Novel Ruthenium-Catalyzed Cross-Carbonylation of Alkynes and 2-Norbornenes to Hydroquinones

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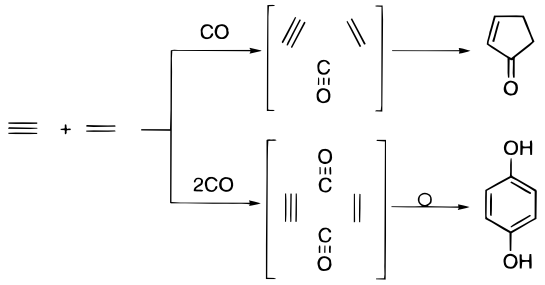
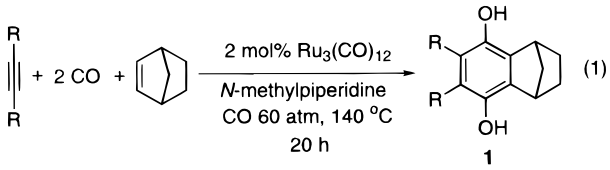
Summary: Unsymmetrically substituted hydroquinones were obtained in high yields by the novel ruthenium-catalyzed cross-carbonylation of alkynes and 2-norbornenes. For example, treatment of 4-octyne and 2-norbornene with 2 mol % $Ru_3(CO)_{12}$ in N-methylpiperidine under 60 atm of carbon monoxide at 140 °C for 20 h gave the corresponding hydroquinone, 4,5-dipropyltricyclo[6.2.1.0^{2,7}]undeca-2(7),3,5-triene-3,6-diol, in 85% yield. The reaction apparently involves a maleoylruthenium intermediate which is generated by the reaction of an alkyne and two molecules of carbon monoxide on the ruthenium.

Metal-mediated [2 + 2 + 1] cocyclization of alkynes, alkenes, and carbon monoxide to produce cyclopentenones, represented by the Pauson−Khand reaction, is now established as an important route to natural products and novel materials.[1] Many advances relating to this method have recently been reported, including the development of cyclization using a catalytic amount of complexes with transition metals, such as Co,[2] Ti,[3] and Ru.[4] In sharp contrast, neither the metal-mediated nor metal-catalyzed cocyclization of alkynes, alkenes, and two molecules of carbon monoxide to produce hydroquinones has yet been reported (Scheme 1), although Reppe's synthesis of hydroquinone from two molecules of alkyne and two molecules of carbon monoxide in the presence of water is well-known.[5]

Since hydroquinone and its derivatives are important in the chemical industry as a photographic developer, polymerization inhibitor, antioxidant, and intermediates for numerous dyes, they have recently been the subject of increasing interest.[6] On the basis of our study of ruthenium-catalyzed carbonylation reactions,[4a,7] we have found the first example of the ruthenium-catalyzed cross-carbonylation of alkynes and alkenes. We report here the development of this new catalyst system for the selective synthesis of unsymmetrically substituted hydroquinones from alkynes, 2-norbornenes, and carbon monoxide (eq 1).

Scheme 1





The effects of the catalyst and the solvent as well as the molar ratio of 2-norbornene to alkyne were examined in the reaction of 4-octyne with 2-norbornene. The results are summarized in Table 1 and Figure 1. Among the catalysts examined, $Ru_3(CO)_{12}$ showed the highest catalytic activity. Several other ruthenium complexes, such as $[RuCl_2(CO)_3]_2$ and $[(\eta^6\text{-}C_6H_6)RuCl_2]_2$, were also effective, but 2,3,5,6-tetrapropylcyclohexa-2,5-diene-1,4-dione (**2**), which is the normal Reppe's reaction product, was obtained as a byproduct (4% and 14% yields, respectively). A considerable amount of **2** was also obtained in *N*,*N*-dimethylacetamide, acetonitrile, toluene, or THF. The selective production of **1a** was attained using $Ru_3(CO)_{12}$ in *N*-methylpiperidine.[8] Attempts to effect cross-carbonylation at temperatures lower than 120 °C resulted in drastically diminished

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(7) (a) Mitsudo, T.; Suzuki, N.; Kondo, T.; Watanabe, Y. *J. Org. Chem.* **1994**, *59*, 7759. (b) Kondo, T.; Kodoi, K.; Mitsudo, T.; Watanabe, Y. *J. Chem. Soc., Chem. Commun.* **1994**, 755. (c) Mitsudo, T.; Suzuki, N.; Kondo, T.; Watanabe, Y. *J. Mol. Catal., A: Chemical* **1996**, *109*, 219.

(8) We have already found that *N*-methylpiperidine is the best solvent in several ruthenium-catalyzed reactions. (a) Mitsudo, T.; Zhang, S.-W.; Satake, N.; Kondo, T.; Watanabe, Y. *Tetrahedron Lett.* **1992**, *33*, 5533. (b) Zhang, S.-W.; Mitsudo, T.; Kondo, T.; Watanabe, Y. *J. Organomet. Chem.* **1993**, *450*, 197. (c) Zhang, S.-W.; Mitsudo, T.; Kondo, T.; Watanabe, Y. *J. Organomet. Chem.* **1995**, *485*, 55.

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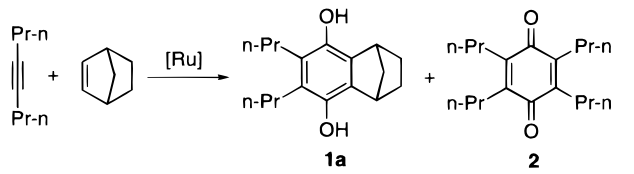
Table 1. Effects of the Catalyst and the Solvent on the Synthesis of 1a by Cross-Carbonylation of 4-Octyne and 2-Norbornene[a]



catalyst	solvent	yield[b] (%) 1a	2
$Ru_3(CO)_{12}$	*N*-methylpiperidine	85(72)	trace
$Ru_3(CO)_{12}$	*N*,*N*-dimethylacetamide	78	14
$Ru_3(CO)_{12}$	CH_3CN	78	20
$Ru_3(CO)_{12}$	toluene	61	35
$Ru_3(CO)_{12}$	THF	51	32
$[RuCl_2(CO)_3]_2$	*N*-methylpiperidine	76	4
$[(\eta^6\text{-}C_6H_6)RuCl_2]_2$	*N*-methylpiperidine	64	14
$RuCl_2(PPh_3)_3$	*N*-methylpiperidine	trace	trace
$RuH_2(PPh_3)_4$	*N*-methylpiperidine	trace	trace

[a] 4-Octyne (2.5 mmol), 2-norbornene (7.5 mmol), solvent (2.0 mL), Ru complex (0.15 mmol as metal atom), CO (60 atm), 140 °C, 20 h. [b] Determined by GLC based on the amount of 4-octyne charged. Number in parentheses is an isolated yield.

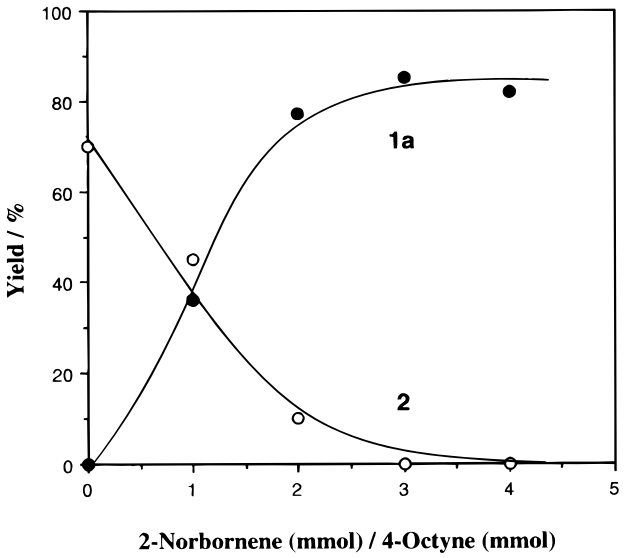


Figure 1. Effect of the molar ratio of 2-norbornene/4-octyne on the synthesis of **1a** by $Ru_3(CO)_{12}$-catalyzed cross-carbonylation of 4-octyne and 2-norbornene. Reaction conditions: $Ru_3(CO)_{12}$ (0.050 mmol), *N*-methylpiperidine (2.0 mL), 4-octyne (2.5 mmol), CO (60 atm), 140 °C, 20 h.

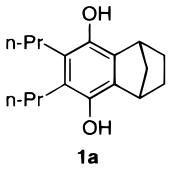
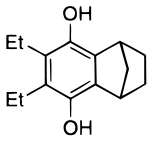
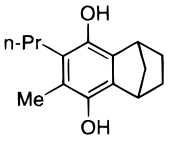
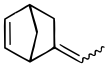
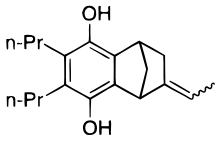
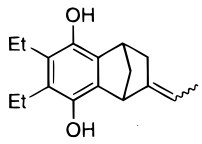
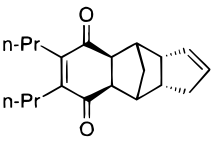
conversion to product. However, the reaction is not sensitive to CO pressure from 20 (**1a**, 72%) to 80 atm (**1a**, 90%).

In addition, the present reaction is strongly affected by the molar ratio of 2-norbornene to 4-octyne (Figure 1). The treatment of 4-octyne with an equimolar amount of 2-norbornene gave the corresponding hydroquinone **1a** in only 35% yield together with byproduct **2** (45% yield). The best result was obtained by using an excess (3-fold) amount of 2-norbornene to 4-octyne (**1a**, 85% yield).[9]

The results obtained for several alkynes and 2-norbornenes under optimum conditions are listed in Table

(9) Excess norbornene substrates used in the present reaction can be recovered from the product mixture. For example, 3.1 mmol of 2-norbornene (41%) was recovered after the cross-carbonylation of 4-octyne with 2-norbornene.

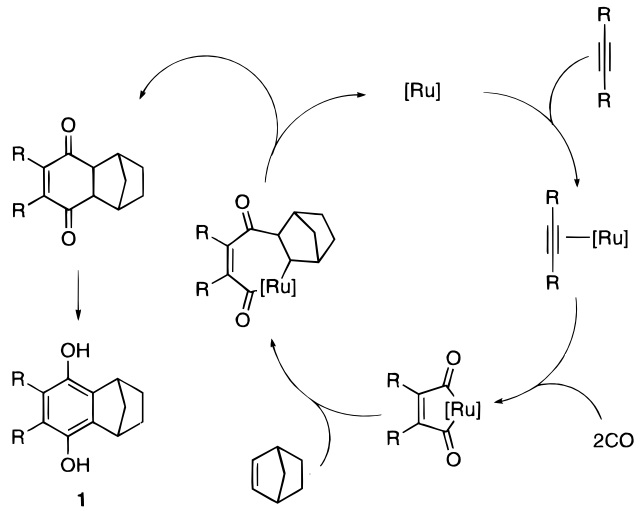
Table 2. $Ru_3(CO)_{12}$-Catalyzed Cross-Carbonylation of Alkynes and 2-Norbornenes[a]

alkyne	2-norbornene derivative	product	yield[b] (%)
		 **1a**	72
		 **1b**	65
		 **1c**	83
		 **1d**	98
		 **1e**	75
		 **1f**	74

[a] Alkyne (2.5 mmol), 2-norbornene derivative (7.5 mmol), $Ru_3(CO)_{12}$ (0.050 mmol), *N*-methylpiperidine (2.0 mL), CO (60 atm), 140 °C, 20 h. [b] Isolated yield.

2. In all cases, starting alkynes were completely consumed and the corresponding hydroquinones were obtained in high yields. No byproduct, such as **2**, could be detected by GLC. It should be noted that the norbornene skeleton is essential for the present reaction. For example, the reaction of 5-ethylidene-2-norbornene with either 4-octyne or 3-hexyne exclusively gave hydroquinones **1d** and **1e** in yields of 98% and 75%, respectively, which means that the reaction selectively occurred on the olefinic moiety in the norbornene skeleton rather than on the ethylidene moiety. Attempts to obtain hydroquinones with less strained or less reactive alkenes, e.g., ethylene, 1-hexene, and cyclopentene, were not successful. No reaction occurred with terminal alkynes, such as 1-octyne, phenylacetylene, and methyl prop-2-ynoate. In the reaction of 4-octyne with dicyclopentadiene, the primary product

Scheme 2



changed from hydroquinone to cyclohex-2-en-1,4-dione (**1f**), probably due to the limited further isomerization to hydroquinone.

While the reaction mechanism is not yet clear, we believe that a maleoylruthenium complex, which would be obtained by the reaction between an alkyne and two molecules of carbon monoxide on the ruthenium, is a key intermediate in the present reaction (Scheme 2). It then reacts with 2-norbornenes by insertion−reductive elimination and further isomerization to give the hydroquinones. Although the reaction of several maleoyl metal complexes with alkynes has been studied in detail,[10] the reaction with alkenes has not yet been reported.

In conclusion, we have found the first practically useful catalytic system for the formation of hydroquinones from alkynes, alkenes, and carbon monoxide. This reaction will open up new opportunities in maleoyl metal chemistry.

Experimental Section

General. GLC analyses were carried out on gas chromatographs equipped with a glass column (3 mm i.d. × 3 m) packed with Silicone OV-17 (2% on Chromosorb W(AW-DMCS), 80−100 mesh) and a capillary column (Shimadzu capillary column HiCap-CBP10-M25-025 (polarity similar to OV-1701); 0.22 mm i.d. × 25 m). The ^{1}H NMR spectra were recorded at 270 and/or 400 MHz. ^{13}C NMR spectra were recorded at 68 and/or 100 MHz. Samples were analyzed in THF-d_8 and $CDCl_3$, and the chemical shift values are expressed relative to Me_4Si as an internal standard. High-resolution mass spectra (HRMS) were obtained on a JEOL JMS-SX102A mass spectrometer. Elemental analyses were performed at the Microanalytical Center of Kyoto University.

Materials. The reagents used in this study were dried and purified before use by standard procedures. Carbon monoxide (>99.9%) was used without further purification. $Ru_3(CO)_{12}$ and $[RuCl_2(CO)_3]_2$ were obtained commercially and used without further purification. $[(\eta^6\text{-}C_6H_6)RuCl_2]_2$,[11] $RuCl_2(PPh_3)_3$,[12] and $RuH_2(PPh_3)_4$[13] were prepared as described in the literature. All of the new compounds are characterized below.

Ruthenium-Catalyzed Cross-Carbonylation of Alkynes and 2-Norbornenes. A mixture of an alkyne (2.5 mmol), a 2-norbornene derivative (7.5 mmol), $Ru_3(CO)_{12}$ (0.032 g, 0.050 mmol), and *N*-methylpiperidine (2.0 mL) was placed in a 50 mL stainless autoclave. Carbon monoxide was then pressurized to 60 atm at room temperature, and the mixture was magnetically stirred at 140 °C for 20 h. After the reaction mixture was cooled, the products were isolated by Kugelrohr distillation.

4,5-Dipropyltricyclo[6.2.1.0^{2,7}]undeca-2(7),3,5-triene-3,6-diol (1a): White solid; mp 128 °C; bp 120−125 °C (1.0 mmHg, Kugelrohr); ^{1}H NMR (400 MHz, THF-d_8) δ 0.94 (t, J = 7.4 Hz, 6H), 1.13 (d, J = 6.9 Hz, 2H), 1.39 (d, J = 7.9 Hz, 1H), 1.45−1.51 (m, 4H), 1.53 (d, J = 7.9 Hz, 1H), 1.79 (d, J = 6.9 Hz, 2H), 2.52 (m, 4H), 3.49 (s, 2H), 6.57 (s, 2H); ^{13}C{^{1}H} NMR (100 MHz) δ 14.9, 24.6, 27.7, 29.7, 40.9, 49.1, 127.1, 131.2, 142.2; MS (70 eV) m/z 260 (M^+). Anal. Calcd for $C_{17}H_{24}O_2$: C, 78.42; H, 9.29. Found: C, 78.27; H, 9.45.

4,5-Diethyltricyclo[6.2.1.0^{2,7}]undeca-2(7),3,5-triene-3,6-diol (1b): White solid; mp 137 °C; bp 120−125 °C (1.0 mmHg, Kugelrohr); ^{1}H NMR (270 MHz, THF-d_8) δ 1.06 (t, J = 7.8 Hz, 6H), 1.13 (d, J = 8.3 Hz, 2H), 1.39 (d, J = 8.3 Hz, 1H), 1.56 (d, J = 8.3 Hz, 1H), 1.79 (d, J = 8.3 Hz, 2H), 2.52−2.66 (m, 4H), 3.49 (s, 2H), 6.61 (s, 2H); ^{13}C{^{1}H} NMR (68 MHz) δ 15.9, 20.8, 28.1, 41.2, 49.5, 128.6, 131.6, 142.4; MS (70 eV) m/z 232 (M^+). Anal. Calcd for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68. Found: C, 77.27; H, 8.88.

4-Ethyl-5-methyltricyclo[6.2.1.0^{2,7}]undeca-2(7),3,5-triene-3,6-diol (1c): White solid; mp 136 °C; bp 110−115 °C (1.0 mmHg, Kugelrohr); ^{1}H NMR (270 MHz, THF-d_8) δ 0.93 (t, J = 7.8 Hz, 3H), 1.10−1.14 (m, 2H), 1.39 (d, J = 8.3 Hz, 1H), 1.40−1.50 (m, 2H), 1.53−1.57 (m, 1H), 1.77−1.80 (m, 2H), 2.07 (s, 3H), 2.45−2.62 (m, 2H), 3.49 (s, 2H), 6.59 (s, 1H), 6.63 (s, 1H); ^{13}C{^{1}H} NMR (68 MHz) δ 12.1, 14.7, 23.8, 27.6, 27.7, 29.7, 40.9 (two overlapping signals), 49.1, 121.9, 127.3, 131.0, 131.1, 142.1, 142.5; MS (70 eV) m/z 260 (M^+). Anal. Calcd for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68. Found: C, 77.05; H, 8.65. Exact mass calcd for $C_{15}H_{20}O_2$: 232.1463. Found: 232.1457.

9-Ethylidene-4,5-diisopropyltricyclo[6.2.1.0^{2,7}]undeca-2(7),3,5-triene-3,6-diol (1d): White solid; mp 164 °C; bp 130−135 °C (1.0 mmHg, Kugelrohr); ^{1}H NMR (400 MHz, THF-d_8) δ 0.94 (t, J = 8.3 Hz, 3H), 0.95 (t, J = 8.3 Hz, 3H), 1.46 (d, J = 6.8 Hz, 3H), 1.45−1.51 (m, 4H), 1.58 (d, J = 8.3 Hz, 1H), 1.72−1.80 (m, 2H), 2.32 (d, J = 14.7 Hz, 1H), 2.44−2.59 (m, 4H), 3.59 (s, 1H), 3.79 (s, 1H), 5.45 (q, J = 6.8 Hz, 1H), 6.56 (s, 1H), 6.67 (s, 1H); ^{13}C{^{1}H} NMR(100 MHz) δ 14.7, 14.9 (two overlapping signals), 24.5, 24.6, 29.8 (two overlapping signals), 33.5, 40.6, 49.4, 50.7, 112.8, 127.2, 127.3, 129.6, 131.0, 142.4, 142.6, 143.6; MS (70 eV) m/z 286 (M^+). Anal. Calcd for $C_{19}H_{26}O_2$: C, 79.68; H, 9.15. Found: C, 79.61; H, 9.34.

9-Ethylidene-4,5-diethyltricyclo[6.2.1.0^{2,7}]undeca-2(7),-3,5-triene-3,6-diol (1e): White solid; mp 154 °C; bp 140−145 °C (1.0 mmHg, Kugelrohr); ^{1}H NMR (400 MHz, THF-d_8) δ 1.06 (t, J = 7.3 Hz, 3H), 1.07 (t, J = 7.3 Hz, 3H), 1.46 (d, J = 6.3 Hz, 3H), 1.58 (d, J = 8.3 Hz, 1H), 1.74−1.80 (m, 2H), 2.30−2.34 (m, 1H), 2.54−2.62 (m, 4H), 3.58 (s, 1H), 3.81 (s, 1H), 5.47 (q, J = 6.8 Hz, 1H), 6.74 (s br, 2H); ^{13}C{^{1}H} NMR (100 MHz) δ 14.0, 14.8 (two overlapping signals), 19.7 (two overlapping signals), 32.8, 39.9, 48.7, 50.1, 112.2, 127.7, 127.8, 129.0, 130.4, 141.4, 141.7, 142.9; MS (70 eV) m/z 258 (M^+). Anal. Calcd for $C_{17}H_{22}O_2$: C, 78.86; H, 8.61. Found: C, 79.03; H, 8.58.

***rel*-(2*R*,7*S*,9*R*,13*R*)-4,5-Dipropyltetracyclo[6.5.1.0^{2,7}.-0^{9,13}] tetradeca-4,10-diene-3,6-dione (1f):** Colorless liquid; bp 140 °C (1.0 mmHg); IR (neat) 1661 (C=O) cm^{-1}; ^{1}H NMR

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(13) Young, R.; Wilkinson, G. *Inorg. Synth.* **1977**, *17*, 75.

(400 MHz, $CDCl_3$) δ 0.96 (t, J = 7.3 Hz, 6H), 1.28−1.36 (m, 2H), 1.32−1.47 (m, 4H), 2.30−2.38 (m, 2H), 2.35−2.51 (m, 4H), 2.59 (d, J = 5.1 Hz, 1H), 2.60 (d, J = 8.7 Hz, 1H), 2.66 (m, 1H), 2.70 (d, J = 8.7 Hz, 1H), 2.87 (d, J = 5.1 Hz, 1H), 3.15−3.24 (m, 1H), 5.62−5.65 (m, 1H), 5.71−5.74 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz) δ 14.4 (two overlapping signals), 22.4 (two overlapping signals), 29.2 (two overlapping signals), 32.6, 37.5, 42.2, 45.6, 46.3, 47.2, 49.2, 52.4, 131.7, 132.0, 151.1, 151.5, 199.5, 200.0; MS (70 eV) m/z 298 (M^+). Anal. Calcd for $C_{20}H_{26}O_2$: C, 80.50; H, 8.78. Found: C, 80.00; H, 8.83. Exact mass calcd for $C_{20}H_{26}O_2$: 298.1933. Found: 298.1934.

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