Pt- and Au-catalyzed oxidative cyclization of 2-ethenyl-1-(prop-2′-yn-1′-ol)benzenes to naphthyl aldehydes and ketones: catalytic oxidation of metal-alkylidene intermediates using H_2O and H_2O_2†

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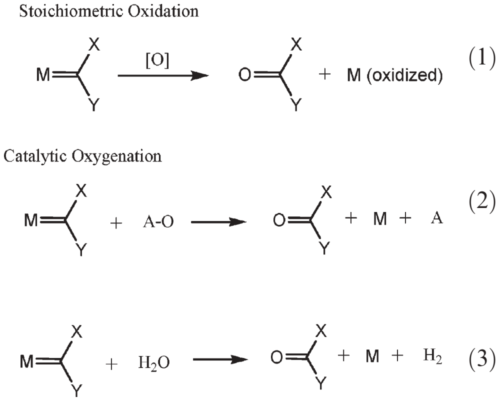
Received (in Cambridge, UK) 16th January 2007, Accepted 2nd March 2007
First published as an Advance Article on the web 20th March 2007
DOI: 10.1039/b700659d

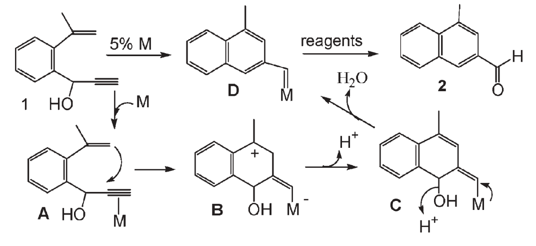
2-Ethenyl-1-(prop-2′-yn-1′-ol)benzenes was cyclized through catalytic oxidation with $PtCl_2/CO/H_2O$ and PEt_3AuCl/H_2O_2; the metal–naphthylidene intermediates were identified and oxygenated with water and H_2O_2, respectively; for the efficiency of cyclization, the Au catalytic system is superior to that of the $PtCl_2$-catalysis because of its compatibility toward diverse alcohol substrates including both internal alkynes and terminal alkynes.

One advance in contemporary catalytic science is the generation of reactive metal carbenoids from metal-implemented cyclization of acyclic organic alkynes; this approach avoids the use of hazardous diazoalkane precursors.[1–5] Pt(II) and Au(I) carbenoids generated in this protocol are catalytically active in diversified reaction modes including cyclopropanation of olefins,[2] C–H bond insertion into sp^2- (or sp^3)-hydrocarbons,[3] formation of alkenes *via* a 1,2-hydrogen shift,[4] and skeletal rearrangement of enynes.[1] Organic carbonyl compounds are important functionalities, and formation of these species *via* oxidation of metal carbenoid species has attracted considerable attention.[5–7] Most literature reports focused on the use of oxidant reagents; in such cases metal–carbene species are used in stoichiometric proportion because of an inevitable oxidation of metal species (eqn (1)).[5] To the best of our knowledge, very few examples[6,7] were reported for catalytic oxidation of metal–carbenoid intermediates generated from alkyne precursors. Trost and co-workers.[6] reported the use of *N*-hydroxysuccinimide to oxygenate ruthenium–oxacarbene intermediates generated in catalytic cyclization of 1-alkyn-4-ols; this protocol is depicted in eqn (2). An alternative approach involves the use of water,[7] which undergoes disproportion into hydrogen gas and organic carbonyl compounds as depicted in eqn (3); such a process has been postulated in Rh(I)-catalyzed oxidative cyclization of enynebenzaldehydes without mechanistic evidences.[7] We report here a new catalytic oxidative cyclization of 2-ethenyl-1-(prop-2′-yn-1′-ol)benzenes using Au(I)/H_2O_2 and Pt(II)/H_2O catalytic systems, corresponding to protocols in eqn (2) and (3), respectively.‡



Trost's oxidative cyclization is limited strictly to ruthenium oxacarbenes, which are likely too stable to be oxygenated by water and other mild oxidants such as H_2O_2. 2-Ethenyl-1-(prop-2′-yn-1′-ol)benzene **1** was selected for study because it is a designed precursor for generation of reactive metal–naphthylidene intermediate **D** as depicted in Table 1. Treatment of alcohol **1** with $PtCl_2$ (5 mol%) in dry THF at 25 °C for 48 h produced naphthyl aldehyde **2** in 41% yield with recovery of substrate **1** in 47% yield.

Table 1 Catalytic oxidative cyclization of 2-ethenyl-1-(prop-2′-yn-1′-ol) **1** with various catalysts



Entry	Catalyst (M)[a,b]	Reagent	*T*/°C (*t*/h)	Yield[a] **2** (%)
1	$PtCl_2$	—	25 (48)	41
2	$PtCl_2$	H_2O	25 (4)	69
3	$PtCl_2/CO$	H_2O	25 (4)	75
4	$PPh_3AuCl/AgOTf$	H_2O	25 (8)	55
5	$PPh_3AuCl/AgSbF_6$	H_2O	25 (8)	17
6	PPh_3AuCl	H_2O	70 (8)	15
7	PPh_3AuCl	H_2O_2	70 (6)	74
8	PEt_3AuCl	H_2O_2	70 (6)	80
9	AuCl	H_2O_2	70 (6)	31
10	$AuCl_3$	H_2O_2	70 (6)	26
11	$PtCl_2/CO$	H_2O_2	70 (6)	56

[a] 25 °C for $PtCl_2$, 20 equiv. H_2O, [substrate] = 0.27 M THF. [b] 70 °C, H_2O_2 (3 equiv.), DCE, [substrate] = 0.27 M. [c] Yields are reported after purification on silica column.

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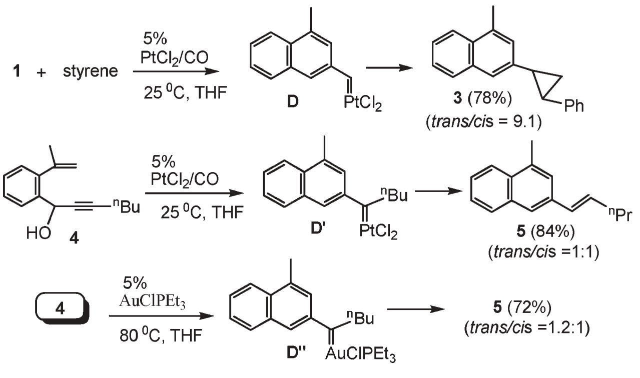
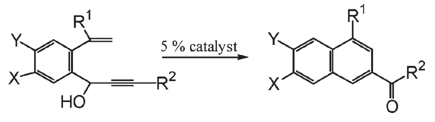
† Electronic supplementary information (ESI) available: (1) Theoretical calculation for oxygenation of Pt-carbenoids with water. (2) Experimental procedures for the metal-catalyzed cyclization, cyclopropanation and measurement of hydrogen evolvement. (3) Spectral data for compounds **1**–**42**. See DOI: 10.1039/b700659d



Scheme 1

In the presence of water (20 equiv. entries 2, 3), the yield of aldehyde **2** was increased to 69% at short times (4 h), and further improved to 75% in the presence of CO (1 atm).[8] In entry 3, the content of H_2 in the gaseous phase as determined by GC-analysis (MS-5A column) amounted to 34% of the theoretical value. The proportion of hydrogen in the THF solution was not determined. The cationic Au catalysts PPh_3AuOTf, PPh_3AuSbF_6 and PPh_3AuCl were less efficient for production of aldehyde **2** (yields < 55%, entries 4–6). In the presence of aqueous H_2O_2 solution (30%, 3 equiv.), PPh_3AuCl (5%) and its triethylphosphine (5%) analogue showed effective catalytic efficiency in hot dichloroethane (DCE, 70 °C) and gave the desired aldehyde **2** in 74–80% yields (entries 7, 8). This H_2O_2-oxidation method failed to work efficiently with AuCl and $AuCl_3$, which gave aldehyde **2** in low yields (<30%) (entries 9, 10). In the $PtCl_2$/CO system, the use of H_2O_2 gave aldehyde **2** less efficiently (56%) than the water case (75%).

Table 2 Catalytic oxidative cyclization of various 2-ethenyl-1-(prop-2′-yn-1′-ol)benzenes



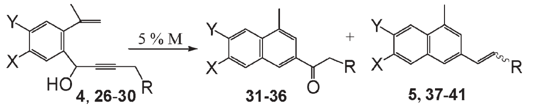
Entry	Substrate	Product	Yield^a (%) (t/h)	
			$PtCl_2$/ H_2O^b	PEt_3AuCl/ $H_2O_2{}^c$
1	R^1 = Me; X = Y = H; R^2 = Ph (**6**)	**16**	48 (55)	76 (24)
2	R^1 = Me; X = Y = H; R^2 = CO_2Me (**7**)	**17**	Messy (10)	81 (8)
3	R^1 = Me; X = Y = H; R^2 = 2-thienyl (**8**)	**18**	78 (38)	65 (17)
4	R^1 = Me; X = Y = H; R^2 = 2-furyl (**9**)	**19**	68 (48)	81 (19)
5	R^2 = X = Y = H; R^1 = Ph (**10**)	**20**	75 (4)	77 (5)
6	R^1 = Me; X = R^2 = H; Y = F (**11**)	**21**	85 (3)	90 (6)
7	R^1 = Me; X = R^2 = H; Y = OMe (**12**)	**22**	80 (4)	82 (6)
8	R^1 = Me; Y = R^2 = H; X = F (**13**)	**23**	83 (4)	91 (6)
9	R^1 = Me; Y = R^2 = H; X = OMe (**14**)	**24**	81 (3)	85 (6)
10	R^1 = Me; R^2 = H; X, Y = –OCH_2O– (**15**)	**25**	78 (4)	83 (6)

[a] Yields were reported after purification on silica column. [b] 25 °C, CO (1 atm), 20 equiv. H_2O, [substrate] = 0.27 M, THF, [c] 70 °C, H_2O_2, (3 equiv.), DCE, [substrate] = 0.27 M.

Scheme 1 shows our experimental evidence to support the formation of platinum–naphthylidene intermediate **D**. $PtCl_2$-catalyzed cyclization of alcohol **1** with styrene (10 equiv.) in dry THF at 25 °C gave a 78% yield of cyclopropane product **3** that is thought to arise from the cyclopropanation of platinum–naphthylidene intermediate **D**.[2,9] Treatment of alcohol **4** with $PtCl_2$/CO alone led to formation of olefin product **5** (84%), presumably generated from a 1,2-hydrogen shift of hypothetical platinum–alkylidene intermediate **D**′.[3,10] Compound **5** was also obtained in 72% yield upon heating alcohol **4** with PEt_3AuCl (5%) in dichloroethane (DCE), indicative of formation of a similar Au–alkylidene intermediate **D**″. The formation mechanism of carbene species **D** is proposed to involve 6-*exo-dig* cyclization of Pt–alkyne species **A**, followed by deprotonation of intermediate **B** and proton-catalyzed dehydroxylation of vinylplatinum species **C** as depicted in Scheme 1. In this catalytic sequence, one molecule of water is released before the formation of platinum–naphthylidene intermediate **D**, as depicted in Table 1; the added water serves to accelerate the reaction that is intrinsically slow in dry THF because water is a poor nucleophile (see entry 1, Table 1).

As shown in Table 2 we have prepared various 2-ethenyl-1-(prop-2′-yn-1′-ol)benzenes **6–15** to assess the generality of this catalytic oxidative cyclization using $PtCl_2$/CO/H_2O and PEt_3AuCl/H_2O_2 respectively; the former was performed at 25 °C in wet THF and the latter was heated with H_2O_2 (3 equiv.) in DCE at 70° for 6 h. Entries 1–5 show the oxidative cyclization of internal alkynes **6–9** bearing aryl, methoxycarbonyl, thienyl and furyl groups respectively; the Au-catalysis seems superior to the platinum system in the production of ketone compounds **16–18** except thienyl product **18**. We prepared also various terminal alkynes **10–15** bearing fluoro, methoxy and methylenedioxy groups at the phenyl X- and Y-positions, and catalytic oxidations of these substrates proceeded smoothly in the two catalytic systems; the resulting aldehydes were obtained with yields exceeding 75%.

Table 3 Catalytic oxidative cyclization of various 2-ethenyl-1-(prop-2′-yn-1′-ol)benzenes

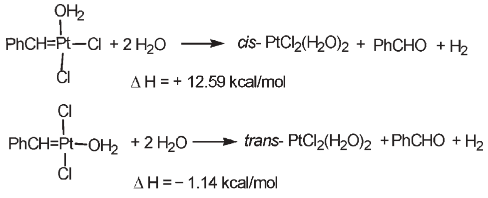


Entry	Substrate	Product	Yield^a (%)	
			$PtCl_2/H_2O^b$	$AuClPEt_3/H_2O_2{}^c$
1	X = Y = H,	**31**	6	83
	R = ^{n}Pr (**4**)	**5**	78	—
2	X = Y = H,	**32**	4	80
	R = H (**26**)	**37**	68	—
3	X = OMe, Y = H,	**33**	3	89
	R = $^nC_7H_{15}$ (**27**)	**38**	84	3
4	X = H, Y = OMe,	**34**	4	82
	R = $^nC_7H_{15}$ (**28**)	**39**	83	4
5	X, Y = –OCH_2O–,	**35**	7	83
	R = $^nC_7H_{15}$ (**29**)	**40**	78	—
6	X = F, Y = H,	**36**	3	80
	R = $^nC_7H_{15}$ (**30**)	**41**	85	—

[a] Yields were reported after purification on silica column. [b] 25 °C, CO (1 atm), 20 equiv. H_2O, [substrate] = 0.27 M THF. [c] 70 °C, H_2O_2(3 equiv.) DCE, [substrate] = 0.27 M.

The metal–naphthylidene intermediates in the preceding oxidative cyclizations are considered to be kinetically stable because of the lack of a C$_\beta$-alkyl hydrogen for a competitive 1,2-hydrogen shift.[10] We therefore studied oxidative cyclization of alcohol **4** with PEt$_3$AuCl/H$_2$O$_2$ in hot dichloroethane (70 °C, 6 h), which afforded desired ketone **31** with a yield up to 83% whereas olefin product **5** (78%) was dominant over ketone **31** (6%) in the PtCl$_2$/H$_2$O catalysis, as depicted in Table 3 (entry 1). For this Au-catalyzed cyclization, the preference for the oxygenation reaction is manifested with additional examples shown in Table 3. We prepared also benzyl alcohols **26–30** with alternative alkynyl CH$_2$R (R = *n*-propyl or *n*-heptyl) substituents as well as phenyl X, Y groups (entries 2–6); PEt$_3$AuCl/H$_2$O$_2$ effects the efficient transformation of these alcohols into the corresponding ketones **32–36** (yields > 80%), with olefin byproducts **38** and **39** (<4%) given in two examples in small proportions. In contrast, PtCl$_2$ failed to give desired ketones products significantly (<7%) because a rapid 1,2-hydrogen shift reaction gave olefin products **37–41** in large proportions (68–85%). In the PtCl$_2$ case, when we attempted the oxidative cyclization of alcohol **4** with H$_2$O$_2$ rather than H$_2$O in DCE (70 °C, 8 h), we obtained ketone **31** and olefin **5** in 52 and 4% yields respectively. This information reveals that the poor nucleophilicity of water accounts for its preference for formation of olefin **5** in the PtCl$_2$-catalysis.

Despite its lower efficiency, the use of water in PtCl$_2$/CO catalysis is economically and environmentally interesting because useful H$_2$ is also produced. To examine the feasibility of this process, we have calculated the enthalpy change for the water-oxygenation of platinum–benzylidene species using the Gaussian 98 program.[11] The ΔH value is more favorable for *trans*-PhCH=PtCl$_2$(H$_2$O) (ΔH = −1.14 kcal mol^{-1}) than its *cis* isomer (ΔH = +12.59 kcal mol^{-1}).



$$\mathrm{PhCH{=}Pt(OH_2)(Cl)Cl} + 2\,\mathrm{H_2O} \longrightarrow cis\text{-}\mathrm{PtCl_2(H_2O)_2} + \mathrm{PhCHO} + \mathrm{H_2} \qquad \Delta H = +12.59\ \mathrm{kcal/mol}$$

$$\mathrm{PhCH{=}Pt(Cl)(OH_2)Cl} + 2\,\mathrm{H_2O} \longrightarrow trans\text{-}\mathrm{PtCl_2(H_2O)_2} + \mathrm{PhCHO} + \mathrm{H_2} \qquad \Delta H = -1.14\ \mathrm{kcal/mol}$$

In summary, we have examined a new oxidative cyclization[12] of 2-ethenyl-1-(prop-2′-yn-1′-ol)benzenes to give naphthyl aldehydes and ketones using PtCl$_2$/CO/H$_2$O[13] and PEt$_3$AuCl/H$_2$O$_2$ systems;[14] the resulting metal–naphthylidene intermediates in such cyclizations were identified and oxygenated by water and H$_2$O$_2$, respectively. The Au-catalyst is far superior to platinum system for the production of the desired ketones and aldehydes from diverse alcohol substrates. Further use of this approach to oxidative cyclization of 1,5- and 1,6-enynes are under current investigation.

Notes and references

‡ *Representative procedure* for AuClEt$_3$ cyclization: To a solution of alcohol **1** (230 mg, 1.33 mmol) and AuClEt$_3$ (21.5 mg, 0.066 mmol) in DCE (5 ml) was added H$_2$O$_2$ (136 mg, 4 mmol). After this reaction mixture was stirred at 70 °C for 6 h, water (7 ml) was added to quench the reaction. The mixture was extracted with ether twice. The combined extracts were dried over MgSO$_4$. After removal of solvent under reduced pressure, the residue was purified on silical column (hexane–AcOEt 9 : 1) to give aldehyde **2** (181 mg, 1.07 mmol) in 80% yield as a colorless liquid. ^{1}H NMR (400 MHz, CDCl$_3$): δ 10.07 (s, 1H), 8.13 (s, 1H), 8.00–7.95 (m, 2H), 7.75 (s, 1H), 7.64 (t, 1H, J = 7.6 Hz), 7.55 (t, 1H, J = 7.6 Hz), 2.68 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$): δ 192.3, 135.7, 133.6, 133.2 × 2, 132.6, 130.1, 128.9, 126.6, 124.3, 12.7, 19.2. IR (neat) ν 2978, 1650 cm^{-1}. HRMS: calc. for C$_{12}$H$_{10}$O ([M + H]$^+$) 170.0732, found 170.0729.

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12 For oxidative cleavage of C–C multiple bonds using Au catalysts and oxidants, see: (*a*) Y. Liu, F. Song and S. Guo, *J. Am. Chem. Soc.*, 2006, **128**, 11332; (*b*) D. Xing, B. Guan, G. Cai, Z. Fang, L. Yang and Z. Shi, *Org. Lett.*, 2006, **8**, 693.

13 The experimental procedure for measurement of the evolved H$_2$ in the PtCl$_2$/CO/H$_2$O system is provided in ESI†.

14 PtCl$_2$/CO/H$_2$O did not catalyze the oxidation of alcohol **42** to aldehyde **2** under air or nitrogen. However, we obtained aldehyde **2** in 15% yield with a 63% recovery of unreacted **42** in the PEt$_3$AuCl/H$_2$O$_2$ system. We cannot exclude the possibility that some portions of aldehyde products arise from their alcohol precursors *via* decomposition of Au–carbenoid species with water.