

$\rho_{\text{calc}} = 1.383 \text{ g cm}^{-3}$, $F(000) = 2256$, $\text{Mo}_{\text{K}\alpha}$ ($\lambda = 0.71069 \text{ \AA}$, $\mu(\text{Mo}_{\text{K}\alpha}) = 4.38 \text{ cm}^{-1}$; crystal dimensions $0.23 \times 0.29 \times 0.34 \text{ mm}$. For 2505 unique observed reflections [$I > 2\sigma(I)$] collected at $T = 295 \text{ K}$ on a Rigaku AFC6S diffractometer ($6 < 2\theta < 50^\circ$) the conventional R value is 0.026 ($wR2 = 0.043$ for the 4570 unique reflections having $I > 0$ used in the refinement). Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Center as supplementary publication no. CCDC-101526. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

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[12] The synthesis and structure of $[\text{Me}_8\text{N}_4\text{Na}_4(\text{thf})_2]$ will be reported in a forthcoming paper. The alternative use of the sodium instead of the lithium porphyrinogen is dictated by easier separation of NaCl from the reaction mixture.

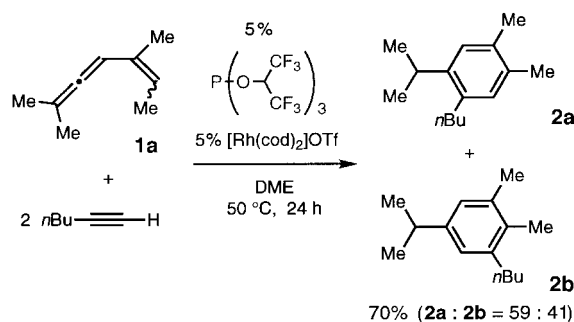
Rhodium-Catalyzed Intermolecular [4+2] Cycloaddition of Unactivated Substrates**

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Cycloaddition reactions have played a prominent role in the construction of complex cyclic compounds.^[1] In particular, [4+2] Diels–Alder cycloaddition is arguably the most important synthetic tool for the preparation of six-membered rings.^[2] Virtually the only requirement for [4+2] cycloaddition reactions to be effective is that the two components have complementary electronic properties. This is typically achieved by employing an electron-rich 1,3-diene and an electron-deficient dienophile. In fact, 1,3-dienes and dienophiles in which the multiple bonds are not activated by electron-withdrawing or electron-releasing substituents fail to undergo cycloaddition except under the most severe conditions. The use of transition metal catalysts has proven to be a valuable solution to this limitation. Complexation of unactivated substrates to such catalysts promotes both inter-^[3] and intramolecular^[4] [4+2] cycloadditions. Recently, we developed new [4+1] and [4+2] cycloaddition reactions of unactivated vinylallenes based on our study of their bonding interactions with transition metals.^[5–7] Here we report a rhodium-catalyzed intermolecular [4+2] cycloaddition reaction between a vinylallene and an ordinary alkyne which proceeds under mild conditions without the need for electron-withdrawing or electron-releasing substituents. With this method, 1,3,5-tri-

substituted benzene derivatives can be synthesized in a highly regioselective manner.

We first examined the reaction of vinylallene **1a** with the unactivated dienophile 1-hexyne in the presence of $[\text{Rh}(\text{dppe})(\text{cod})]\text{PF}_6$ (dppe = 1,2-bis(diphenylphosphanyl)ethane, cod = (Z,Z)-1,5-cyclooctadiene), a potent catalyst for the [4+1] cycloaddition of vinylallene with carbon monoxide.^[5a] However, [4+2] cycloaddition failed to occur even under forcing conditions,^[8] which led us to examine the electronic perturbation of the catalyst.^[9] Screening of various combinations of catalyst precursors and phosphorus ligands under different reaction conditions revealed that a complex prepared in situ from $[\text{Rh}(\text{cod})_2]\text{OTf}$ and $\text{P}[\text{OCH}(\text{CF}_3)_2]_3$, one of the most strongly electron-accepting ligands available, efficiently catalyzed the [4+2] cycloaddition.^[10] 1,2-Dimethoxyethane (DME) was the solvent of choice. Thus, a mixture of **1a**, 1-hexyne (2 equiv), $[\text{Rh}(\text{cod})_2]\text{OTf}$ (5 mol %), and $\text{P}[\text{OCH}(\text{CF}_3)_2]_3$ (5 mol %) in DME was heated at 50°C for 24 h (Scheme 1). Isomerization (i.e. aromatization) ensued after cycloaddition to afford the corresponding tetrasubstituted benzene in 70% yield as a mixture of regioisomers (**2a** and **2b**).



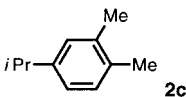
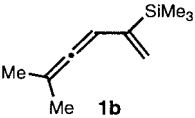
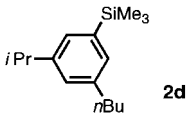
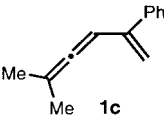
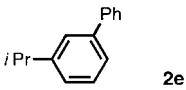
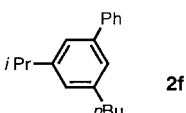
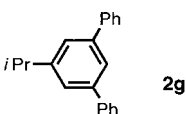
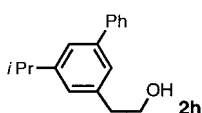
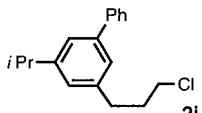
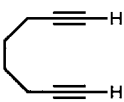
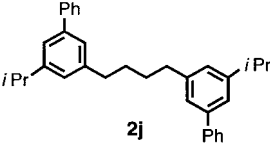
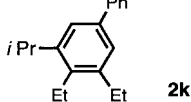
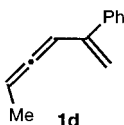
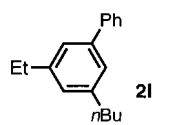
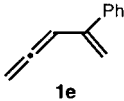
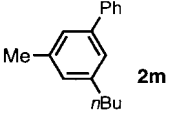
Scheme 1. [4+2] Cycloaddition of vinylallene **1a** with 1-hexyne.

A variety of substrates were allowed to react under the standard reaction conditions to produce the corresponding aromatic compounds (Table 1).^[11] It is noteworthy that synthetically useful results were obtained with substrates lacking directive heteroatom functionalities. For example, ethyne was found to be a reactive dienophile. Furthermore, when a terminal alkyne and a vinylallene lacking substituents at the vinylic terminus were used, 1,3,5-trisubstituted benzene derivatives (**2d**, **2f–j**) were produced in a highly regioselective manner.^[12] Hydroxyl and chloro functionalities are compatible with the present reaction conditions (**2h**, **2i**). In the case of 1,7-octadiyne, a tethered bis-benzene derivative (**2j**) was obtained in 82% yield, without formation of the [2+2+2] cycloadduct.^[13] An internal alkyne could also be employed in the reaction. Vinylallenes in which the allenic terminus is monosubstituted (**1d**) and nonsubstituted (**1e**) gave lower yields of the corresponding cycloadducts (**2l**, **2m**). These results can be explained in terms of the preference for η^2 over η^4 coordination. With **1d** and **1e**, η^2 coordination at the allenic π bond distal to the vinyl group would be favored over η^4 coordination owing to steric reasons.^[5a, 14]

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Table 1. [4+2] Cycloaddition of vinylallenes with alkynes.

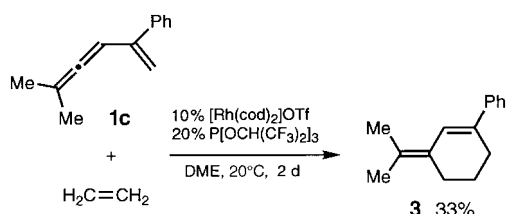
Vinylallene	Alkyne	Amount of alkyne	$T[^\circ\text{C}]$	$t[\text{h}]$	Product	Yield [%] ^[a]
1a	$\text{H}-\text{C}\equiv\text{C}-\text{H}$	10^6 Pa	20	16	 2c	93
 1b	$n\text{Bu}-\text{C}\equiv\text{C}-\text{H}$	2 equiv	20	3	 2d	87
 1c	$\text{H}-\text{C}\equiv\text{C}-\text{H}$	10^6 Pa	20	16	 2e	81
1c	$n\text{Bu}-\text{C}\equiv\text{C}-\text{H}$	1.5 equiv	20	2	 2f	84
1c	$\text{Ph}-\text{C}\equiv\text{C}-\text{H}$	2 equiv	70	40	 2g	48
1c	$\text{Ph}-\text{C}\equiv\text{C}-\text{H}$	2 equiv	70	72		55 ^[b]
1c	$\text{H}-\text{C}\equiv\text{C}-\text{CH}_2\text{CH}_2\text{OH}$	2 equiv	20	4	 2h	94
1c	$\text{H}-\text{C}\equiv\text{C}-\text{CH}_2\text{CH}_2\text{CH}_2\text{Cl}$	2 equiv	20	4	 2i	93
1c		0.3 equiv	70	23	 2j	82 ^[b, c]
1c	$\text{Et}-\text{C}\equiv\text{C}-\text{Et}$	1.3 equiv	60	13	 2k	65 ^[d]
 1d	$n\text{Bu}-\text{C}\equiv\text{C}-\text{H}$	5 equiv	20	48	 2l	24
 1e	$n\text{Bu}-\text{C}\equiv\text{C}-\text{H}$	5 equiv	20	96	 2m	15

[a] Yield of isolated product based on **1**. [b] 2 equiv of $\text{P}[\text{OCH}(\text{CF}_3)_2]_3$ based on Rh. [c] Yield of isolated product based on 1,7-octadiyne. [d] 5 equiv of $\text{P}[\text{OCH}(\text{CF}_3)_2]_3$ based on Rh.

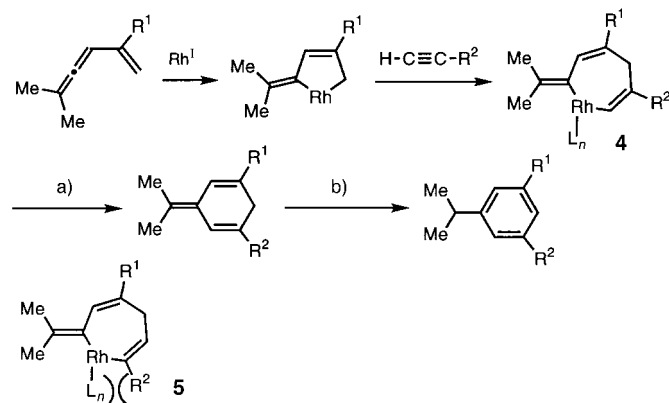
Under the present conditions, even ethene, one of the most sluggish dienophiles, underwent cycloaddition with **1c** to give cyclohexene **3** at temperatures as low as 20°C , albeit in low yield (33 %, Scheme 2).

A plausible mechanism for the production of **2** is shown in Scheme 3. A five-membered rhodacycle is initially formed

from the vinylallene substrate.^[5a, b] After coordination of the alkyne to the rhodium center, C–C bond formation takes place to afford a seven-membered rhodacycle. The regiochemical outcome observed with terminal alkynes can be regarded as a consequence of the selective formation of **4** by insertion of an alkyne into the $\text{Rh}-\text{C}_{\text{sp}^3}$ bond. Competing



Scheme 2. [4+2] Cycloaddition of vinylallene **1c** with ethene (2×10^6 Pa).



Scheme 3. Proposed mechanism of the rhodium-catalyzed [4+2] cycloaddition; a) reductive elimination, b) aromatization.

formation of a seven-membered rhodacycle with the alternative alkyne orientation (**5**) would be disfavored because of repulsive steric interactions between the alkyne substituent R^2 and the ligands on the metal. This interpretation also accounts for the nonregioselective cyclization of **1a**; the preference for an intermediate analogous to **4** would be balanced due to an additional steric interaction between the alkyne substituent R^2 and the methyl group at the vinylic terminus of **1a**.^[15] Finally, reductive elimination followed by isomerization completes the formation of the substituted arenes.

In summary, intermolecular [4+2] cycloaddition reactions of vinylallenes with alkynes, without the necessity of activating heteroatoms, is successfully mediated by use of an electronically tuned rhodium catalyst. Although the precise reason of the beneficial effect of employing an electron-accepting ligand is unclear, the present work indicates that optimization of a ligand set by electronic tuning will offer great potential for the regulated incorporation of unreactive substances, including readily available carbon feedstocks such as ethene and ethyne, into carbon skeletons.

Experimental Section

2a and **2b**: A mixture of $[\text{Rh}(\text{cod})_2]\text{OTf}$ (9.6 mg, 20.5 μmol), $\text{P}[\text{OCH}(\text{CF}_3)_2]_3$ (10.9 mg, 20.5 mmol), **1a** (50.0 mg, 409 μmol), and 1-hexyne (67.2 mg, 818 μmol) in DME (2 mL) was stirred at 50 °C for 24 h. After the mixture was cooled, the solvent was removed under vacuum. The residue was subjected to gel permeation chromatography to afford a mixture of **2a** and **2b** (58.2 mg, 70 %). **2a**: ^1H NMR (300 MHz, CDCl_3): δ = 0.94 (t, J = 7.3 Hz, 3H), 1.22 (d, J = 6.8 Hz, 6H), 1.35–1.45 (m, 2H), 1.48–1.58 (m, 2H), 2.20 (s, 3H), 2.23 (s, 3H), 2.57 (t, J = 7.9 Hz, 2H), 3.11 (septet, J = 6.8 Hz, 1H), 6.90 (s, 1H), 7.01 (s, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3): δ = 14.0, 19.2, 19.5, 22.9, 24.2, 28.2, 32.2, 34.3, 126.5, 130.8, 133.4, 134.0, 137.0, 143.8. **2b**: ^1H NMR (300 MHz, CDCl_3): δ = 0.95 (t, J = 7.3 Hz, 3H), 1.23 (d, J = 6.8 Hz, 6H), 1.35–1.45 (m, 2H), 1.48–1.58 (m, 2H), 2.16 (s, 3H), 2.27 (s, 3H), 2.60 (t, J = 7.7 Hz, 2H), 2.81 (septet, J = 6.8 Hz, 1H), 6.86

(s, 1H), 6.87 (s, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3): δ = 14.0, 14.7, 20.8, 22.9, 24.1, 33.0, 33.6, 34.0, 125.0, 125.5, 131.7, 136.6, 140.9, 145.7. Elemental analysis calcd for $\text{C}_{15}\text{H}_{24}$ (204.36): C 88.16, H 11.84; found: C 87.91, H 11.72.

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- [11] The use of two or more equivalents of $\text{P}[\text{OCH}(\text{CF}_3)_2]_3$ (based on rhodium) gave better yields of **2** in some cases, especially when heating was required.
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