which does not employ aluminum as the Lewis acid (Table 3, entries 17 and 18).



4



5

Use of the Binger or Hilt catalysts with **1f** (Table 3, entries 14−16) were also unsuccessful in promoting the homo-Diels−Alder reaction, leading to either polymer formation or no reaction at all. Also of note, enol ether **5** was isolated as a major byproduct (27%) from the [4 + 2 + 2] reaction of **1e** using the modified Duan catalyst, presumably the result of a cobalt-catalyzed double-bond migration to give the exocyclic olefin. In a control experiment, when **1e** was subjected to the reaction conditions in the absence of 1,3-butadiene, complete conversion to **5** was observed. Transition metal-catalyzed olefin isomerizations have long been known including examples using cobalt systems.[33] Since isomerization of 2-substituted norbornenes and norbornadienes to exocyclic olefins are also known,[29c,33d] the production of **5** was not surprising. The stereochemistry of **5** was established by NOEs as shown.

In view of the contrast between the variable regioselectivity observed in the cobalt- and nickel-catalyzed [2 + 2 + 2] cycloadditions with alkynes and alkenes[11,12] and the exclusive regioselectivity in the [4 + 2 + 2] reactions observed in this work, other conditions and substrates were sought that would succeed in yielding cycloadducts with an original norbornadiene C2 substituent located on C2 (cyclopropyl carbon) of the adduct. Lautens had previously noted that the regioisomer distribution in the $Ni(COD)_2$-catalyzed [2 + 2 + 2] cycloadditions of 2-substituted norbornadienes, including both **1f** and **1g**, was sensitive to the identity of the phosphorus ligand in the reactions, with substituents on the cyclopropyl ring of the adduct often being the major product.[11] Triisopropyl phosphite was also successfully employed as a ligand in this [2 + 2 + 2] chemistry. However, when triisopropyl phosphite was used in place of dppe in the modified Lyons catalyst [$Co(acac)_2$/2(i-PrO)$_3$P/Et_2AlCl, tol, 60 °C] for the reaction of **1d** with 1,3-butadiene, only a very complex product mixture resulted with no cycloadducts detected. Attempts to use the Carbonaro catalyst [$Fe(acac)_3$/dppe/Et_2AlCl, tol, 60 °C] with **1d** also resulted in a messy reaction with no cycloadducts detected, and no reaction occurred at all when dppf[34] was used in place of dppe in the Duan system (CoI_2/dppf/Zn).

In an attempt to force the formation of cycloadducts with a substituted cyclopropane ring, 2,3-disubstituted norbornadienes **1j** and **1l** were prepared from straightforward cycloadditions of cyclopentadiene and appropriate alkynes, while **1k** was made by basic hydrolysis of **1j** followed by anhydride closure, and **1j**−**l** were then subjected to the cobalt-catalyzed [4 + 2 + 2] reaction conditions using the modified Duan catalyst (CoI_2/dppe/Zn, Scheme 4). Norbornadiene **1l** was of special interest since it was hoped that the electronic distinction between the norbornadiene substituents would lend insight into the impact of electronic effects on the cycloaddition if the [4 + 2 + 2] adducts would be formed.

No reaction occurred with dimethyl norbornadiene-2,3-dicarboxylate (**1j**) even after prolonged heating (90−100 °C, 46 h, 5 mol % Co). The reaction of anhydride **1k** with

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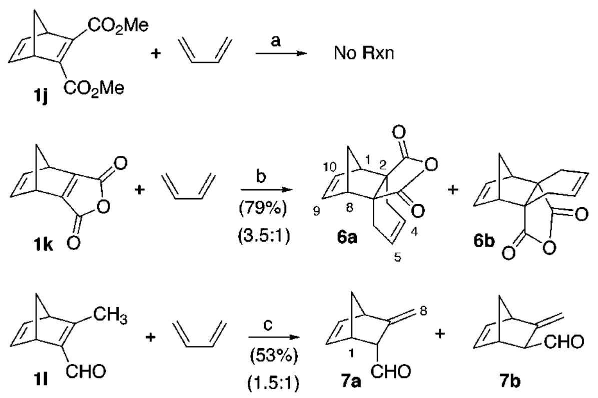
[31] Pretsch, E.; Seibl, J.; Simon, W.; Clerc, T. In *Tables of Spectral Data for Structure Determination of Organic Compounds*; Springer-Verlag: Berlin, 1983.

[32] The $H11_{endo}$ and $H11_{exo}$ hydrogens were assigned by analogy with those of **2a** wherein the corresponding allylic methylene hydrogens also appeared as broadened and sharp multiplets. NOEs from H6 to the broadened resonance (and, hence, the exo hydrogens), and from H2/3 to the sharp resonance (hence the endo hydrogens) on **2a** distinguished these methylene hydrogens. Furthermore, the lack of resolved coupling between $H11_{exo}$ and H10, and the lack of observable coupling between $H11_{exo}$ with C12 in the HMBC spectra of **2e** and **2h** are in accord with near 90° dihedral angles anticipated for the most stable pseudochair conformation of the seven-membered ring.

[33] For example: (a) Karapiuka, G. L.; Orchin, M. *J. Org. Chem.* **1961**, *26*, 4187−4190. (b) Goetz, R. W.; Orchin, M. *J. Am. Chem. Soc.* **1963**, *85*, 1549−1550. (c) Roos, L.; Orchin, M. *J. Am. Chem. Soc.* **1965**, *87*, 5502−5504. For an older review: (d) Hubert, A. J.; Reimlinger, H. *Synthesis* **1970**, 405−430.

[34] dppf = 1, 1′-bis(diphenylphosphino)ferrocene.

Scheme 4[a]



[a] Key: (a) CoI$_2$/dppe/Zn (1:2:10; 5 mol % Co), ClCH$_2$CH$_2$Cl, 90−100 °C, 46 h; (b) CoI$_2$/dppe/Zn (1:2:10; 2.5 mol % Co), ClCH$_2$CH$_2$Cl, 80 °C, 45 h; (c) CoI$_2$/dppe/Zn (1:2:10; 2.5 mol % Co), ClCH$_2$CH$_2$Cl, 80 °C, 56 h.

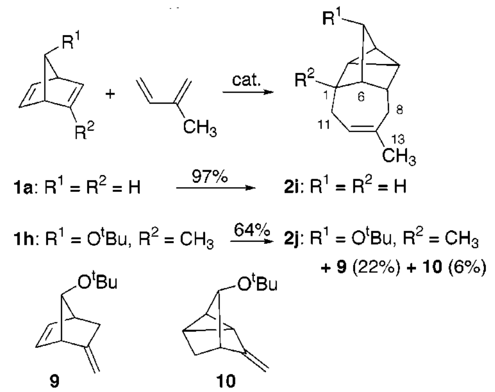
1,3-butadiene under similar conditions (1,2-dichloroethane, 80 °C, 45 h, 2.5 mol % Co) gave only the normal Diels−Alder cycloadducts **6a** and **6b** (3.5:1, endo/exo, separable by flash chromatography) in a combined 79% yield (Scheme 4, see the Experimental Section for characterization) with no [4 + 2 + 2] cycloadduct detected. The formation of **6a** and **6b** (in a 1:6 ratio) from the Diels−Alder reaction of **1k** with 1,3-buadiene in refluxing benzene has been previously reported.[35] Finally, the reaction of **1l** produced only isomerized products **7a** and **7b** (1.5:1, 53% combined yield) along with recovered **1l** (18%), again with no detected [4 + 2 + 2] adducts. In light of the isolation of **5** from the product mixture in the cobalt-catalyzed [4 + 2 + 2] cycloadditions of **1e** noted earlier, and the reported base-catalyzed isomerization of **1d** to the exocyclic olefin,[29c] formation of **7a** and **7b** was not surprising, though disappointing.

The lack of reactivity of 2,3-disubstituted norbornadienes has also been noted in [2 + 2 + 2] homo-Diels−Alder chemistry under both thermal and attempted nickel promotion. For example, Kelly noted that 2,3-dimethylnorbornadiene failed to react with several electron-deficient dienophiles (DMAD, TCNE, and others) known to produce [2 + 2 + 2] adducts with unsubstituted norbornadiene.[36] Lautens later reported that the Ni(COD)$_2$-catalyzed reaction between **1j** and *N*-phenylmaleimide yielded only the [2 + 2] adduct **8** with the cycloaddition occurring on the unsubstituted double bond of **1j**.[11,37]

8

[4 + 2 + 2] Cycloadditions with Substituted 1,3-Butadienes. The [4 + 2 + 2] cycloaddition between **1a** and isoprene is a well-known reaction, with Lyons reporting a 96% yield of **2i** using [Co(acac)$_3$/dppe/Et$_2$AlCl] as the catalytic system,[8h] which was reproduced in this work with the modified Duan catalyst (CoI$_2$/dppe/Zn) (97%, Scheme 5).[38] Lautens has since accomplished this reaction as well as that of other 2-substituted 1,3-butadienes with good enantioselectivity (72% ee).[12,15] We therefore examined the cycloaddition of isoprene with 2,7-disubstituted norbornadiene **1h**.

Scheme 5



The cycloaddition between 7-*tert*-butoxy-2-methylnorbornadiene (**1h**) and isoprene using the modified Duan catalyst [CoI$_2$(5 mol %)/dppe/Zn] in ClCH$_2$CH$_2$Cl] gave only one regioisomer **2j** (64%) along with **9** (22%) and **10** (6%), the products of isomerization of **1h** (Scheme 5). The modified Lyons catalyst [Co(acac)$_2$(5 mol %)/dppe/Et$_2$AlCl in toluene] gave a considerably less clean product mixture with cycloadduct formed as indicated by the NMR spectrum of this crude mixture, while lesser amounts of this catalyst (1 mol %) give little reaction. This reaction with isoprene was noticeably slower than that of **1h** with 1,3-butadiene (Table 3, entry 20), requiring a longer reaction time (27 h) and higher temperature (80 °C) in addition to more catalyst.

The structure of **2j** was apparent from extensive NMR studies. As noted above, the location of the methyl substituent at C1 rather than on a cyclopropyl carbon was indicated by the appearance of three cyclopropyl methine hydrogens (δ 0.90, dd, $J = 5.5$, 5.5 Hz, H3; 1.00, dd, $J = 4.9$, 5.5 Hz, H2; 1.04, dd, $J = 4.9$, 5.5 Hz, H4) correlating with three relatively high-field methine carbons (δ 16.5, C3; 16.6, C4; 21.8, C2) in the HMQC spectrum. Long-range heteronuclear coupling ($^3J_{C,H}$) observed in the HMBC spectrum between H11$_{endo}$ and the methyl carbon positioned at C1 confirmed the location of this substituent at C1. The identification of the H11 protons were secured from a COSY experiment from the coupling of H11$_{endo}$ (δ 1.95, dd, $J = 8.5$, 16.5 Hz) with the vinyl proton H10, locating the vinyl methyl group at C9, while H8$_{endo}$ (1.99, dd, $J = 7.3$, 16.5 Hz) coupled with H7. Neither H11$_{exo}$ (δ 2.26, bd 2.26, $J = 16.5$ Hz) nor H8$_{exo}$ (δ 2.35, bd, $J = 16.5$ Hz) showed significant coupling to their vicinal partners. Complementary long-range heteronuclear couplings ($^3J_{C,H}$) between H8$_{endo}$/C13 and H7/C9 confirmed the regiochemical assignment.

In contrast to the highly regioselective reaction with **1h**, the cycloaddition between 7-*tert*-butoxynorbornadiene (**1b**) and isoprene gave two inseparable diastereomers **2k** and **2l** in a 1.7:1 ratio, 66% combined yield using the

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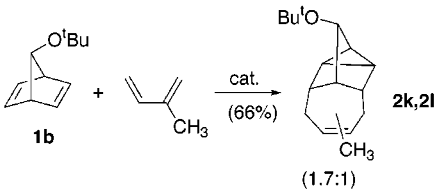
(35) Edman, J. R.; Simmons, H. E. *J. Org. Chem.* **1968**, *33*, 3808−3816.

(36) Kelly, T. R. *Tetrahedron Lett.* **1973**, 437−440.

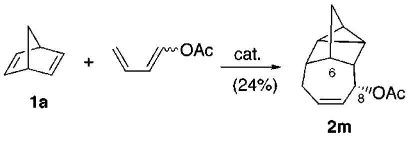
(37) Edwards, L. G.; Lautens, M.; Lough, A. J. *Z. Kristallogr.* **1996**, *211*, 919−923.

(38) In a footnote (ref 20), Carbonaro also noted that a 1:1 adduct was formed between isoprene and norborndiene using their iron catalyst, Fe(acac)$_3$/dppe/Et$_2$AlCl, but did not identify the adduct.

Scheme 6



Scheme 7



modified Lyons catalyst (5 mol %, Scheme 6). With the Duan catalyst, the yield was 67% with a 1.3:1 ratio of diastereomers; the two diastereomers were not distinguished within the mixtures. The production of this near equal mixture of diastereomers, in contrast to the exclusive regioselectivity observed in the cycloaddition of **1h**, illustrates the importance of the 2-methyl substituent on the norbornadiene in the regiocontrol.[39]

Intermolecular [4 + 2 + 2] homo-Diels−Alder reactions of norbornadiene with 1-substituted 1,3-butadienes are rare. Lyons had reported a 94% yield (but with only 40% conversion) of the [4 + 2 + 2] adduct between 1,3-pentadiene and **1a**,[8h,40] and Lautens succeeded with the intramolecular [4 + 2 + 2] cycloaddition of butadienes tethered from the C1-position to the C2 position of norbornadiene, though the yields were modest ($\leq$40%).[12] We therefore undertook an investigation into the cycloaddition of several 1-substituted butadienes with the hope of generating cycloadducts functionalized at the C8/11 position(s).

Commercially available 1-acetoxy-1,3-butadiene (trans/cis, 63:37) did participate in the [4 + 2 + 2] reaction with **1a** using relatively large amounts of the modified Duan catalyst (20 mol % Co) to produce a single, diastereomerically pure adduct **2m**, but in only 24% yield (Scheme 7). It was not clear whether one of the butadiene isomers reacted preferentially in stereoselective fashion, or both olefinic isomers reacted to produce **2m**. The stereochemistry was established by the observation of an NOE between H8 and H6 in a NOESY spectrum. The sluggishness of the reaction was clearly evidenced not only by the reaction time and temperature (46 h, 80 °C), but also by the necessity of continuous addition of **1a** over the course of the reaction just to achieve this low yield. The modified Binger (CoI$_2$/dppe/ZnI$_2$) and Lyons [Co(acac)$_2$/dppe/Et$_2$AlCl] catalysts were unsuccessful in promoting the production of **2m**. Several other 1-substituted 1,3-butadienes were also examined (Figure 2), yet all failed to produce the desired [4 + 2 + 2] cycloadducts.

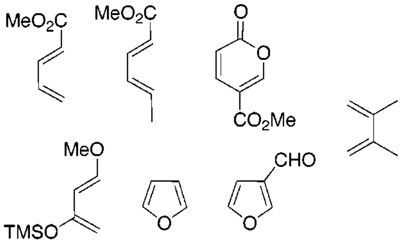
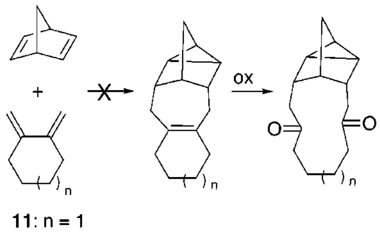


Figure 2. Other dienes that failed to participate in cobalt-catalyzed [4 + 2 + 2] cycloadditions with **1a**.

Scheme 8



One notable disappointment was the lack of reactivity of 1,2-dimethylenecyclohexane[41] (**11**) with **1a**. Successful formation of the cycloadduct would have enabled a relatively facile pathway to an 11-membered ring system, while the corresponding dimethylenecyclopentane would have given rise to the analogous 10-membered ring adduct following oxidative cleavage of the central olefin (Scheme 8). This failure may reflect a lack of reactivity of 2,3-disubstituted butadienes since 2,3-dimethyl-1,3-butadiene also failed to participate in the [4 + 2 + 2] chemistry with **1a** (Figure 2).

[4 + 2 + 2] Cycloadditions of Bicyclo[2.2.2]octa-2,5-dienes. Prior to our preliminary report,[42] there were no examples of transition-metal-catalyzed [2 + 2 + 2] or [4 + 2 + 2] cycloadditions of bicyclo[2.2.2]octa-2,5-dienes, though thermally promoted [2 + 2 + 2] cycloadditions of bicyclo[2.2.2]octa-2,5-diene (**12**),[43] benzobarrelene (**13a**),[44] and barrelene[45] had been reported. Following literature procedures, **12**[46] and benzobarrelenes **13a**−**c**[47] were prepared and subjected to the [4 + 2 + 2] cycloaddition conditions with butadiene using the modified Lyons catalyst, producing the desired cycloadducts **14** and **15** in good yields (Table 4). As with the norbornadienes, the corresponding reaction of **13c** with isoprene was noticeably slower and gave the cycloadduct **15d** in reduced yield (48%) relative to the reactions with butadiene which produced **15c** (70%). As described earlier, the cycloadducts were easily identified by the ^{1}H NMR spectra, though for the benzobarrelene adducts, the benzylic cyclopropyl hydrogens were significantly deshielded (δ 2.14 for **15a** δ 2.7−2.8 for the perchloroderivatives

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[39] The cycloaddition of **1b** with isoprene is an example where two regiochemically distinct pathways produce diastereomers, **2k** and **2l**.

[40] In a footnote, Carbonaro has also mentioned, but did not identify, the production of a 1:1 adduct between **1a** and 1,3-pentadiene: ref 20.

[41] Bailey, W. J.; Golden, H. R. *J. Am. Chem. Soc.* **1953**, *75*, 4780−4782. The preparation of bismethylenocyclohexane of **11** followed a modification of this literature procedure, beginning with commercially available 1,2-cyclohexanecarboxylic anhydride (10 g), LAH reduction then acetylation to the diacetate, with flash vacuum pyrolysis generating **11** in the final step, 57% overall yield for three steps.

[42] Kiattansakul, R.; Snyder, J. K. *Tetrahedron Lett.* **1999**, *40*, 1079−1082.

[43] (a) Allred, E. L.; Johnson, A. L. *J. Am. Chem. Soc.* **1971**, *93*, 3, 1300−1301. (b) Fickes, G. N.; Metz, T. E. *J. Org. Chem.* **1978**, *43*, 4057−4061.

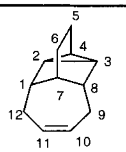
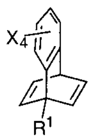
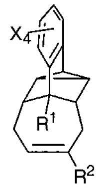
[44] Adam, W.; Balci, M.; Cakmak, O.; Peters, K.; Saha-Moeller, C. R.; Schulz, M. *Tetrahedron* **1994**, *50*, 9009−9012.

[45] (a) Zimmerman, H. E.; Grunewald, G. L. *J. Am. Chem. Soc.* **1964**, *86*, 1434−1436. (b) Zimmerman, H. E.; Boettcher, R. J.; Buehler, N. E.; Keck, G. E.; Steinmetz, M. G. *J. Am. Chem. Soc.* **1976**, *98*, 7680−7689.

[46] Preparation of **12**: Williams, R. V.; Chauhan, K.; Gadgil, V. R. *J. Chem. Soc., Chem. Commun.* **1994**, 1739−1740.

[47] Preparation of **13a-c**: (a) Hales, N. J.; Heany, H.; Hollinshead, J. H. *Synthesis* **1975**, 707−708. (b) Hales, N. J.; Heany, H.; Hollinshead, J. H.; Singh, P. *Organic Syntheses*; Wiley: New York, 1973; Collect. Vol. VI, pp 82−86.

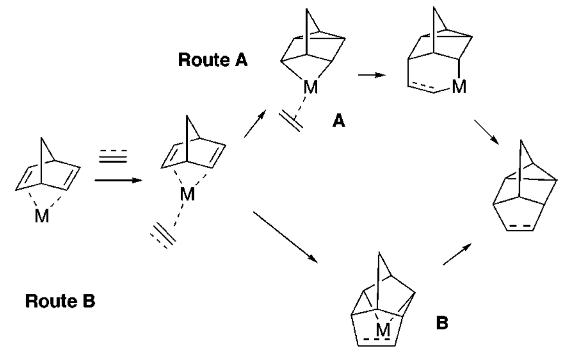
Table 4. Cobalt-Catalyzed [4 + 2 + 2] Cycloadditions of Bicyclo[2.2.2]octa-2,5-dienes[a]

Bicyclooctadiene	Cycloadduct (% Yield)[b]	Cat. mol%	Temp (°C)	Time (h)
 **12**	 **14** (87)	20	50	6
				
13a: $R^1 = X = H$	**15a**: $R^1 = R^2 = X = H$ (80)	5	60	24
13b: $R^1 = H, X = Cl$	**15b**: $R^1 = R^2 = H, X = Cl$ (95)	20	55	6
13c: $R^1 = OMe, X = Cl$	**15c**: $R^1 = OMe, R^2 = H, X = Cl$ (70)	20	100	53
	15d: $R^1 = OMe, R^2 = Me, X = Cl$ (48)	25	110	48

[a] All reactions were run in toluene, using $Co(acac)_2$/dppe/Et_2AlCl (1/1.5/10) mol % based on Co, with excess butadiene (see the Experimental Section). [b] Isolated yields.

15b−d) compared to H4 in **14** (δ 0.79) due to their location in the aromatic plane. More extensive NMR studies on **15c** confirmed the presence of three cyclopropane methines, thus locating the methoxy group at C7 (rather than C4). An HMQC spectrum identified the three cyclopropyl carbons (δ 22.2, C2/3; 19.6, C4) with the diagnostically large ^1J values ($^1J_4 = 166$ Hz; $^1J_{2/3} = 175$ Hz, determined from a heteronuclear 2D−J experiment).[48] This regioselectivity is consistent with that observed in the cycloadditions of 2-substituted norbornadienes described above with the original homo diene substituent located away from the cyclopropyl face in the cycloadduct.

Scheme 9



Discussion

Two very obvious differences between in the results observed with the transition-metal-catalyzed [4 + 2 + 2] and those reported for [2 + 2 + 2] cycloadditions are: (1) the requirement of a second metal (Zn or Al were used in this work) for the [4 + 2 + 2] reaction, and (2) the high regioselectivity in the cycloadditions of 2-substituted norbornadienes in the [4 + 2 + 2] reactions. Moreover, nickel based catalysts, which function well in the [2 + 2 + 2] reactions, failed in the high order [4 + 2 + 2] counterparts. We believe these features point to a difference in the true catalyst in the two reactions, though the identities of these catalysts are still unknown. Moreover, dppe is the ligand which works best in the [4 + 2 + 2] cycloadditions, yet is argued to retard the [2 + 2 + 2] reactions. In contrast, PPh_3 is the preferred ligand for these later cycloadditions, yet is not successful in the [4 + 2 + 2] reactions. Thus, differences in the mechanisms of the two reactions may exist.

Various mechanistic rationales of the transition-metal-catalyzed [2 + 2 + 2] cycloaddition have been proposed over the years beginning with a highly concerted pathway proposed by Schrauzer wherein the cycloadducts are assembled on the metal catalyst from the homo diene and homo dienophile reactants in one step.[8a−c] More recently, a stepwise mechanism originally proposed by Noyori beginning from quadricyclane,[10] then later expanded upon by both Lyons[8h] and Lautens[11,12] to include observed side reactions, has emerged as most prominent. This features a cyclopropane closure to intermediate **A** as the initial carbon−carbon bond-forming step following complexation of the norbornadiene on the metal center (Scheme 9, route A). Though later preferring the Noyori mechanism, Lyons had also proposed an alternative mechanism for the [2 + 2 + 2] cycloaddition with alkynes in which the initial carbon−carbon bond-forming step leads to formation of the cyclopentene ring (Scheme 9, route B),[8f] thereby adopting the key intermediate **B** initially proposed by Katz to explain the rhodium-catalyzed dimerization of norbornadiene to produce homo Diels−Alder adducts.[9g] Tetrameric complex **17**, which has the basic structure of intermediate **B**, had been reported in 1972 from the reaction of $[RhCl(nbd)]_2$ with 1,1,1,4,4,4-hexafluorobut-2-yne, which supported this later pathway.[49] Calculations by Gugelchuk to probe the stereochemical outcome of the [2 + 2 + 2] cycloadditions catalyzed by nickel suggested that either **A** or **B** could be key intermediates in the reaction pathway, though another potential intermediate **C**, which is a possible

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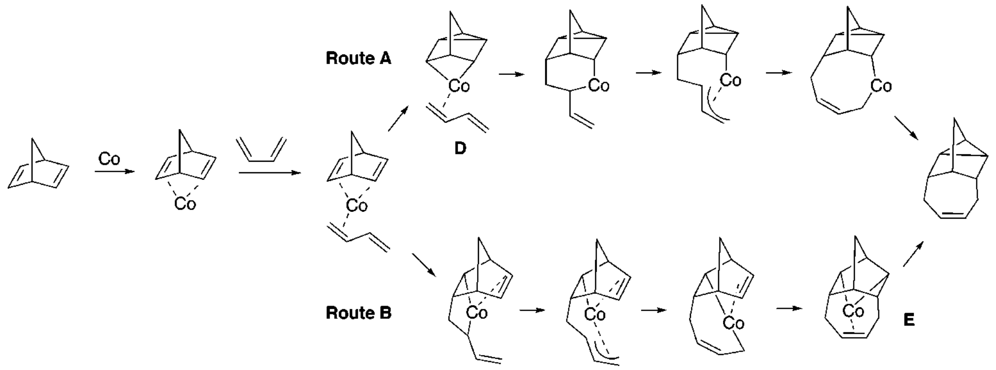
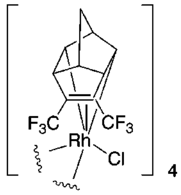
(48) Mooney, E. F.; Winson, P. H. In *Annual Review of NMR Spectrscopy*; Mooney, E. F., Ed.; Academic: New York, 1996; Vol. 2, pp 176−196.

(49) Evans, J. A.; Kemmitt, R. D. W.; Kimura, B. Y.; Russell, D. R. *J. Chem. Soc., Chem. Commun.* **1972**, 509−510.

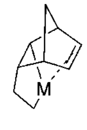
Scheme 10



precursor to **B**, was considered less likely by these authors on the basis of the preferred *exo* stereochemical outcome of the [2 + 2 + 2] cycloaddition with substituted olefins.[81,50]



17



C

Either of these mechanisms can be adapted to the [4 + 2 + 2] cycloaddition with initial cyclopropane (**D**) or cycloheptene (**E**) ring closure (Scheme 10). The exclusive regioselectivity for the formation of C1-substituted adducts **2d**–**f** and **2h** from C2-substituted norbornadienes, which stands in contrast to the [2 + 2 + 2] cycloadditions, can be rationalized on steric grounds by the Katz-type intermediate **E**, or steps leading to this intermediate (Figure 3). Steric interactions between the norbornadiene C2 substituent in **E′** and a phenyl ring of dppe should disfavor formation of an adduct with the substituent located on the cyclopropane ring, as was found in the [2 + 2 + 2] reactions. Such a steric interaction does not exist in intermediate **E** leading to the observed C1-substituted cycloadducts **2d**–**f**. It is more difficult to rationalize the observed exclusive regioselectivity of the cobalt-catalyzed [4 + 2 + 2] cycloaddition with the Noyori-type intermediate **D**, particularly in light of the contrasting regioselectivity in the corresponding [2 + 2 + 2] reactions. It must be emphasized, however, that neither of the pathways depicted in Scheme 10 for the [4 + 2 + 2] reaction clarifies the critical role of the second metal (Zn or Al) beyond that of a simple reducing agent to generate the active cobalt species, nor do they explain the improvement in the reaction when using dppe in comparison to PPh_3, and thus cannot be considered complete. Perhaps the role of this metal is to guide the reaction course to the Katz-type intermediate in an as yet unspecified manner.

Conclusions

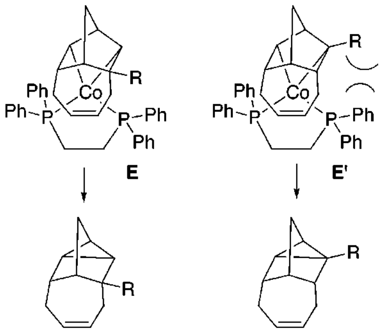


Figure 3. Intermediate **E** in proposed cycloaddition mechanism with steric interactions between the phenyl rings of dppe and the substituent "R" controlling the regioselectivity in favor of the unhindered 1-substituted adducts.

The transition-metal-catalyzed [4 + 2 + 2] cycloadditions of norbornadienes and some bicyclo[2.2.2]octa-2,5-dienes with 1,3-butadienes proceed in excellent yields using cobalt-based catalytic systems. Two key distinctions between these [4 + 2 + 2] cycloadditions and the corresponding transition-metal-catalyzed [2 + 2 + 2] counterparts are the requirement of a bimetal catalytic system with a bidentate bisphosphine ligand for the former, and the exclusive regioselectivity in the [4 + 2 + 2] reaction of 2-substituted norbronadienes to produce 1-substituted adducts. These distinctions may indicate two distinct mechanisms for the [4 + 2 + 2] and [2 + 2 + 2] reactions. In the subsequent paper, opening of the cycloadducts **2** to the target bicyclo[5.3.0]decanes is described, thereby completing one of the goals in pursuing the transition-metal-catalyzed homo Diels–Alder reactions.

Experimental Section

General Methods. Melting points were determined in capillaries and are uncorrected; ^1H NMR and ^{13}C NMR spectra data were recorded at 93.94 kG (^1H 400 MHz), 70.5 kG (^1H 300 MHz, ^{13}C 75 MHz) or 63.41 kG (^{13}C 67.5 MHz) at ambient temperature in $CDCl_3$. Proton chemical shifts (in ppm) are referenced to the residual $CHCl_3$ resonance at δ 7.24. For ^{13}C NMR, the center line of the $CDCl_3$ triplet was used as the internal reference: δ 77.0. Unless otherwise noted, each carbon resonance represents a single carbon (relative intensity); carbon resonances of more than a single carbon in relative intensity were established from integration under inverse gated decoupled conditions (delay between transients = 10 s). Where given, ^1H and ^{13}C assignments were made on the basis of extensive 1D (DNOE, APT) and 2D (^1H,^1H–COSY, ^1H,^{13}C–COSY, NOESY, HMQC, HMBC) techniques. Mass spectra (HRMS) were recorded in either CI (140 eV) or EI (70 eV) mode as noted. Infrared spectra were recorded on NaCl plates. Solid samples were prepared by depositing a solution of the sample (typically in $CDCl_3$) on the plate and allowing the solvent to evaporate prior to recording the IR spectra.

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(50) Gugelchuk, M. M.; Wisner, J. *Organometallics* **1995**, *14*, 1834–1839.

All reaction solvents were anhydrous and distilled immediately prior to use (toluene, Et_2O, and THF from sodium, $ClCH_2CH_2Cl$ and CH_2Cl_2 from CaH_2);[51] chromatography solvents were distilled prior to use. Norbornadiene (**1a**) was distilled prior to use and stored under argon; powdered zinc was activated prior to use by sequential washing with 5% aqueous HCl, EtOH, and Et_2O (twice with each solvent with twice the volume of the solid zinc) on a glass fritted funnel with vacuum filtration. Other commercially available reagents were used without further purification. All reactions were carried out in oven-dried (105 °C) glassware. The glass vessels used for the low boiling point reactants were heavy-walled tubes (25.4 × 102 mm) with Teflon plugs and FETFE O-rings, designated as "pressure tube" in the text. Dry ice−acetone baths were used to maintain reactions at −78 °C, dry ice-50% aqueous acetone baths maintain temperatures of −30 °C. Flash chromatography was performed using silica gel-60 (43−60 μm); TLC was performed on silica gel plates, and visualization was accomplished with ammonium molybdate stain: ammonium molybdate (4 g)/H_2O (60 mL)/H_2SO_4 (4 mL). Workup of many reactions began as noted by passing the reaction mixture through a "silica gel plug", this refers to vacuum filtration through a pad of silica gel approximately 2 cm in height, typically on a Hirsch funnel. Compounds **1b**,[26] **1c**,[27] **1f**,[29a,30] **1g**,[29a,30] **1j**,[52] **12**,[42] and **13a**−**c**[43] were prepared according to literature procedures without significant modification. For the preparation and characterizing data of **1k**,[35,53,54] **1l**,[36,55,56] **6a** and **6b**,[35] and **7a**[57] and **7b**, see the Supporting Information. For the preparation and structure assignments of **1d**,**e**,**h**, **2a**,**b**,**d**−**f**,**h**,**j**, **5**, **9**, and **10**, see the Supporting Information of our previous communication.[5b] General procedures for the cycloadditions in Table 1 are also given in the previous communication;[5b] specific conditions for the preparation of new cycloadducts are given below.

General Observations on the [4 + 2 + 2] Cycloadditions of Norbornadienes. In all the cases, the active catalysts were initially generated as described below, and were indicated by the formation of a cloudy brown solution that was sensitive to air. Addition of the 1,3-butadiene and norbornadiene into the solution of the active catalyst was either separate or as a preformed solution via cannula. 1,3-Butadiene (bp −5 °C) was transferred via cannula as a liquid trapped at −78 °C. After the catalyzed cycloadditions were run, all reaction mixtures were passed through a silica gel plug to remove the spent catalyst prior to solvent removal and flash chromatography.

5-Tetracyclo[5.4.0.0^{2,4}.0^{3,7}]undec-9-enyl benzoate (2c). To a solution of the active catalyst [CoI_2 (15.6 mg, 0.05 mol), dppe (39.8 mg, 0.1 mmol) and Zn (32.7 mg, 0.5 mmol)] in $ClCH_2CH_2Cl$ (0.6 mL) in a pressure tube at 0 °C under Ar were added **1c** (212 mg, 1 mmol) and 1,3-butadiene (0.1 mL, 1.16 mmol) with stirring, and then reaction vessel was removed from the ice bath and immediately capped. The brown cloudy solution was then heated to 80 °C in an oil bath for 24 h. After being cooled to room temperature, the reaction mixture was passed through a silica gel plug washing with CH_2Cl_2 (3 × 10 mL). The washings were collected, and the solvent was removed in vacuo to give the crude oily product which was purified by flash chromatography (hexanes/EtOAc 10:1) to give pure **2c** (R_f = 0.6, 236.3 mg, 89%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.17 (br d, J = 5.3 Hz, 2H), 1.40 (br dd, J = 5.3, 5.3 Hz, 1H), 1.98 (br s, 1H), 2.04−2.05 (br s, 1H), 2.22−2.38 (m, 3H), 2.42−2.52 (m, 2H), 4.86 (br s, 1H), 5.47−5.59 (m, 2H), 7.41 (t, J = 7.4 Hz, 2H), 7.53 (tt, J = 7.4, 1.4 Hz, 1H), 8.03 (dd, J = 7.4, 1.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.7, 15.5, 17.7, 29.7, 30.6, 37.9, 38.3, 44.5, 81.3, 126.9, 127.8, 128.2 (2C), 129.5 (2C), 130.6, 132.7, 166.4; IR (NaCl) 1716 cm^{-1}; HRMS (CI, CH_4, 140 eV) m/z 266.1326 ([M]$^+$, 0.4), calcd for $C_{18}H_{18}O_2$ 266.1307.

9-Methyltetracyclo[5.4.0.0^{2,4}.0^{3,7}]undec-9-ene (2i).[8h] To a solution of the active catalyst [CoI_2 (78.2 mg, 0.25 mmol), dppe (149.4 mg, 0.38 mmol), and Zn (163.4 mg, 2.5 mmol)] in $ClCH_2CH_2Cl$ (3.1 mL) in a pressure tube at 0 °C under Ar were added **1a** (460.7 mg, 5 mmol) and 2-methyl-1,3-butadiene (isoprene, 1 mL, 10 mmoL) with stirring, and then the reaction vessel was removed from the cold bath and immediately capped. The brown, cloudy solution was then heated to 80 °C in an oil bath for 22 h. After being cooled to room temperature, the reaction mixture was passed through a silica gel plug washing with CH_2Cl_2 (3 × 10 mL). The washings were collected, and the solvent was removed in vacuo. Flash chromatography (hexanes) gave pure **2i** (R_f = 0.8, hexanes, 776.5 mg, 97%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.81−0.85 (m, 2H), 1.00 (br dd, J = 5.5, 5.5 Hz, 1H), 1.24 (br s, 2H), 1.58 (br s, 1H), 1.69−1.72 (m, 5H), 2.10 (dd, J = 17.0, 5.5 Hz, 1H), 2.21 (br s, 2H), 2.33 (br d, J = 17.0 Hz, 2H), 5.27 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.8, 13.7, 13.9, 27.5, 29.7, 35.3, 35.9, 40.6, 40.9, 41.1, 121.4, 134.9; HRMS (EI, 70 eV) m/z 160.1257 ([M]$^+$, 47), calcd for $C_{12}H_{16}$ 160.1252.

***anti*-5-*tert*-Butoxy-9-methyltetracyclo[5.4.0.0^{2,4}.0^{3,7}]undec-9-ene (2k) and *syn*-5-*tert*-Butoxy-9-methyltetracyclo[5.4.0.0^{2,4}.0^{3,7}]undec-9-ene (2l).** To a solution of the active catalyst [Co(acac)$_2$ (25.7 mg, 0.1 mmol), dppe (59.8 mg, 0.15 mmol), and Et_2AlCl (1.8 M in toluene, 0.6 mL, 1 mmol)] in toluene (2 mL) in a pressure tube at 0 °C under Ar was added a solution of 7-*tert*-butoxybicyclo[2.2.1]hepta-2,5-diene (**1b**, 328.0 mg, 2 mmol) and 2-methyl-1,3-butadiene (isoprene, 0.6 mL, 6 mmol) in toluene (2 mL). After removal of the ice bath and immediate capping of the pressure tube, the reaction mixture was warmed to 80 °C in an oil bath for 18 h. After the mixture was cooled to room temperature, MeOH was added dropwise (<1 mL) to quench the excess Et_2AlCl until it became green, and the green mixture was passed through a silica gel plug washing with CH_2Cl_2 (3 × 5 mL). The organic solutions were combined, and the solvent was removed in vacuo. Flash chromatography (hexanes/EtOAc = 10:1) gave **2k** and **2l** as an inseparable mixture (R_f = 0.7, 306.4 mg, 66%, 1.7:1, from ^{1}H NMR integration) as a colorless oil. The ^{1}H NMR and MS spectra were recorded on the mixture of **2k** and **2l**, the characteristic and resolved peaks are reported. **2k** (major component): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.98 (br d, J = 4.9 Hz, 2H), 1.06 (br dd, J = 4.9, 4.9 Hz, 1H), 1.18 (s, 9H), 1.53−1.78 <overlapped peaks>, 2.06 (dd, J = 16.9, 5.6 Hz, 1H), 2.15−2.40 <overlapped peaks>, 3.57 (br s, 1H), 5.31 (br d, J = 7.3 Hz, 1H). **2l** (minor component): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.98 (br d, J = 4.9 Hz, 2H), 1.06 (br dd, J = 4.9, 4.9 Hz, 1H), 1.18 (s, 9H), 1.53−1.78 <overlapped peaks>, 2.15−2.40 <overlapped peaks>, 3.57 (br s, 1H), 5.23 (br s, 1H); HRMS (EI, CH_4, 140 eV) m/z 232.1825 ([M]$^+$, 0.03), calcd for $C_{16}H_{24}O$ 232.1827. The syn and anti isomers were not distinguished.

***endo*-8-Tetracyclo[5.4.0.0^{2,4}.0^{3,7}]undec-9-enyl Acetate (2m).** To a solution of the active catalyst [CoI_2 (31.3 mg, 0.1 mmol), dppe (39.8 mg, 0.1 mmol) and Zn (32.7 mg, 0.5 mmol)] in $ClCH_2CH_2Cl$ (0.3 mL) in a pressure tube at room temperature under Ar was added a solution of **1a** (216 μL, 2.0 mmol) and 1-acetoxy-1,3-butadiene (cis/trans = 37:63, 56.1 mg, 0.5 mmol) in $ClCH_2CH_2Cl$ (0.2 mL) with stirring. The reaction vessel was immediately capped and the mixture heated to 80 °C in an oil path, and after 9 h, additional **1a** was added (216 μL, 2.0 mmol) and the mixture further heated for 36 h. After being cooled to room temperature, the reaction mixture was passed through a silica gel plug eluting with CH_2Cl_2 (3 × 5 mL). The washings were combined, and the solvent was

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(51) Perrin, D. D.; Armarego, W. L. F.; Perrin, D. R. *Purification of Laboratory Chemicals*, 2nd ed.; Pergamon: New York, 1980.

(52) Tabor, D. C.; White, F. H..; Collier, L. W., IV; Evans, S. A., Jr. *J. Org. Chem.* **1983**, *48*, 1638−1643.

(53) Nelson, S. F.; Seppanen, E. D. *J. Am. Chem. Soc.* **1967**, *89*, 5740−5742.

(54) Bicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxylic acid has been previously prepared from the cycloaddition of cyclopentadiene and acetylene dicarboxylic acid: (a) Diels, O.; Alder, K. *Liebigs Ann. Chem.* **1931**, *490*, 236−242. (b) Bartlett, P. D.; Roof, A. A. M.; Subramanyam, R.; Winter, W. J. *J. Org. Chem.* **1989**, *49*, 1875−1880.

(55) Monti, H.; Corriol, C.; Bertrand, M. *Tetrahedron Lett.* **1982**, *23*, 947−948.

(56) Lunt, J. C.; Sondheimer, F. *J. Chem. Soc.* **1950**, 3361−3367.

(57) Previous preparation reported only IR data: Nakuzaki, M.; Naemura, K.; Harada, H.; Narutaki, H. *J. Org. Chem.* **1982**, *47*, 3470−3474.

removed in vacuo. Flash chromatography (hexanes/EtOAc, 10:1) gave pure **2m** ($R_f = 0.5$, 24.7 mg, 24%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.90 (br dd, *J* = 5.2, 5.2 Hz, *H*2), 1.10 (br dd, *J* = 5.2, 5.2 Hz, *H*4), 1.16 (br dd, *J* = 5.2, 5.2 Hz, *H*3), 1.31 (dd, *J* = 1.4, 1.4 Hz, 2H: *H*5/5′), 1.76 (br s, *H*6), 1.77−1.79 (m, *H*1), 1.85−1.87 (m, *H*7), 2.07 (d, 3H: C*H*$_3$), 2.27 (dddd, $J = 17.9_{(AB)}$, 7.1, 3.1, 3.1 Hz, *H*11), 2.34 (m, *H*11′), 5.33 (ddd, *J* = 11.9, 4.6, 2.7 Hz, *H*9), 5.50−5.56 (m, 2H: *H*8/10); ^{13}C NMR (75 MHz, $CDCl_3$) 10.5 (*C*4), 11.5 (*C*3), 13.9 (*C*2), 21.5 (*C*H$_3$), 29.9 (*C*11), 36.3 (*C*5), 36.7 (*C*6), 41.1 (*C*1), 46.2 (*C*7), 74.0 (*C*8), 126.7 (*C*10), 129.4 (*C*9), 170.5 (*C*=O); IR (NaCl) 1757, 1736 cm^{-1}; HRMS (CI, NH_3, 140 eV) *m/z* 222.1482 ($[M + NH_4]^+$, 6.8), calcd for $C_{13}H_{20}O_2$ 222.1494. The stereochemistry at C8 was assigned by a NOESY experiment: H8 ↔ H6.

General Procedure for the [4 + 2 + 2] Homo-Diels−Alder Reactions of Bicyclo[2.2.2]octa-2,5-dienes 12 and 13a−c (Table 4). To a solution of $Co(acac)_2$ and DPPE (1.5 equiv relative to Co) in anhydrous toluene (see individual compounds for optimized amounts) in a pressure tube cooled to −30 °C under argon was added Et_2AlCl (10 equiv relative to Co, 1.8 M in toluene) dropwise with stirring, forming a brown solution. To this active catalyst solution at −30 °C was added the homodiene and 1,3-butadiene (see individual compounds for optimized amounts) either neat or as a solution in toluene as indicated below. The reaction vessel was capped and warmed to the desired temperature for the designated period of time with continuous stirring. After the mixture was cooled to room temperature, excess Et_2AlCl was quenched by the dropwise addition of MeOH until the reation mixture turned green (usually < 1 mL), then the solution was filtered by suction through a silica gel plug (2 cm) on a glass frit to remove the catalyst. The silica gel was washed with CH_2Cl_2 (3×5 mL) and the combined CH_2Cl_2 solutions (now colorless) were evaporated to dryness in vacuo to provide the crude product mixture. Flash chromatography gave the target cycloadducts as indicated below.

Tetracyclo[5.5.0.0^{2,4}.0^{3,8}]dodec-10-ene (14). Prepared according to the general procedure using **12** (212 mg, 2 mmol), 1,3-butadiene (1 mL, 11.65 mmol), $Co(acac)_2$ (103 mg, 0.40, mmol), and dppe (240 mg, 0.60 mmol) in toluene (2 mL). The reaction was maintained at 50 °C for 6 h and the product purified by flash chromatography (hexanes, $R_f = 0.8$) to give **14** as a colorless oil (278.4 mg, 87%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.79 (tt, *J* = 7.4, 2.4 Hz, 1H), 1.02 (br d, *J* = 7.4 Hz, 2H), 1.49 (m, 2H), 1.56 (br s, 1H), 1.77 (m, 2H), 2.01 (br dd, *J* = 3.4, 3.4 Hz, 2H), 2.15 (br dd, *J* = 16.4 Hz, 3.2 Hz, 2H), 2.30 (dddd, *J* = 16.4, 3.4, 3.4, 1.2 Hz, 2H), 5.42−5.44 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.6, 16.5, 22.0 (2C), 30.0, 35.6 (2C), 40.4 (2C), 43.9, 126.9 (2C); HRMS (CI, NH_3, 140 eV) *m/z* 160.1251 ($[M]^+$, 0.9) calcd for C_{12} H_{16} 160.1252.

5,6-*o*-Benzenotetracyclo[5.5.0.0^{2,4}.0^{3,8}]dodec-10-ene (15a). Prepared according to the general procedure using **13a** (548 mg, 3.6 mmol), 1,3-butadiene (2 mL, 21.9 mmol), $Co(acac)_2$ (46 mg, 0.18, mmol), and dppe (107 mg, 0.27 mmol) in toluene (12 mL). The reaction was maintained at 60 °C for 24 h and the product purified by flash chromatography (hexanes, $R_f = 0.4$) to give **15a** as a colorless oil (596.1 mg, 80%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.38 (dd, *J* = 7.4, 1.0 Hz, 2H), 1.49 (dd, *J* = 3.8, 2.9 Hz, 2H), 2.14 (t, *J* = 7.4 Hz, 1H), 2.34 (bdd, *J* = 16.1, 2.9 Hz, 2H), 2.46 (dddd, *J* = 16.1, 3.8, 3.8, 1.8 Hz, 2H), 2.60 (br s, 1H), 5.52 (m, 2H), 6.96 (dd, *J* = 7.3, 1.0 Hz, 1H), 7.04 (ddd, *J* = 7.3, 7.3, 1.0 Hz, 1H), 7.11 (ddd, *J* = 7.3, 7.3, 1.5 Hz, 1H), 7.22 (br d, *J* = 7.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.1, 20.7 (2C), 33.7 (2C), 38.5 (2C), 49.9, 122.3, 124.0, 125.7, 126.3, 126.8 (2C), 135.0, 143.4; HRMS (EI, 70 eV) *m/z* 208.1250 ($[M]^+$, 28), calcd for $C_{16}H_{16}$ 208.1252.

5,6-*o*-Tetrachlorobenzenotetracyclo[5.5.0.0^{2,4}.0^{3,8}]dodec-10-ene (15b). Prepared according to the general procedure using **13b** (100 mg, 0.34 mmol), 1,3-butadiene (1 mL, 11.65 mmol), $Co(acac)_2$ (17.5 mg, 0.068 mmol), and dppe (40.6 mg, 0.102 mmol) in toluene (2 mL). The reaction was maintained at 55 °C for 6 h and the product purified by flash chromatography (hexanes, $R_f = 0.6$) to give **15b** as a colorless oil (112.6 mg, 95%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.46 (dd, *J* = 3.8, 3.8 Hz, 2H), 1.55 (dd, *J* = 7.3, 1.0 Hz, 2H), 2.39 (br dd, *J* = 16.6, 3.0 Hz, 2H), 2.50 (dddd, *J* = 16.6, 3.8, 3.8, 1.8 Hz, 2H), 2.70 (t, *J* = 7.3 Hz, 1H), 3.25 (br s, 1H), 5.54 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.5, 21.4 (2C), 33.2 (2C), 37.5 (2C), 46.3, 126.3, 126.5 (2C), 128.0, 129.5, 130.4, 134.4, 140.6; HRMS (CI, NH_3, 140 eV) *m/z* 344.9780 ($[M + H]^+$), 0.12), calcd for $C_{16}H_{13}{}^{35}Cl_4$, 344.9772.

5,6-*o*-Tetrachlorobenzeno-7-methoxytetracyclo[5.5.0.-0^{2,4},0^{3,8}]dodec-10-ene (15c). Prepared according to the general procedure using **15c** (20 mg, 0.06 mmol), 1,3-butadiene (0.03 mL, 0.37 mmol), $Co(acac)_2$ (3.2 mg, 0.0124, mmol), and dppe (7.4 mg, 0.0186 mmol) in toluene (0.31 mL). The reaction was maintained at 100 °C for 53 h and the product purified by flash chromatography (3% CH_2Cl_2 in hexanes, $R_f = 0.7$) to give **15c** as a colorless oil (16.3 mg, 70%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.62 (d, *J* = 7.6 Hz, 2H), 1.78 (dd, *J* = 3.4, 2.4 Hz, 2H), 2.30 (dddd, *J* = 16.1, 3.9, 3.4, 2.0 Hz, 2H), 2.70 (br dd, *J* = 16.1, 2.4 Hz, 2H), 2.80 (t, *J* = 7.6 Hz, 1H), 3.53 (br s, 3H), 5.53 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.6, 22.2 (2C), 29.5 (2C), 40.7 (2C), 55.9, 88.3, 125.3, 126.2 (2C), 130.0, 130.3, 130.6, 137.0, 139.6; HRMS (CI, NH_3, 140 eV) *m/z* 373.9824 ($[M]^+$, 26), calcd for $C_{17}H_{14}O^{35}Cl_4$ 373.9800.

5,6-*o*-Tetrachlorobenzeno-7-methoxy-10-methyltetracyclo[5.5.0.0^{2,4}.0^{3,8}]dodec-10-ene (15d). Prepared according to the general procedure using **13d** (36.4 mg, 0.11 mmol), 1,3-butadiene (0.06 mL, 0.56 mmol), $Co(acac)_2$ (7.3 mg, 0.028 mmol), and dppe (16.9 mg, 0.042 mmol) in toluene (0.38 mL). The reaction was maintained at 110 °C for 48 h, and the product purified by flash chromatography (1% CH_2Cl_2 in hexanes, $R_f = 0.8$) to give **15d** as a colorless oil (21.2 mg, 48%) along with recovered **13d** (7.3 mg, 20%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.62 (d, *J* = 7.8 Hz, 2H), 1.71 (dd, *J* = 3.9, 3.4 Hz, 1H), 1.73 (dd, *J* = 3.9, 3.4 Hz, 1H), 1.77 (br s, 3H), 2.11 (dd, *J* = 17.4, 3.9 Hz, 1H), 2.21 (ddd, *J* = 17.8, 6.6, 3.9 Hz, 1H), 2.66 (br d, *J* = 17.4 Hz, 1H), 2.73 (br d, *J* = 17.8, 1H), 2.79 (t, *J* = 7.8 Hz, 1H), 3.52 (s, 3H), 5.32 (br d, *J* = 6.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.6, 22.1, 22.3, 27.8, 28.8, 34.0, 40.1, 40.5, 55.8, 87.9, 120.7, 125.4, 130.0, 130.3, 130.6, 133.2, 137.1, 139.4; HRMS (CI, NH_3, 140 eV) *m/z* 387.9940 ($[M]^+$, 1.5), calcd for $C_{18}H_{16}O^{35}Cl_4$ 387.9955.

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Supporting Information Available: Experimental procedures and characterization data for **1k**,**l**, **6a**,**b**, and **7a**,**b** and copies of ^{1}H and ^{13}C NMR spectra of previously unreported compounds **2c**,**i**,**k**/**l**,**m**, **6a**, **7a**/**b**, **14**, and **15a**−**d**. This material is available free of charge via the Internet at http://pubs.acs.org.

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