

Synthesis of Furans by Cyclization of 2-En-4-yn-1-ols in the Presence of Ruthenium and Palladium Catalysts

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ABSTRACT: Substituted furans have been synthesized in the presence of ruthenium catalysts under neutral and mild conditions *via* cyclization of primary and secondary enynols of type (Z)-HC≡C-C(Me)=CH-CH(R)OH containing a terminal triple bond. The intramolecular addition of the hydroxy group to the triple bond of internal (Z)-enynols is also possible upon palladium catalysis.

Furans are key structural units in many natural products and have found a variety of applications as pharmaceuticals, flavor and fragrance compounds.¹ They are also reactive synthetic intermediates for the access to heterocyclic and acyclic compounds mainly upon Diels-Alder, oxidation and metalation reactions.²

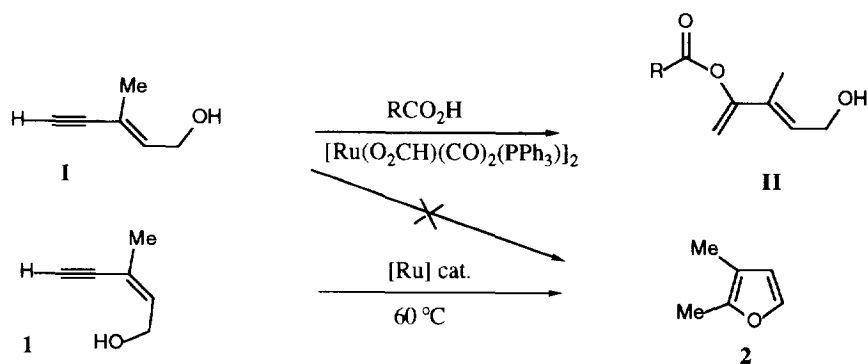
Many syntheses of furans are based on intramolecular cyclization of 1,4-diketones³ and polycarbonyl compounds⁴, or modification of unsubstituted furans by introduction of lateral groups usually *via* metalation.^{2,5} Recently, strategies involving cyclization of functional acetylenic compounds in the presence of a base or a metal catalyst have been developed. Potassium *tert*-butoxide and sodium hydroxide are suitable bases for the preparation of furans from enynols,⁶ alkynyloxiranes⁷, haloalkynes,⁸ and propargyl benzotriazole.⁹ Aluminum,¹⁰ silver¹¹ and titanium¹² reagents have been used as catalysts in furan syntheses from ketonic or hydroxylated allenes and alkynes. Opening of alkynyloxiranes in the presence of catalytic amounts of mercury(II)¹³ or Mo(CO)₆¹⁴ provides a synthetic route to functional furans containing an alcohol or a ketone functionality. The utilization of palladium catalysts makes possible the formation of furans from β-hydroxyalkynes containing a leaving group at the Cα carbon atom¹⁵ and α,α'-dihydroxyalkynes.¹⁶ Acetylenic ketones also undergo rearrangement into furan rings with palladium catalyst precursors,¹⁷ with concomitant allylation¹⁸ or cross-carbonylation with aryl iodides.¹⁹ Reaction of carbonucleophiles with allenylpalladium moieties leads to functional furans.²⁰ A catalytic synthesis of furans based on initial ruthenium-catalyzed condensation of terminal alkynes with allylic alcohol, followed by osmium-catalyzed

dihydroxylation has recently been reported.²¹ The copper-catalyzed cyclization of (*Z*)-3-methylpent-2-en-4-yn-1-ol allows the preparation of 2,3-dimethylfuran in large scale.²²

We now report a new method of synthesis of furans under neutral conditions *via* ruthenium-catalyzed cyclization of enynols (*Z*)-HC≡C-C(Me)=CH-CH(R)OH. Following our initial study,²³ this paper describes in detail the synthesis of trisubstituted furans from easily accessible *terminal* (*Z*)-2-en-4-yn-1-ols, by activation of the triple bond with ruthenium catalysts and intramolecular addition of the hydroxy group. We also show that this reaction can be extended to (*Z*)-enynols bearing an *internal* triple bond, in the presence of palladium catalysts.

RUTHENIUM-CATALYZED SYNTHESIS OF FURANS FROM TERMINAL 2-EN-4-YN-1-OLS

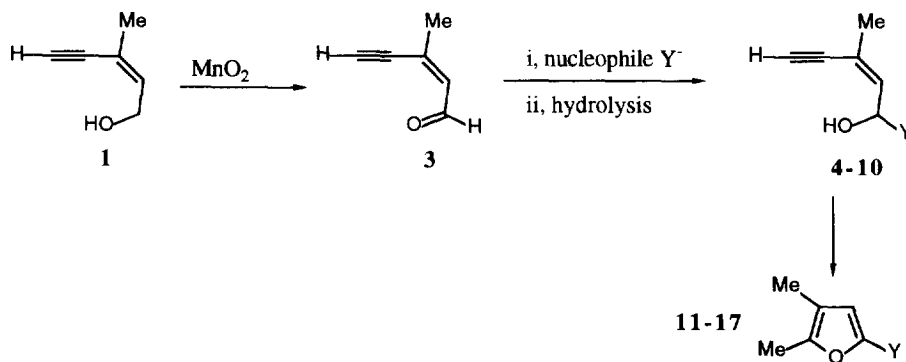
The ruthenium-catalyzed addition of carboxylic acids to alkynes constitutes an elegant way to produce functional alkenes.²⁴ Whereas the addition of carboxylic acids to (*E*)-3-methylpent-2-en-4-yn-1-ol **I** selectively led to hydroxylated dienyl esters **II** in the presence of a ruthenium catalyst,²⁵ our attempts to add benzoic acid to its stereoisomer (*Z*)-3-methylpent-2-en-4-yn-1-ol **1** failed and a faster reaction involving only the enynol took place, giving 2,3-dimethylfuran **2** (Scheme 1).



[Ru] cat. :	(arene)RuCl ₂ (PPh ₃)	2 h	conversion : 100%
	[Ru(O ₂ CH)(CO) ₂ (PPh ₃) ₂]	2 h	conversion : 100%
	Ru ₃ (CO) ₁₂ , (dppe) ₂ RuCl ₂	20 h	conversion : 50%
	CpRuCl(PPh ₃) ₂	20 h	conversion : 0%

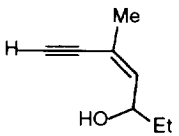
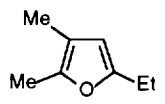
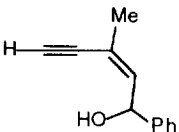
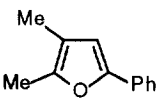
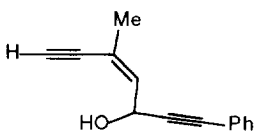
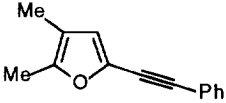
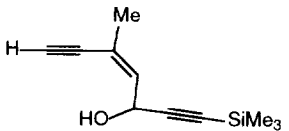
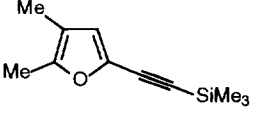
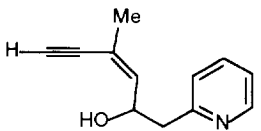
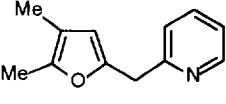
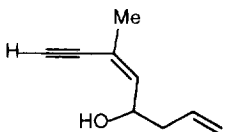
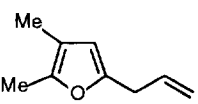
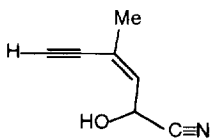
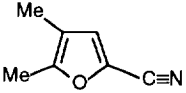
Scheme 1

Thus, in the presence of 1 mol% of (*p*-cymene)RuCl₂(PPh₃), 10 mmol of (*Z*)-3-methylpent-2-en-4-yn-1-ol **1** reacted at 60 °C for 2 h without a solvent to give a quantitative conversion into 2,3-dimethylfuran **2** isolated in 74% yield by transfer under reduced pressure. A variety of ruthenium complexes were tested and we found that (arene)RuCl₂(PMe₃) (arene = *p*-cymene and hexamethylbenzene) and the binuclear compound [Ru(O₂CH)(CO)₂(PPh₃)₂]₂ exhibited similar activities leading to the complete conversion of 10 mmol of enynol **1** within 2 h at 60 °C. Ru₃(CO)₁₂ and [bis(diphenylphosphino)ethane]₂RuCl₂ were less efficient : they gave only a 50% conversion of **1** after 20 h at 60 °C, and (cyclopentadienyl)RuCl(PPh₃)₂ was inactive under similar conditions. The geometry of the double bond of the enynol is an important factor as no cyclization took place when (*E*)-3-methylpent-2-en-4-yn-1-ol **1** was reacted at 60 °C in the presence of (*p*-cymene)RuCl₂(PPh₃). The ruthenium-catalyzed reaction is specific to terminal alkynes as no conversion was observed when (*Z*)-3-methylhex-2-en-4-yn-1-ol (MeC≡C-C(Me)=CH-CH₂OH) was treated in the presence of (*p*-cymene)RuCl₂(PPh₃), even at 110 °C. This specific isomerization takes place *via* a ruthenium-catalyzed intramolecular addition of the OH group at the internal carbon of the triple bond and provides a direct synthesis of substituted furans under neutral conditions. The interest and generality of this novel catalytic reaction was demonstrated by the synthesis of a variety of trisubstituted furans from various secondary (*Z*)-2-en-4-yn-1-ols substituted at C(1), including base sensitive and fragile substrates. Secondary alcohols were prepared in two steps from the commercially available (*Z*)-3-methylpent-2-en-4-yn-1-ol **1**, by oxidation into aldehyde **3** with manganese dioxide, followed by condensation with nucleophiles after isolation of **3** (Scheme 2). Organomagnesium derivatives were used to prepare (*Z*)-enynols **4** and **5**, organolithium derivatives afforded (*Z*)-enynols **6**, **7**, **8**, whereas the allylic compound **9** was obtained from an allylzinc derivative, and the cyanohydrin **10** resulted from the reaction of **3** with CN⁻ under acidic conditions.



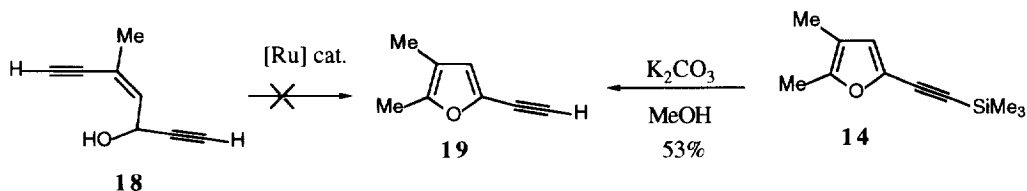
Scheme 2

Table 1. Ruthenium-Catalyzed Preparation of Furans **11-17** from Secondary (Z)-Enynols **4-10**

(Z)-Enynol		Furan		Yield (%)
	4		11	89
	5		12	85
	6		13	53
	7		14	58
	8		15	67
	9		16	74
	10		17	50

Under the experimental conditions required for the cyclization of **1**, the enynol **4** led to 2,3-dimethyl-5-ethylfuran **11** in 89% yield after 2 h at 60 °C without a solvent, and the allylic compound **9** gave

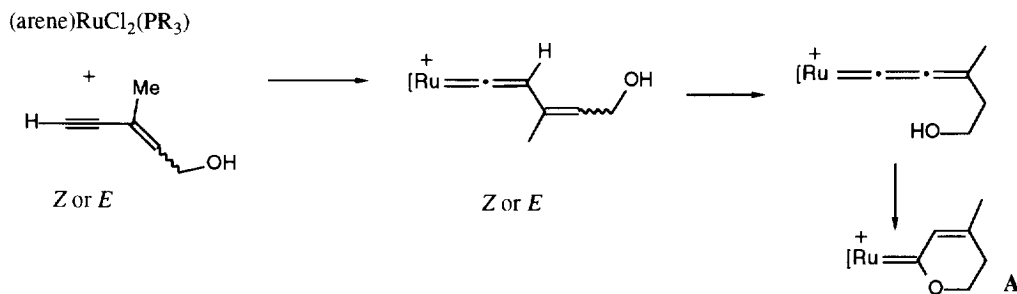
5-allyl-2,3-dimethylfuran **16** in 74% yield after 15 h of reaction at 80 °C in hexane. The other (*Z*)-enynols containing more bulky substituents reacted in toluene at 110 °C to afford the corresponding furans **12-15**, **17**, in good yields (Table 1). This catalysis with $\text{RuCl}_2(\text{PPh}_3)(p\text{-cymene})$ taking place under neutral conditions makes possible the access to furans from substrates containing reactive functionalities such as trialkylsilylalkynyl or cyano groups. The generality of the reaction has been shown, but the alcohol **18** bearing a propargylic structure with a terminal proton was not reactive under our conditions. This difficulty could be overcome and furan **19** was obtained by cleavage of the trimethylsilyl group from furan **14** in the presence of K_2CO_3 in methanol at room temperature (Scheme 3).



Scheme 3

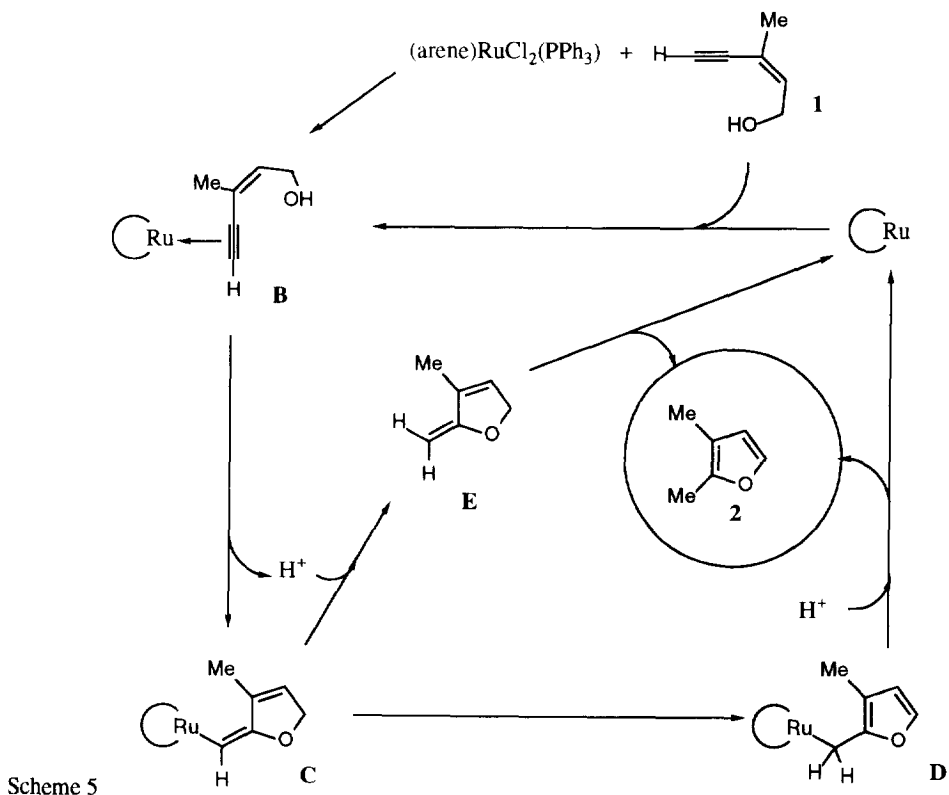
MECHANISM

The mechanism of this catalytic reaction was investigated on the basis of $(\text{arene})\text{RuCl}_2(\text{PR}_3)$ complexes which appeared to be the most efficient catalyst precursors. Under stoichiometric conditions, $(\text{arene})\text{RuCl}_2(\text{PR}_3)$ complexes react with (*Z*)-3-methylpent-2-en-4-yn-1-ol in the presence of NaPF_6 in CH_2Cl_2 to produce the cyclic unsaturated carbene **A** via vinylidene and allenylidene-ruthenium intermediates and intramolecular nucleophilic addition of the OH group to the electrophilic C(α) (Scheme 4).²⁶



Scheme 4

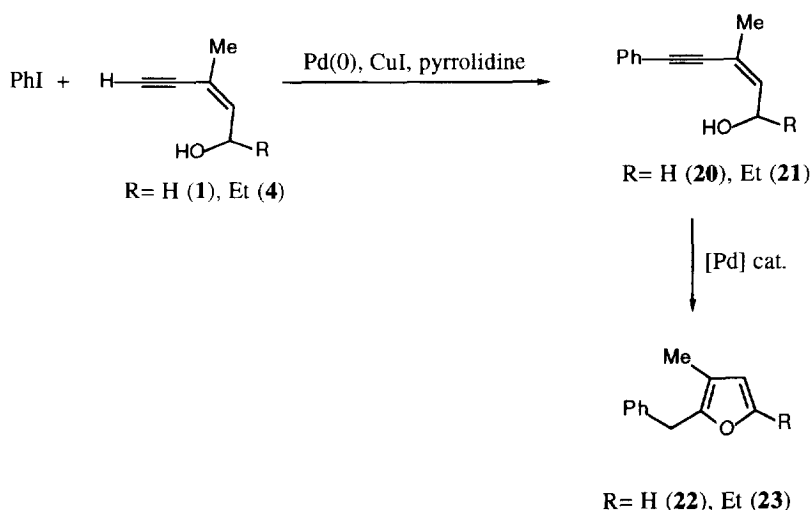
It is noteworthy that the carbene ruthenium complex **A** is also a catalyst for the synthesis of furans as it leads to the complete conversion of 10 mmol of **1** at 60 °C for 2 h. However, the catalytic synthesis of furans from the (*E*)-enynol **1** was not possible with (arene)RuCl₂(PPh₃) complexes, which rules out the involvement of the cyclic ruthenium carbene **A** as a key species of the catalytic cycle. The reaction with labelled enynol **1**, containing deuterium atoms in both hydroxy and terminal alkyne groups indicated that the two deuterium atoms were incorporated into the methyl group of the furan attached to C(2). Under stoichiometric conditions, the use of the deuteriated enynol (*Z*)-D-C≡C-C(Me)=CH-CH₂OD would lead to a cyclic unsaturated carbene **A** with the two deuterium atoms attached to two different carbon atoms. These considerations suggest that the reactive species involved in the catalytic cycle are different from the stable compounds resulting from stoichiometric reaction. The catalytic cycle that we proposed (Scheme 5) is based on the activation of the triple bond of the enynol by an electrophilic ruthenium species formed after liberation of a vacant site at the metal centre to give the metal (η^2 -alkyne) intermediate **B**. Intramolecular oxyruthenation of the triple bond would lead to the vinyl ruthenium species **C**. The elimination of the furan ring by protonolysis may take place either from the coordinated vinylic ligand in **C** (**C** → **E** → **2**) or after proton migration and formation of a furanic ligand in **D** (**C** → **D** → **2**).



**PALLADIUM-CATALYZED SYNTHESIS OF FURANS FROM INTERNAL
2-EN-4-YN-1-OLS**

Ruthenium catalysts were inefficient to transform internal enynols into furans. Some examples of palladium-catalyzed intramolecular addition of a hydroxy group to a triple bond reported in the literature^{15,27} prompted us to test the activity of palladium precursors to perform the cyclization of (*Z*)-enynols containing an internal triple bond.

The starting alkynols **20** and **21** were prepared in 95 and 93% respective yields from iodobenzene and the terminal (*Z*)-enynols **1** and **4** via palladium(0), copper(I)-catalyzed cross-coupling reaction in the presence of pyrrolidine.²⁸ The treatment of **20** at 100 °C for 2 h in tetrahydrofuran in the presence of 2 mol% of Pd(OAc)₂ gave 2-benzyl-3-methylfuran **22** in 60% isolated yield. Similarly, in tetrahydrofuran at 110 °C in the presence of 1 mol% of Pd(PPh₃)₄ the enynol **21** led to the trisubstituted furan **23** in 60% yield (Scheme 6).



Scheme 6

However, the reaction has some limitations and we were not able to carry out the cyclization of internal enynols bearing a conjugated double bond such as $\text{MeCH}=\text{C}(\text{Me})-\text{C}\equiv\text{C}-\text{C}(\text{Me})=\text{CHCH}_2\text{OH}$ or $\text{Me}_2\text{C}=\text{CH}-\text{C}\equiv\text{C}-\text{C}(\text{Me})=\text{CHCH}_2\text{OH}$.

CONCLUSION

The ruthenium-catalyzed cyclization of terminal (*Z*)-2-en-4-yn-1-ols gives a simple access to 2-methylfurans under mild and neutral conditions. This reaction represents a novel application of ruthenium catalysts in organic synthesis. Furans containing base-sensitive substituents have been synthesized in good yields. This reaction with ruthenium catalysts is specific to (*Z*)-enynols containing a terminal alkynyl group. The utilization of palladium catalysts enlarges the scope of this rearrangement to (*Z*)-enynols with an internal triple bond for preparing furans containing a different substituent at C(2).

EXPERIMENTAL

Preparation of (p-cymene)RuCl₂(PPh₃). The catalyst precursor (*p*-cymene)RuCl₂(PPh₃) was prepared in two steps from commercially available RuCl₃·xH₂O : formation of the dimer [(*p*-cymene)RuCl₂]₂ by heating 60 mmol of the ruthenium salt in the presence of 280 mmol of α -phellandrene in 300 ml of ethyl alcohol (95%) under reflux for 6 h,³⁰ followed by reaction of two equivalents of triphenylphosphine in dichloromethane at room temperature for 4 h.³¹

(Z)-3-methylpent-2-en-4-yn-1-ol (3). 1.92 g of (*Z*)-3-methylpent-2-en-4-yn-1-ol **1** (20 mmol) was added over 15 min to a suspension of 13.7 g of activated MnO₂ (supplied from Aldrich) (143 mmol) in 50 ml of anhydrous CH₂Cl₂, and the mixture was stirred at room temperature for 16 h. The solution was filtered and the filtrate was evaporated and distilled under reduced pressure to give 1.66 g (88%) of **3** as a colorless liquid, bp 20 °C (2 mm Hg) ; IR (film) ν /cm⁻¹ 3275 (H-C \equiv C), 2095 (C \equiv C) and 1670 (H-C=O) ; ¹H NMR δ (300 MHz, CDCl₃) 2.07 (s, 3 H, CH₃), 3.56 (s, 1 H, H-C \equiv C), 6.17 (d, 1 H, ³J = 8.1 Hz, HC=C), 9.95 (dm, 1 H, ³J = 8.1 Hz, H-C=O). Found : C, 76.65 ; H, 6.35. Calcd for C₆H₆O : C, 76.57 ; H, 6.43.

(Z)-5-methylhept-4-en-6-yn-3-ol (4). A solution of EtBr (1.66 ml, 20 mmol) in 4 ml of diethyl ether was added over 30 min to a suspension of 0.486 g of Mg (20 mmol) in 10 ml of anhydrous ether, and the mixture was stirred at room temperature for 30 min. The aldehyde **3** (0.94 g, 10 mmol) in 4 ml of ether was then added at 0 °C. The mixture was stirred at room temperature for 1 h, washed with 10 ml of a saturated NH₄Cl solution, extracted with ether, dried over MgSO₄ and evaporated. 0.875 g (70%) of **4** was isolated as a colorless liquid by distillation under reduced pressure, bp 70 °C (2 mm Hg) ; IR (film) ν /cm⁻¹ 3305 (H-C \equiv C), 2095 (C \equiv C) and 1635 (C=C) ; ¹H NMR δ (300 MHz, CDCl₃) 0.86 (t, 3 H, ³J = 7.4 Hz, CH₃-CH₂), 1.46 (m, 1 H,

CH₃-CHH), 1.56 (m, 1 H, CH₃-CHH), 1.82 (d, 3 H, ⁴J = 1.4 Hz, CH₃), 1.95 (broad signal, 1 H, OH), 3.07 (s, 1 H, H-C≡C), 4.45 (dt, 1 H, ³J = 8.6 Hz, ³J = 6.7 Hz, CHOH), 5.66 (dm, 1 H, ³J = 8.6 Hz, CH=C). Found : C, 77.55 ; H, 9.55. Calcd for C₈H₁₂O : C, 77.38 ; H, 9.74.

(Z)-3-methyl-1-phenylpent-2-en-4-yn-1-ol (**5**). A solution of PhI (2 ml, 17.8 mmol) in 4 ml of ether was added over 30 min to a suspension of Mg (0.4 g, 17.8 mmol) in 10 ml of anhydrous ether, and the mixture was stirred at room temperature for 30 min. The aldehyde **3** (0.84 g, 8.9 mmol) in 4 ml of ether was then added at 0 °C. The mixture was stirred at room temperature for 1 h, washed with 10 ml of a saturated NH₄Cl solution, extracted with ether, dried over MgSO₄ and evaporated. 1.09 g (71%) of **5** was isolated as a colorless liquid by distillation under reduced pressure, bp 110 °C (2 mm Hg) ; IR (film) ν/cm⁻¹ 3290 (H-C≡C), 2095 (C≡C) and 1630 (C=C) ; ¹H NMR δ (300 MHz, CDCl₃) 1.90 (d, 3 H, ⁴J = 1.4 Hz, CH₃), 2.33 (s, 1 H, OH), 3.23 (s, 1 H, H-C≡C), 5.75 (d, 1 H, ³J = 8.9 Hz, CHOH), 5.93 (dm, 1 H, ³J = 8.9 Hz, CH=C), 7.25-7.63 (m, 5 H, Ph). Found : C, 83.91 ; H, 6.90. Calcd for C₁₂H₁₂O : C, 83.69 ; H, 7.02.

Typical procedure for compounds 6-8 :

20 mmol of lithium derivative, prepared at -78 °C by addition of BuLi to a solution of acetylenic compound or 2-picoline in THF, were added over 30 min to a solution of *(Z)*-3-methylpent-2-en-4-yn-1-ol **3** (0.95 g, 10 mmol) in 10 ml of THF at -78 °C. The mixture was stirred for 30 min at -78 °C and then 1 h at room temperature, quenched with 10 ml of a saturated NH₄Cl solution, extracted with ether, dried over MgSO₄ and evaporated. Pure products were obtained by distillation or silica gel chromatography with a (80/20) hexane-ether mixture as eluent.

(Z)-5-methyl-1-phenylhept-4-ene-1,6-diyne-3-ol (**6**). 44% yield ; colorless liquid ; IR (film) ν/cm⁻¹ 3290 (H-C≡C), 2230 and 2100 (C≡C), 1635 (C=C) ; ¹H NMR δ (300 MHz, CDCl₃) 1.86 (s, 3 H, CH₃), 2.19 (s, 1 H, OH), 3.17 (s, 1 H, H-C≡C), 5.50 (d, 1 H, ³J = 8.9 Hz, CHOH), 5.89 (dm, 1 H, ³J = 8.9 Hz, CH=C), 7.20-7.39 (m, 5 H, Ph). Found : C, 85.71 ; H, 5.98. Calcd for C₁₄H₁₂O : C, 85.68 ; H, 6.16.

(Z)-5-methyl-1-trimethylsilylhept-4-ene-1,6-diyne-3-ol (**7**). 75% yield ; colorless liquid ; IR (film) ν/cm⁻¹ 3400 (OH), 3295 (H-C≡C), 2170 (C≡C-Si), 2100 (C≡C-) and 1630 (C=C) ; ¹H NMR δ (300 MHz, CDCl₃) 0.17-0.14 (m, 9 H, Si(CH₃)₃), 1.89 (d, 3 H, ⁴J = 1.5 Hz, CH₃-C=), 2.10 (broad signal, 1 H, OH), 3.19 (s, 1 H, H-C≡C), 5.29 (d, 1 H, ³J = 9.0 Hz, CHOH), 5.83 (dm, 1 H, ³J = 9.0 Hz, HC=C). Found : C, 68.28 ; H, 8.60. Calcd for C₁₁H₁₆OSi : C, 68.69 ; H, 8.39.

(*Z*)-4-methyl-1-(2-pyridyl)hex-3-en-5-yn-2-ol (**8**). 50% yield ; colorless liquid ; IR (film) ν/cm^{-1} 3300 (H-C \equiv C), 2095 (C \equiv C) and 1635 (C=C) ; ^1H NMR δ (300 MHz, CDCl_3) 1.87 (d, 3 H, $^4J = 1.4$ Hz, CH_3), 2.98-3.01 (m, 3 H, CH_2+OH), 3.14 (s, 1 H, H-C \equiv C), 5.03 (dt, 1 H, $^3J = 7.8$ Hz, $^3J = 4.6$ Hz, CHOH), 5.86 (dm, 1 H, $^3J = 9.0$ Hz, $\text{HC}=\text{C}$), 7.18-7.14 (m, 2 H, pyridyl-H), 7.62 (td, 1 H, $^3J = 7.7$ Hz, $^4J = 1.8$ Hz, pyridyl-H), 8.47 (dd, 1 H, $^3J = 5.2$ Hz, $^4J = 2.1$ Hz, pyridyl-H).

(*Z*)-3-methylocta-3,7-dien-1-yn-5-ol (**9**). According to Pétrier,²⁹ (*Z*)-3-methylpent-2-en-4-yn-1-al **3** (0.94 g, 10 mmol), allylbromide (0.43 ml, 5 mmol), zinc powder (0.327 g, 5 mmol) were stirred at room temperature for 15 h in a mixture of 1 ml of THF and 5 ml of a saturated NH_4Cl solution. The mixture was extracted with ether, dried over MgSO_4 and evaporated. 0.291 g (43%) of **9** was isolated by distillation, bp 75 °C (2 mm Hg) ; IR (film) ν/cm^{-1} 3500 (OH), 3300 (H-C \equiv C), 2100 (C \equiv C) and 1635 (C=C) ; ^1H NMR δ (300 MHz, CDCl_3) 1.84 (d, 3 H, $^4J = 1.5$ Hz, CH_3), 2.02 (broad signal, 1 H, OH), 2.24-2.32 (m, 2 H, CH_2), 3.10 (s, 1 H, H-C \equiv C), 4.61 (dm, 1 H, $^3J = 9.0$ Hz, CHOH), 5.08 (dd, 1 H, $^3J_{\text{cis}} = 10.1$ Hz, $^2J = 2.1$ Hz, = CHH), 5.11 (dd, 1 H, $^3J_{\text{trans}} = 17.0$ Hz, $^2J = 2.1$ Hz, = CHH), 5.73 (dm, 1 H, $^3J = 9.0$ Hz, $\text{MeC}=\text{CH}$), 5.79 (ddt, 1 H, $^3J_{\text{trans}} = 17.0$ Hz, $^3J_{\text{cis}} = 10.1$ Hz, $^3J = 7.0$ Hz, $\text{CH}_2\text{CH}=\text{}$). Found : C, 79.42 ; H, 8.68. Calcd for $\text{C}_9\text{H}_{12}\text{O}$: C, 79.37 ; H, 8.88.

(*Z*)-1-cyano-3-methylpent-2-en-4-yn-1-ol (**10**). To a solution of (*Z*)-3-methylpent-2-en-4-yn-1-al **3** (0.6 g, 6.4 mmol), KCN (1.04 g, 16 mmol) in 10 ml of ether and 16 ml of water, was added under vigorous stirring 4.2 ml of 6N HCl solution over 15 min at 0 °C. The mixture was stirred 30 min at 0 °C and 2 h at 20 °C, extracted with ether, dried (MgSO_4) and evaporated. 0.75 g (100%) of **10** was obtained without further purification because of its instability ; IR (film) ν/cm^{-1} 3500 (OH), 3330 (H-C \equiv C), 2250 (C \equiv N), 2100 (C \equiv C) and 1635 (C=C). ^1H NMR δ (300 MHz, CDCl_3) 1.93 (d, 3 H, $^4J = 1.6$ Hz, CH_3), 3.34 (s, 1 H, H-C \equiv C), 3.91 (broad signal, 1 H, OH), 5.38 (d, 1 H, $^3J = 8.8$ Hz, CHOH), 5.85 (dm, 1 H, $^3J = 8.8$ Hz, $\text{HC}=\text{C}$). Found : M^+ , 121.0517. Calcd for $\text{C}_7\text{H}_7\text{NO}$: M, 121.0528.

Typical procedure for the preparation of furans 2,11-17:

5 mmol of (*Z*)-enynol, 0.05 mmol of (*p*-cymene) $\text{RuCl}_2(\text{PPh}_3)$ were stirred at 60-110 °C for 2-20 h in 5 ml of solvent (hexane, toluene or no solvent) under an inert atmosphere of nitrogen. The products were isolated by transfer or distillation under reduced pressure or by silica gel chromatography.

2,3-dimethylfuran (**2**). 74% yield, colorless liquid, bp 20 °C (2 mm Hg) ; IR (film) ν/cm^{-1} 1605 (C=C) ; ^1H NMR δ (300 MHz, CDCl_3) 1.94 (s, 3 H, CH_3), 2.19 (s, 3 H, CH_3), 6.14 (d, 1 H, $^3J = 1.8$ Hz, H), 7.19 (d,

1 H, $^3J = 1.8$ Hz, H). Found : C, 74.89 ; H, 8.42 ; M⁺, 96.057. Calcd for C₆H₈O : C, 74.97 ; H, 8.39 ; M, 96.057.

5-ethyl-2,3-dimethylfuran (11). 50% yield, colorless liquid ; IR (film) ν/cm^{-1} 1645 and 1580 (C=C) ; $^1\text{H NMR}$ δ (300 MHz, CDCl₃) 1.21 (t, 3 H, $^3J = 7.6$ Hz, CH₂-CH₃), 1.92 (s, 3 H, CH₃), 2.18 (s, 3 H, CH₃), 2.58 (q, 2 H, $^3J = 7.6$ Hz, CH₂-CH₃), 5.77 (s, 1 H, CH). Found : C, 77.65 ; H, 9.68. Calcd for C₈H₁₂O : C, 77.38 ; H, 9.74.

2,3-dimethyl-5-phenylfuran (12). 85% yield, colorless liquid, bp 140 °C (2 mm Hg) ; IR (film) ν/cm^{-1} 1600 and 1555 (C=C) ; $^1\text{H NMR}$ δ (300 MHz, CDCl₃) 1.96 (s, 3 H, CH₃), 2.26 (s, 3 H, CH₃), 6.42 (s, 1 H, H-C=C), 7.15-7.60 (m, 5 H, Ph). Found : C, 83.83 ; H, 6.97. Calcd for C₁₂H₁₂O : C, 83.69 ; H, 7.02.

2,3-dimethyl-5-(phenylethynyl)furan (13). 53% yield, colorless liquid ; IR (film) ν/cm^{-1} 2205 (C≡C) and 1625 (C=C) ; $^1\text{H NMR}$ δ (300 MHz, CDCl₃) 1.96 (s, 3 H, CH₃), 2.25 (s, 3 H, CH₃), 6.47 (s, 1 H, H-C=C), 7.32-7.52 (m, 5 H, Ph). Found : C, 86.05 ; H, 6.24. Calcd for C₁₄H₁₂O : C, 85.68 ; H, 6.16.

2,3-dimethyl-5-(trimethylsilylethynyl)furan (14). 48% yield, colorless liquid, bp 125 °C (2 mm Hg) ; IR (film) ν/cm^{-1} 2155 (C≡C), 1625 (C=C) and 1250 (Si-C) ; $^1\text{H NMR}$ δ (300 MHz, CDCl₃) 0.21 (s, 9 H, Si(CH₃)₃), 1.89 (s, 3 H, CH₃), 2.18 (s, 3 H, CH₃), 6.37 (s, 1 H, H-C=C). Found : M⁺, 192.0964. Calcd for C₁₁H₁₆SiO : M, 192.0970.

2,3-dimethyl-5-((2-pyridyl)methyl)furan (15). 67% yield, colorless oil ; IR (film) ν/cm^{-1} 1590, 1570 (C=C) ; $^1\text{H NMR}$ δ (300 MHz, CDCl₃) 1.88 (s, 3 H, CH₃), 2.14 (s, 3 H, CH₃), 4.06 (s, 2 H, CH₂), 5.88 (s, 1 H, furanic H), 7.10 (dd, 1 H, $^3J = 6.9$ Hz, $^3J = 5.2$ Hz), 7.17 (d, 1 H, $^3J = 7.8$ Hz), 7.57 (td, 1 H, $^3J = 7.7$ Hz, $^4J = 1.8$ Hz), 8.52 (dm, 1 H, $^3J = 4.9$ Hz). Found : C, 76.85 ; H, 6.86 ; N, 7.62. Calcd for C₁₂H₁₃NO : C, 76.98 ; H, 7.00 ; N, 7.48.

2,3-dimethyl-5-(prop-2-en-1-yl)furan (16). 74% yield, colorless liquid, bp 40 °C (2 mm Hg) ; IR (film) ν/cm^{-1} 1600 (C=C) ; $^1\text{H NMR}$ δ (300 MHz, CDCl₃) 1.90 (s, 3 H, CH₃), 2.17 (s, 3 H, CH₃), 3.31 (d, 2 H, $^3J = 6.6$ Hz, CH₂), 5.09 (dm, 1 H, $^3J_{\text{cis}} = 10.1$ Hz, =CHH), 5.14 (dm, 1 H, $^3J_{\text{trans}} = 17.0$ Hz, =CHH), 5.80 (s, 1 H, MeC=CH), 5.92 (ddt, 1 H, $^3J_{\text{trans}} = 17.0$ Hz, $^3J_{\text{cis}} = 10.1$ Hz, $^3J = 6.6$ Hz, HC=CH₂). Found : M⁺, 136.0886. Calcd for C₉H₁₂O : M, 136.0888.

5-cyano-2,3-dimethylfuran (17). 50% yield, colorless liquid, bp 80 °C (2 mm Hg) ; IR (film) ν/cm^{-1} 2225 (C≡N) and 1620 (C=C) ; $^1\text{H NMR}$ δ (300 MHz, CDCl₃) 1.95 (s, 3 H, CH₃), 2.24 (s, 3 H, CH₃), 6.84 (s, 1 H, CH) ; $^{13}\text{C NMR}$ δ (75.5 MHz, CDCl₃) 9.5, 11.8, 112.3, 116.5, 123.1, 125.2, 154.1. Found : M⁺, 121.0517. Calcd for C₇H₇NO : M, 121.0528.

5-ethynyl-2,3-dimethylfuran (19). Furan **14** (0.5 g, 2.6 mmol) was stirred with K_2CO_3 (0.6 g, 4.3 mmol) in 10 ml of methanol for 4 h at room temperature. The mixture was washed with 5 ml of saturated NH_4Cl solution, extracted with ether, dried ($MgSO_4$) and evaporated. 0.312 g (53%) of furan **19** was isolated by distillation as a colorless liquid, bp 60 °C (2 mm Hg) ; IR (film) ν/cm^{-1} 3295 (H-C \equiv C), 2110 (C \equiv C) and 1625 (C=C) ; 1H NMR δ (300 MHz, $CDCl_3$) 1.91 (s, 3 H, CH_3), 2.19 (s, 3 H, CH_3), 3.37 (s, 1 H, H-C \equiv C), 6.42 (s, 1 H, H).

Typical procedure for compounds 20-21.

To a solution of PhI (0.56 ml, 5 mmol), CuI (0.095 g, 0.5 mmol), $Pd(PPh_3)_4$ (0.145 g, 0.125 mmol) in 5 ml of pyrrolidine, was slowly added the compound **1** or **4** (10 mmol) at 0 °C under vigorous stirring. After 15 min at 0 °C and 30 min at room temperature, the mixture was washed with 10 ml of saturated NH_4Cl solution, extracted with ether, dried ($MgSO_4$) and evaporated. The pure products were obtained by silica gel chromatography with a (50/50) ether-pentane mixture (for **20**) or with ether (for **21**) as eluent.

(Z)-3-methyl-5-phenylpent-2-en-4-yn-1-ol (20). 95% yield, colorless liquid ; IR (film) ν/cm^{-1} 3500 (OH), 2200 (C \equiv C) and 1630 (C=C) ; 1H NMR δ (300 MHz, $CDCl_3$) 1.78 (s, 1 H, OH), 1.96 (d, 3 H, $^4J = 1.3$ Hz, CH_3), 4.40 (dd, 2 H, $^3J = 6.8$ Hz, $^3J = 1.1$ Hz, CH_2), 5.92 (tq, 1 H, $^3J = 6.8$ Hz, $^4J = 1.3$ Hz, C=CH), 7.28-7.46 (m, 5 H, Ph). Found : C, 83.36 ; H, 7.01. Calcd for $C_{12}H_{12}O$: C, 83.69 ; H, 7.02.

(Z)-5-methyl-7-phenylhept-4-en-6-yn-3-ol (21). 93% yield, colorless liquid ; IR (film) ν/cm^{-1} 3500 (OH), 2200 (C \equiv C) and 1630 (C=C) ; 1H NMR δ (300 MHz, $CDCl_3$) 0.89 (t, 3 H, $^3J = 7.4$ Hz, CH_3-CH_2), 1.50 (m, 1 H, CH_3-CH_2), 1.60 (m, 1 H, CH_3-CH_2), 1.76 (broad signal, 1 H, OH), 1.89 (d, 3 H, $^4J = 1.4$ Hz, CH_3), 4.54 (dt, 1 H, $^3J = 8.5$ Hz, $^3J = 6.7$ Hz, CH_2OH), 5.64 (dq, 1 H, $^3J = 8.5$ Hz, $^4J = 1.4$ Hz, C=CH), 7.21-7.39 (m, 5 H, Ph). Found : C, 83.86 ; H, 8.11. Calcd for $C_{14}H_{16}O$: C, 83.96 ; H, 8.05.

2-benzyl-3-methylfuran (22). Compound **20** (0.5 g, 2.9 mmol) and $Pd(OAc)_2$ (0.013 g, 0.058 mmol) were stirred in 7.5 ml of THF at 100 °C for 2 h. 0.295 g (60%) of **22** was isolated as a colorless liquid by silica gel chromatography with a (90/10) pentane-ether mixture as eluent. IR (film) ν/cm^{-1} 1595 (C=C) ; 1H NMR δ (300 MHz, $CDCl_3$) 2.06 (s, 3 H, CH_3), 3.98 (s, 2 H, CH_2), 6.25 (d, 1 H, $^3J = 1.8$ Hz, H), 7.22-7.36 (m, 6 H, Ph + 1 H). Found : C, 83.67 ; H, 6.97. Calcd for $C_{12}H_{12}O$: C, 83.69 ; H, 7.02.

2-benzyl-5-ethyl-3-methylfuran (23). Compound **21** (0.3 g, 1.5 mmol) and $Pd(PPh_3)_4$ (0.017 g, 0.015 mmol) were stirred in 4 ml of THF at 110 °C for 15 h. 0.18 g (60%) of **23** was isolated as a colorless liquid by distillation under reduced pressure, bp 160 °C (2 mm Hg) ; IR (film) ν/cm^{-1} 1650 (C=C) ; 1H NMR δ (300

MHz, CDCl_3) 1.07 (t, 3 H, $^3J = 7.5$ Hz, $\text{CH}_3\text{-CH}_2$), 1.85 (s, 3 H, CH_3), 2.45 (q, 2 H, $^3J = 7.5$ Hz, CH_3CH_2), 3.78 (s, 2 H, PhCH_2), 5.69 (s, 1 H, CH), 7.05-7.20 (m, 5 H, Ph). Found : C, 83.86 ; H, 8.11. Calcd for $\text{C}_{14}\text{H}_{16}\text{O}$: C, 83.96 ; H, 8.05.

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