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[Ru(η^3-2-C_3H_4Me)(CO)(dppf)][SbF_6]: a mononuclear 16e$^-$ ruthenium(II) catalyst for propargylic substitution and isomerization of HC≡CCPh$_2$(OH)†

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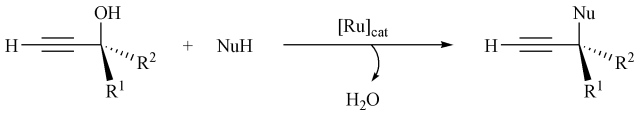
The 16e$^-$ derivative [Ru(η^3-2-C_3H_4Me)(CO)(dppf)][SbF_6] catalyzes: (*i*) the propargylic substitution reaction of 1,1-diphenyl-2-propyn-1-ol with alcohols to produce propargylic ethers, and (*ii*) the formal isomerization of 1,1-diphenyl-2-propyn-1-ol into 3,3-diphenyl-2-propenal.

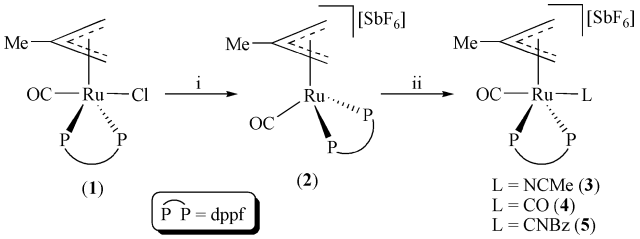
Although the Nicholas reaction constitutes a direct and widely used methodology for stoichiometric propargylic substitutions,[1] the search for a catalytic route has been a main synthetic goal. Nevertheless, only a few examples have been reported to date.[2] In this context, M. Hidai, S. Uemura and co-workers have recently disclosed an efficient ruthenium-catalyzed substitution reaction of terminal propargylic alcohols with various heteroatom- and carbon-centered nucleophiles (see Scheme 1).[3] We note that while secondary propargylic alcohols HC≡CCHR(OH) have been extensively used in these transformations, only a few examples involving tertiary alcohols HC≡CCR$_2$(OH) have been reported.[3a]



Scheme 1 Ruthenium-catalyzed propargylic substitution reactions.

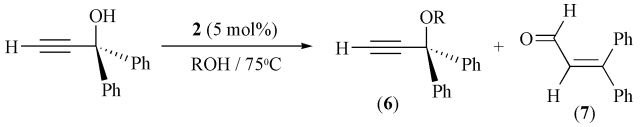
These catalytic processes proceed *via* an allenylidene-ruthenium intermediate [Ru]=C=C=CR^{1}R^2, which is generated from chalcogenolate-bridged diruthenium(III) complexes [Cp*RuCl(μ_2-XR)$_2$RuCp*Cl] and [Cp*RuCl(μ_2-XR)$_2$RuCp*(H$_2$O)][OTf] (Cp* = η^5-C_5Me_5; X = S, Se) by dehydration of the propargylic alcohol, and subsequent attack of the nucleophile at the electrophilic C$_\gamma$ atom.[4] Surprisingly, mononuclear Ru(II) derivatives such as [$RuCl_2(PPh_3)_3$], [$RuCl_2$(dppe)$_2$], [RuCl(PPh_3)$_2$Cp] (Cp = η^5-C_5H_5) or [RuCl(η^5-C_9H_7)(PPh_3)$_2$] are inactive despite their known ability to generate allenylidene complexes from propargylic alcohols.[4–6] Intramolecular charge transfer across the Ru–Ru bond in the dinuclear species has been proposed as a key factor to promote such catalytic transformations (synergistic effect).[3e] In contrast to these results, we have now found that the 16e$^-$ mononuclear (η^3-allyl)-ruthenium(II) derivative [Ru(η^3-2-C_3H_4Me)(CO)(dppf)][SbF_6] (**2**; dppf = 1,1′-bis(diphenylphosphino)ferrocene) is an efficient catalyst for the propargylic substitution reaction of 1,1-diphenyl-2-propyn-1-ol with a large variety of alcohols, demonstrating that the presence of a Ru–Ru framework is not essential.

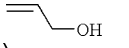
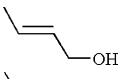
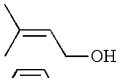
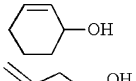
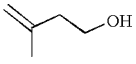
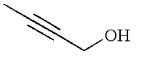
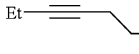
The cationic 16e$^-$ complex **2** was prepared in 97% yield by treatment of a dichloromethane solution of [RuCl(η^3-2-C_3H_4Me)(CO)(dppf)][7] with 1 equiv. of $AgSbF_6$ (Scheme 2). Complex **2**, which has been isolated as an air-stable yellow solid, has been characterized by conductance measurements, mass spectrum (FAB), elemental analyses and IR and NMR spectroscopy, all data being fully consistent with the structural proposal.‡ In accord with its unsaturated nature, **2** readily reacts with two-electron donor ligands such as acetonitrile, carbon monoxide and benzyl isocyanide to afford the corresponding 18e$^-$ derivatives [Ru(η^3-2-C_3H_4Me)(CO)(L)(dppf)][SbF_6] (**3–5**) in excellent yields (91–95% yield; see Scheme 2).§ The structure of complex **5** has been unequivocally confirmed by X-ray crystallography (see ESI¶). However, the reaction of complex **2** with 1,1-diphenyl-2-propyn-1-ol, using different solvents and conditions, does not lead to the



Scheme 2 Synthesis and reactivity of the 16e$^-$ complex **2**. *Reagents and conditions*: i, $AgSbF_6$ (1 equiv.), CH_2Cl_2, r.t.; ii, L (excess), CH_2Cl_2, r.t.

Table 1 Ru-catalyzed propargylic substitution reactions of 1,1-diphenyl-2-propyn-1-ol with alcohols[a]



Entry	ROH	Time	Yield of **6**[b]	Yield of **7**[b]
1	MeOH	4 h	**6a**, 80% (75%)	10%
2	EtOH	6 h	**6b**, 76% (72%)	19%
3		5 h	**6c**, 94% (87%)	4%
4		8 h	**6d**, 86% (80%)	14%
5		24 h	**6e**, 73% (68%)	24%
6		24 h	**6f**, 62% (56%)	31%
7		24 h	**6g**, 93% (89%)	7%
8		11 h	**6h**, 90% (81%)	10%
9		10 h	**6i**, 93% (90%)	0%

[a] Reactions performed under N_2 atmosphere at 75 °C using 1 mmol of HC≡CCPh$_2$(OH) (1.0 M in the corresponding alcohol) and 0.05 mmol of **2**. [b] Yields determined by GC (isolated yields in parentheses).

† Electronic supplementary information (ESI) available: experimental section. See http://www.rsc.org/suppdata/cc/b4/b410812d/

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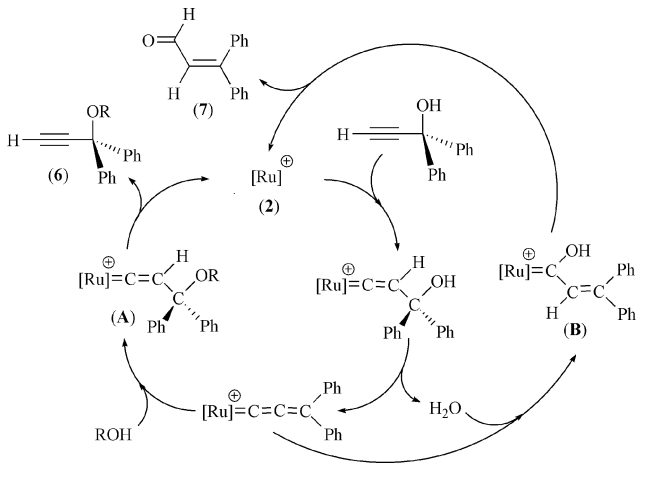
expected 18e$^-$ diphenylallenylidene derivative [Ru(=C=C=CPh$_2$)-(η^3-2-C$_3$H$_4$Me)(CO)(dppf)][SbF$_6$], giving instead a complex reaction mixture. Remarkably, GC/MS analysis of the reaction with an excess of HC≡CCPh$_2$(OH) in methanol at 75 °C shows the total disappearance of the propargylic alcohol with concomitant formation of HC≡CCPh$_2$(OMe) (**6a**). On the basis of these observations a catalytic reaction was performed (5 mol% of **2**) in methanol and ethanol at 75 °C affording the corresponding propargylic ethers **6a,b** in 80 and 76% GC yield, respectively (75 and 72% isolated yield; entries 1–2 in Table 1). The generality of this catalytic transformation has been confirmed by using functionalized alcohols such as allylic (entries 3–6), homoallylic (entry 7), propargylic (entry 8) and homopropargylic (entry 9) alcohols, allowing the isolation of the corresponding enynes (**6c–g**) and diynes (**6h,i**) in high yields (56–90%). Minor amounts of 3,3-diphenyl-2-propenal **7** are in all the cases formed (with the exception of entry 9), its proportion being dependent on the steric properties of the alcohol used (compare entries 3–6). Remarkably, this α,β-unsaturated aldehyde, which results from the formal isomerization of the propargylic alcohol,[8] can be selectively obtained (95% yield) if the catalytic reaction is carried out in the absence of alcohol using undistilled THF as solvent (5 mol% of Ru, 1 M solution, 1.5 h at 75 °C; see ESI). The formal isomerization of propargylic alcohols into the corresponding α,β-unsaturated aldehydes is a useful synthetic process which proceeds with a total atom economy.

The catalytic activity of complex **2** is higher than that shown by the dimers [Cp*RuCl(μ_2-XR)$_2$RuCp*Cl], *i.e.* using 5 mol% of [Cp*RuCl(μ_2-SMe)$_2$RuCp*Cl] (10 mol% of Ru) and 10 mol% of NH_4BF_4 as co-catalyst HC≡CCPh$_2$(OH) was transformed into HC≡CCPh$_2$(OEt) in 62% yield after 20 h at 60 °C in EtOH (to be compared with entry 2).[3a] It is also worth mentioning that catalyst **2** is also active with functionalized alcohols (entries 3–9) showing a remarkable chemoselectivity towards the coordination of the terminal alkynol *vs.* the C=C and C≡C bonds of the alcohols. No similar activity has been reported previously.

Formation of both **6** and **7** most probably involves a highly reactive Ru-allenylidene intermediate which undergoes the nucleophilic addition of the alcohols and water at the electrophilic C$_\gamma$ and C$_\alpha$ atoms of the unsaturated chain, respectively (intermediates **A** and **B** in Scheme 3).[4] Thus, demetalation of vinylidenes **A** and hydroxycarbene **B** could generate ethers **6** and 3,3-diphenyl-2-propenal **7**, respectively.



Scheme 3 Proposed [Ru]-intermediates in the formation of **6** and **7**.

In summary, a new mononuclear ruthenium(II) catalyst active in both propargylic substitution and isomerization of 1,1-diphenyl-2-propyn-1-ol is reported. Two main features deserve to be mentioned: (*i*) complex **2** is the first mononuclear ruthenium(II) complex active in propargylic substitutions starting from propargylic alcohols, and (*ii*) although other ruthenium(II) catalysts are active in the transformation of propargylic alcohols into α,β-unsaturated aldehydes, this is the first to perform the isomerization with disubstituted derivatives[8a] in one single step.[8b] Further studies on the scope of these catalytic reactions,[9] as well as detailed mechanistic investigations, are now in progress.

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Notes and references

‡ *Synthesis and characterization of* **2**: A solution of ***1*** (0.774 g, 1 mmol) in dichloromethane (50 cm^3) was treated with $AgSbF_6$ (351 mg, 1 mmol) and stirred for 15 min at room temperature in the absence of light. The AgCl formed was then filtered off (Kieselguhr) and the resulting solution evaporated to dryness to afford a yellow solid which was washed with diethyl ether (3 × 50 cm^3) and vacuum-dried. Yield: 0.945 g, 97% (Found: C, 47.92; H, 3.71. $RuFeC_{39}H_{35}F_6P_2OSb$ requires C, 48.08; H, 3.62%); Λ_M (acetone, 20 °C) 113.4 Ω^{-1} cm^2 mol^{-1}; ν/cm^{-1} (CO) 1944s (KBr); δ_P (CD_2Cl_2) 39.79 (s); δ_H (CD_2Cl_2) 1.26 (s, 2 H, CH$H_{(anti)}$), 2.21 (s, 3 H, CH_3), 3.79 (s, 2 H, CH$H_{(syn)}$), 4.31, 4.51, 4.69 and 4.93 (br, 2 H each, C_5H_4), 7.10–7.70 (m, 20 H, Ph); δ_C (CD_2Cl_2) 26.07 (s, CH_3), 60.87 (m, second-order system, CH_2), 72.96, 73.18, 75.16 and 75.47 (br, CH of C_5H_4), 81.24 (d, ^1J(C,P) = 48.8 Hz, C of C_5H_4), 121.72 (s, C), 127.80–135.50 (m, Ph), 205.01 (t, ^2J(C,P) = 16.8 Hz, CO); MS (FAB) *m/z* 739 [M$^+$], 655 [M$^+$ − CO − C$_3$H$_4$Me].

§ Compounds **3–5** have been characterized by NMR spectroscopy and elemental analyses. See ESI.

¶ CCDC 245208. See http://www.rsc.org/suppdata/cc/b4/b410812d/ for crystallographic data in .cif or other electronic format.

1 For reviews on the Nicholas reaction see: K. M. Nicholas, *Acc. Chem. Res.*, 1987, **20**, 207; J. R. Green, *Curr. Org. Chem.*, 2001, **5**, 809; B. J. Teobald, *Tetrahedron*, 2002, **58**, 4133.

2 Cu(I)-, Ti(IV)- and Ir(I)-catalyzed nucleophilic substitution of propargylic esters with alcohols, amines, amides and enoxysilanes are known: Y. Imada, M. Yuasa, I. Nakamura and S.-I. Murahashi, *J. Org. Chem.*, 1994, **59**, 2282; R. Mahrwald and S. Quint, *Tetrahedron*, 2000, **56**, 7463; R. Mahrwald and S. Quint, *Tetrahedron Lett.*, 2001, **42**, 1655; R. Mahrwald, S. Quint and S. Scholtis, *Tetrahedron*, 2002, **58**, 9847; I. Matsuda, K.-I. Komori and K. Itoh, *J. Am. Chem. Soc.*, 2002, **124**, 9072.

3 See for example: (*a*) Y. Nishibayashi, I. Wakiji and M. Hidai, *J. Am. Chem. Soc.*, 2000, **122**, 11019; (*b*) Y. Nishibayashi, I. Wakiji, Y. Ishii, S. Uemura and M. Hidai, *J. Am. Chem. Soc.*, 2001, **123**, 3393; (*c*) Y. Nishibayashi, M. Yoshikawa, Y. Inada, M. Hidai and S. Uemura, *J. Am. Chem. Soc.*, 2002, **124**, 11846; (*d*) Y. Nishibayashi, G. Onodera, Y. Inada, M. Hidai and S. Uemura, *Organometallics*, 2003, **22**, 873; (*e*) Y. Nishibayashi, H. Imajima, G. Onodera, M. Hidai and S. Uemura, *Organometallics*, 2004, **23**, 26; (*f*) Y. Nishibayashi, M. Yoshikawa, Y. Inada, M. Hidai and S. Uemura, *J. Org. Chem.*, 2004, **69**, 3408.

4 For general reviews on the chemistry of allenylidene complexes see: M. I. Bruce, *Chem. Rev.*, 1998, **98**, 2797; V. Cadierno, M. P. Gamasa and J. Gimeno, *Eur. J. Inorg. Chem.*, 2001, 571.

5 We have described a number of stoichiometric propargylic substitution reactions mediated by the indenyl complex [RuCl(η^5-C$_9$H$_7$)(PPh$_3$)$_2$]: V. Cadierno, S. Conejero, M. P. Gamasa and J. Gimeno, *Dalton Trans.*, 2003, 3060 and references therein.

6 Complexes [RuClL$_2$Cp] (L = PPh$_3$; L$_2$ = COD) have been found to catalyze the *S*-propargylation of thiols with internal propargylic carbonates *via* (σ-propargyl)-ruthenium intermediates: T. Kondo, Y. Kanda, A. Baba, K. Fukuda, A. Nakamura, K. Wada, Y. Morisaki and T. Mitsudo, *J. Am. Chem. Soc.*, 2002, **124**, 12960.

7 V. Cadierno, P. Crochet, J. Díez, S. E. García-Garrido, J. Gimeno and S. García-Granda, *Organometallics*, 2003, **22**, 5226.

8 (*a*) One-step isomerization of monosubstituted propargylic alcohols HC≡CCHR(OH) into RCH=CHCHO using [RuCl(PMe$_3$)$_2$Cp] as catalyst under neutral conditions (^{i}PrOH/H$_2$O) has been recently reported (disubstituted propargylic alcohols do not react at all): T. Suzuki, M. Tokunaga and Y. Wakatsuki, *Tetrahedron Lett.*, 2002, **43**, 7531; (*b*) A general two-step transformation of propargylic alcohols into α,β-unsaturated aldehydes using a [Ru(η^3-2-C$_3$H$_4$Me)$_2$(dppe)]/PhCO$_2$H/PTSA catalytic system is known: M. Picquet, A. Fernández, C. Bruneau and P. H. Dixneuf, *Eur. J. Org. Chem.*, 2000, 2361.

9 Complex **2** catalyzes also the propargylic substitution reaction of monosubstituted derivatives HC≡CCHR(OH) with alcohols. As an example, under the same reaction conditions, HC≡CCHPh(OH) reacts with CH$_2$=CHCH$_2$OH to afford HC≡CCHPh(OCH$_2$CH=CH$_2$) in 67% yield after 6 h (an uncharacterised by-product is also formed in *ca.* 30% yield).