JOC Article

Ruthenium/TFA-Catalyzed Coupling of Activated Secondary Propargylic Alcohols with Cyclic 1,3-Diones: Furan versus Pyran Ring Formation

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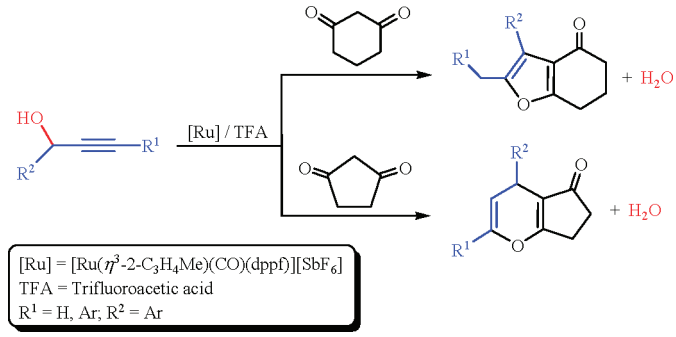

A catalytic system consisting of the 16-electron allyl-ruthenium(II) complex [Ru(η^3-2-C_3H_4Me)(CO)(dppf)][SbF_6] (dppf = 1,1′-bis(diphenylphosphino)ferrocene) and trifluoroacetic acid (TFA) has been used to promote the coupling between secondary propargylic alcohols and cyclic 1,3-diketones. The nature of the resulting products was found to be dependent on the ring size of the dicarbonyl compound employed. Thus, whereas 6,7-dihydro-5*H*-benzofuran-4-ones have been selectively obtained starting from 1,3-cyclohexanediones, via furan-ring formation, the use of 1,3-cyclopentanedione leads instead to 6,7-dihydro-4*H*-cyclopenta[*b*]pyran-5-ones via a pyran-ring formation process.

Introduction

The furan ring is a common structural motif in many biologically active molecules and pharmaceutical substances, furans being also widely employed as versatile building blocks in synthetic organic chemistry.[1] The important role played by these five-membered heterocycles in the field of flavors and fragrances should also be highlighted.[2] As a consequence, the development of synthetic routes to produce furans has been a major research objective for over a century.[1,3] Although several general approaches are presently available, such as the classical cyclocondensation of 1,4-diones (Paal−Knorr synthesis), the search for new methodologies proceeding more efficiently and involving readily available starting materials still remains an active area of research. Among others, relevant contributions to this field have recently emerged by the aid of transition-metal catalysts because they allow the construction of complex furanic molecules from accessible precursors under mild conditions, via

(1) See, for example: (a) Lipshutz, B. H. *Chem. Rev.* **1986**, *86*, 795. (b) Heaney, H.; Ahn, J. S. In *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., ; Rees, C. W., ; Scriven, E. F. V., Eds.; Elsevier: Oxford, 1996; Vol. 2, p 297. (c) Friedrichsen, W. In *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., ; Rees, C. W., ; Scriven, E. F. V., Eds.; Elsevier: Oxford, 1996; Vol. 2, p. 351. (d) Keay, B. A.; Dibble, P. W. In *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., ; Rees, C. W., ; Scriven, E. F. V. Eds.; Elsevier: Oxford, 1996; Vol. 2, p 395. (e) Pozharskii, A. F.; Soldatenkov, A. T.; Katritzky, A. R. In *Heterocycles in Life and Society*; John Wiley & Sons: Chichester, 1997. (f) Wong, H. N. C.; Yu, P.; Yick, C.-Y. *Pure Appl. Chem.* **1999**, *71*, 1041. (g) Lee, H.-K.; Chan, K.-F.; Hui, C.-W.; Yim, H.-K.; Wu, X.-W.; Wong, H. N. C. *Pure Appl. Chem.* **2005**, *77*, 139.

(2) See, for example: (a) Bauer, K.; Garbe, D.; Surburg, H. In *Common Fragrance and Flavor Materials*; Wiley-VCH: Weinheim, 2001. (b) Ash, M.; Ash, I. In *Handbook of Flavors and Fragrances*; Synapse Information Resources, Inc: New York, 2006.

(3) For recent reviews, accounts, and highlights dealing with the synthesis of furans, see: (a) Hou, X. L.; Cheung, H. Y.; Hon, T. Y.; Kwan, P. L.; Lo, T. H.; Tong, S. Y.; Wong, H. N. C. *Tetrahedron* **1998**, *54*, 1955. (b) Keay, B. A. *Chem. Soc. Rev.* **1999**, *28*, 209. (c) Jeevanandam, A.; Ghule, A.; Ling, Y.-C. *Curr. Org. Chem.* **2002**, *6*, 841. (d) Brown, R. C. D. *Angew. Chem., Int. Ed.* **2005**, *44*, 850. (e) Kirsch, S. F. *Org. Biomol. Chem.* **2006**, *4*, 2076. (f) D′Souza, D. M.; Müller, T. J. J. *Chem. Soc. Rev.* **2007**, *36*, 1095. (g) Patil, N. T.; Yamamoto, Y. *ARKIVOC* **2007**, (x), 121. (h) Balme, G.; Bouyssi, D.; Monteiro, N. *Heterocycles* **2007**, *73*, 87.

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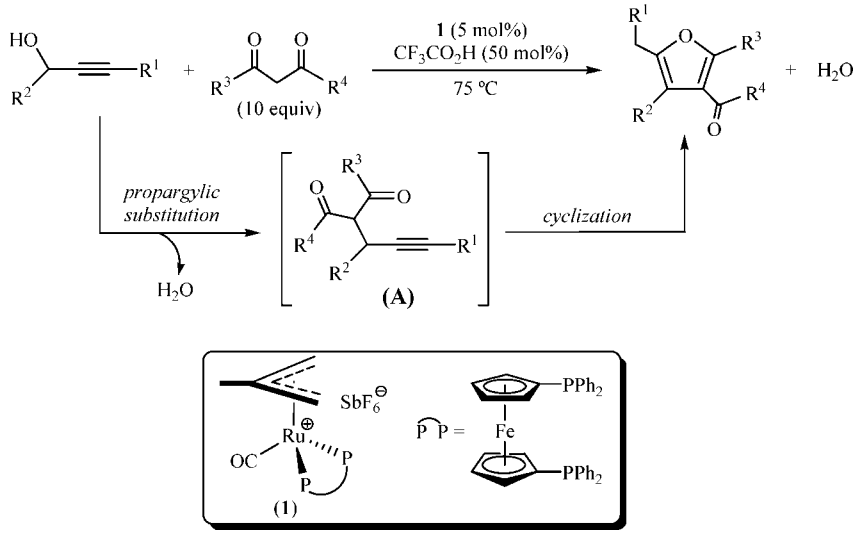
SCHEME 1. Direct Synthesis of Furans from Alkynols and 1,3-Dicarbonyl Compounds



uni- or bimolecular transformations as well as multicomponent reactions (MCR).[3] In the course of current studies focused on the application of ruthenium complexes as catalysts in organic synthesis,[4,5] we recently disclosed a straightforward approach to tetrasubstituted furans from inexpensive secondary propargylic alcohols and acyclic 1,3-dicarbonyl compounds (Scheme 1).[6,7] The process, which proceeds in a one-pot manner, involves the initial trifluoroacetic acid promoted propargylic substitution of the alkynol by the 1,3-dicarbonyl compound[8] and subsequent cyclization of the resulting γ-ketoalkyne **A** catalyzed by the 16-electron allyl-ruthenium(II) complex [Ru(η^3-2-C_3H_4Me)(CO)(dppf)][SbF_6] (**1**; dppf = 1,1′-bis(diphenylphosphino)ferrocene).

By following this synthetic route, a large variety of furans containing carbonyl functionalities on the aromatic ring could be prepared in good yields starting from both terminal and internal secondary alkynols and acyclic β-diketones or β-keto esters.[6] In order to extend the scope of this synthetic methodology to the preparation of novel bicyclic furans, we decided to explore analogous coupling reactions using commercially available cyclic 1,3-diketones (**B** and **C** in Figure 1). However, we have found that the nature of the resulting products is strongly dependent on the ring size of the dicarbonyl compound employed. Thus, whereas the expected 6,7-dihydro-5*H*-benzofuran-4-ones (**D**) are selectively obtained starting from 1,3-cyclohexanediones **B**, the use of 1,3-cyclopentanedione **C** leads instead to 6,7-dihydro-4*H*-cyclopenta[*b*]pyran-5-ones (**E**) in which the formation of a pyran ring takes place. Full details of this research are described in this article.

Results and Discussion

Furan-Ring Formation Reactions: Synthesis of 6,7-Dihydro-5*H*-benzofuran-4-ones and Related Compounds. As shown in Table 1, treatment of terminal propargylic alcohols **2a**−**j** (entries 1−10) with 1 equiv of 1,3-cyclohexanedione (**4**), in THF at 75 °C and in the presence of complex **1** (5 mol %) and TFA (50 mol %), results in the selective formation of 6,7-dihydro-5*H*-benzofuran-4-ones **5a**−**j** after only 3−5 h (except for **5e**, which required 21 h probably as a result of the strong inductive effect of the chloride substituent in the *meta* position of the aromatic ring).[9] Internal alkynols can also participate in this coupling reaction, as clearly exemplified in the synthesis of 2-benzyl-3-(2-methoxyphenyl)-6,7-dihydro-5*H*-benzofuran-4-one (**5k**) starting from 1-(2-methoxyphenyl)-3-phenyl-2-propyn-1-ol (**3a**) (a

(4) Isomerization of allylic alcohols into carbonyl compounds: (a) Cadierno, V.; García-Garrido, S. E.; Gimeno, J. *Chem. Commun.* **2004**, 232. (b) Cadierno, V.; Crochet, P.; García-Garrido, S. E.; Gimeno, J. *Dalton Trans.* **2004**, 3635. (c) Crochet, P.; Díez, J.; Fernández-Zúmel, M. A.; Gimeno, J. *Adv. Synth. Catal.* **2006**, *348*, 93. (d) Crochet, P.; Fernández-Zúmel, M. A.; Gimeno, J.; Scheele, M. *Organometallics* **2006**, *25*, 4846. (e) Cadierno, V.; García-Garrido, S. E.; Gimeno, J.; Varela-Álvarez, A.; Sordo, J. A. *J. Am. Chem. Soc.* **2006**, *128*, 1360. Reduction of allylic alcohols into saturated alcohols: (f) Cadierno, V.; Francos, J.; Gimeno, J.; Nebra, N. *Chem. Commun.* **2007**, 2536. Cycloisomerization of (Z)-enynols into furans: (g) Díaz-Álvarez, A. E.; Crochet, P.; Zablocka, M.; Duhayon, C.; Cadierno, V.; Gimeno, J.; Majoral, J. P. *Adv. Synth. Catal.* **2006**, *348*, 1671. (h) Albers, J.; Cadierno, V.; Crochet, P.; García-Garrido, S. E.; Gimeno, J. *J. Organomet. Chem.* **2007**, *692*, 5234. Intermolecular [2 + 2 + 2] alkyne cyclotrimerizations: (i) Cadierno, V.; García-Garrido, S. E.; Gimeno, J. *J. Am. Chem. Soc.* **2006**, *128*, 15094. Meyer−Schuster and Rupe isomerizations of propargylic alcohols: (j) Cadierno, V.; Díez, J.; García-Garrido, S. E.; Gimeno, J. *Chem. Commun.* **2004**, 2716. (k) Cadierno, V.; García-Garrido, S. E.; Gimeno, J. *Adv. Synth. Catal.* **2006**, *348*, 101. (l) Cadierno, V.; Díez, J.; García-Garrido, S. E.; Gimeno, J.; Nebra, N. *Adv. Synth. Catal.* **2006**, *348*, 2125. Selective deprotection of *N*-allylic amines, amides, and lactams: (m) Cadierno, V.; García-Garrido, S. E.; Gimeno, J.; Nebra, N. *Chem. Commun.* **2005**, 4086. (n) Cadierno, V.; Gimeno, J.; Nebra, N. *Chem. Eur. J.* **2007**, *13*, 6590.

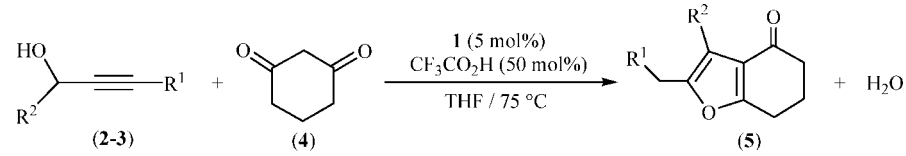
(5) For reviews and books highlighting the burgeoning role of ruthenium catalysts in organic synthesis, see: (a) Bruneau, C.; Dixneuf, P. H. *Chem. Commun.* **1997**, 507. (b) Naota, T.; Takaya, H.; Murahashi, S.-I. *Chem. Rev.* **1998**, *98*, 2599. (c) Trost, B. M.; Toste, F. D.; Pinkerton, A. B. *Chem. Rev* **2001**, *101*, 2067. (d) Trnka, T. M.; Grubbs, R. H. *Acc. Chem. Res.* **2001**, *34*, 18. (e) Ritleng, V.; Sirlin, C.; Pfeffer, M. *Chem. Rev.* **2002**, *102*, 1731. (f) *Ruthenium in Organic Synthesis*; Murahashi, S.-I. Ed.; Wiley-VCH: Weinheim, 2004. (g) *Ruthenium Catalysts and Fine Chemistry*; Bruneau, C., ; Dixneuf, P. H. Eds.; Springer: Berlin, 2004. (h) Trost, B. M.; Frederiksen, M. U.; Rudd, M. T. *Angew. Chem., Int. Ed.* **2005**, *44*, 6630. (i) Bruneau, C.; Dérien, S.; Dixneuf, P. H. *Top. Organomet. Chem.* **2006**, *19*, 295. (j) Bruneau, C.; Dixneuf, P. H. *Angew. Chem., Int. Ed.* **2006**, *45*, 2176. (k) Gimeno, J. Ruthenium Catalyzed Processes. *Curr. Org. Chem.* **2006**, *10* (2), 113–225. (a thematic issue devoted to this topic)

(6) Cadierno, V.; Gimeno, J.; Nebra, N. *Adv. Synth. Catal.* **2007**, *349*, 382.

(7) We note that when a primary amine is introduced in the reaction media pyrroles instead of furans are selectively formed: (a) Cadierno, V.; Gimeno, J.; Nebra, N. *Chem. Eur. J.* **2007**, *13*, 9973.

(8) Brønsted acid catalyzed propargylations of several organic substrates, including 1,3-dicarbonyl compounds, with alkynols have been reported: (a) Sanz, R.; Martínez, A.; Álvarez-Gutiérrez; J. M.; Rodríguez, F. *Eur. J. Org. Chem.* **2006**, 1383. (b) Sanz, R.; Miguel, D.; Martínez, A.; Álvarez-Gutiérrez, J. M.; Rodríguez, F. *Org. Lett.* **2007**, *9*, 727. (c) Sanz, R.; Martínez, A.; Miguel, D.; Álvarez-Gutiérrez, J. M.; Rodríguez, F. *Synthesis* **2007**, 3252. (d) Yadav, J. S.; Reddy, B. V. S.; Rao, T. S.; Krishna, B. B. M.; Kumar, G. G. K. S. N. *Chem. Lett.* **2007**, *36*, 1472. In these works only 5 mol % of the acid is required to promote efficiently the propargylation process. In our case the use of larger quantities of TFA (50 mol %) is imperative in order to avoid the Meyer−Schuster isomerization of the propargylic alcohol catalyzed by the ruthenium complex **1**. See refs 4k and 4l.

TABLE 1. Catalytic Synthesis of 6,7-Dihydro-5*H*-benzofuran-4-ones from Propargylic Alcohols and 1,3-Cyclohexanedione[a]



entry	propargylic alcohol	time (h)	yield (%)[b]
1	R^1 = H; R^2 = Ph (**2a**)	5	**5a**, 77
2	R^1 = H; R^2 = 1-naphthyl (**2b**)	3	**5b**, 74
3	R^1 = H; R^2 = 2-naphthyl (**2c**)	5	**5c**, 76
4	R^1 = H; R^2 = 2-C_6H_4Cl (**2d**)	5	**5d**, 89
5	R^1 = H; R^2 = 3-C_6H_4Cl (**2e**)	21	**5e**, 58
6	R^1 = H; R^2 = 4-C_6H_4Cl (**2f**)	5	**5f**, 87
7	R^1 = H; R^2 = 2-C_6H_4OMe (**2g**)	2	**5g**, 92
8	R^1 = H; R^2 = 3-C_6H_4OMe (**2h**)	5	**5h**, 87
9	R^1 = H; R^2 = 4-C_6H_4OMe (**2i**)	3	**5i**, 90
10	R^1 = H; R^2 = 2-thienyl (**2j**)	3	**5j**, 90
11	R^1 = Ph; R^2 = 2-C_6H_4OMe (**3a**)	21	**5k**, 61

[a] All reactions between propargylic alcohols **2** and **3** (1 mmol) and 1,3-cyclohexanedione (**4**) (1 mmol) were carried out in the presence of complex **1** (0.05 mmol) and CF_3CO_2H (0.5 mmol), in THF (0.5 mL) at 75 °C (sealed tube), for the indicated time. [b] Isolated yield.

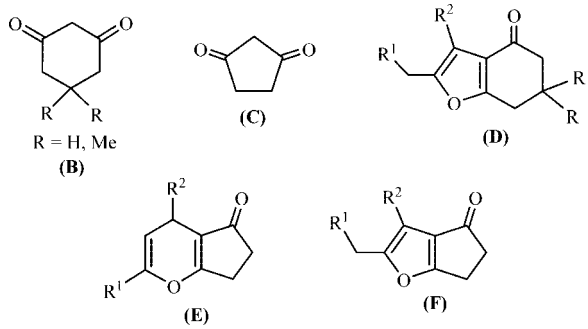


FIGURE 1. Structure of compounds **B**−**F**.

longer reaction time is also in this case required; entry 11). Appropriate chromatographic workup allowed the isolation of bicycles **5** in moderate to good yields (58−90%). The characterization of the novel compounds **5a,c**−**k** was achieved by means of standard spectroscopic techniques (GC/MS, HRMS, IR, and ^{1}H and ^{13}C NMR) and, in the case of solid samples, by elemental analyses, all data being fully consistent with the proposed formulations (details are given in Supporting Information). We note that, as previously observed in our study with acyclic substrates,[6] only secondary aromatic and heteroaromatic alkynols can be employed in this transformation. Thus, attempts to promote related coupling reactions starting from alkyl-monosubstituted propargylic alcohols, such as 1-octyn-3-ol or 3-butyn-2-ol, resulted in the formation of complicated reaction mixtures from which the desired 6,7-dihydro-5*H*-benzofuran-4-ones (ca. 10−20% GC/MS yields in the crude reaction mixtures) could not be separated from the uncharacterized byproduct.

Under the same reaction conditions, the closely related 6,7-dihydro-5*H*-benzofuran-4-ones **7a,i,j** could also be prepared in good yields and with complete regioselectivity starting from commercially available 5,5-dimethyl-1,3-cyclohexanedione (dimedone) and the appropriate alkynol (Scheme 2).

Stimulated by these successful results and having in mind the relevant biological activity of furocoumarins, key structural units in many natural products,[10] we wondered whether this type of heterocycles would be accessible by using our one-pot propargylation−cyclization methodology.[11] Gratifyingly, we found that treatment of 4-hydroxycoumarin **8** with alkynol **2i**, under the standard reaction conditions, results in the selective formation of the substituted furocoumarin **10**, isolated in 72% yield after chromatographic workup (Scheme 3). The molecular structure of **10** was unambiguously confirmed by means of single-crystal X-ray diffraction techniques (see Supporting Information). The related compound **11** could also be synthesized in high yield starting from **2i** and 4-hydroxy-6-methylpyran-2-one **9** (Scheme 3), confirming the generality of this catalytic transformation.

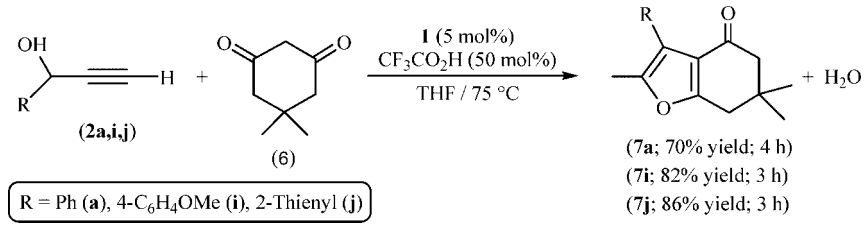
Pyran-Ring Formation Reactions: Synthesis of 6,7-Dihydro-4*H*-cyclopenta[*b*]pyran-5-ones. Remarkably, in contrast to the reactions with 1,3-cyclohexanediones, when 1,3-cyclopentanedione is used as substrate, the expected 5,6-dihydrocyclopenta[*b*]furan-4-ones (**F** in Figure 1) are not formed, the reactions giving instead 6,7-dihydro-4*H*-cyclopenta[*b*-]pyran-5-ones (**E** in Figure 1). Table 2 collects the results obtained when terminal **2a**−**i** and internal **3a**−**c** propargylic alcohols were subjected to react with 1,3-cyclopentanedione (**12**) under our standard reaction conditions, i.e., [alkynol]:[**12**]:[TFA]:[Ru] ratio = 20:20:10:1 in THF at 75 °C. The corresponding 6,7-dihydro-4*H*-cyclopenta[*b*]pyran-5-ones **13** are in all cases formed exclusively, with the isomeric 5,6-dihydro-cyclopenta[*b*]furan-4-ones (**F**) being not detected in the crude reaction mixtures by GC/MS. The characterization of compounds **13**, isolated as solid samples in 61−94% yield

(9) In our previous work involving acyclic 1,3-dicarbonyl compounds (ref 6), the catalytic reactions were performed under "solvent-free" conditions, employing the 1,3-dicarbonyl compound (10 equiv with respect to the alkynol) itself as solvent. In order to avoid the waste of expensive reagents, we decided to reduce the quantity of the 1,3-diketone (1 equiv per equivalent of the alkynol), dissolving all the components of the catalytic reaction in the minimum amount of tetrahydrofuran.

(10) See, for example: (a) Donnelly, D. M. X.; Boland, G. M. *Nat. Prod. Rep.* **1998**, 241. (b) Misky, M.; Jakupovic, J. *Phytochemistry* **1990**, *29*, 1995. (c) Schuster, N.; Christiansen, C.; Jakupovic, J.; Mungai, M. *Phytochemistry* **1993**, *34*, 1179. (d) Grese, T.; Pennington, L. D.; Sluka, J. P.; Adrian, M. D.; Cole, H. W.; Fuson, T. R.; Magee, D. E.; Phillips, D. L.; Rowley, E. R.; Shetler, P. K.; Short, L. L.; Venugopalan, M.; Yang, N. N.; Sato, M.; Glasebrook, A. L.; Bryant, H. U. *J. Med. Chem.* **1998**, *41*, 1272. (e) Wang, X.; Bastow, K. F.; Sun, C.; Lin, Y.; Yu, H.; Don, M.; Wu, T.; Nakamura, S.; Lee, K. *J. Med. Chem.* **2004**, *47*, 5816. (f) Zhao, L.; Brinton, R. D. *J. Med. Chem.* **2005**, *48*, 3463.

(11) Propargylation of coumarin derivatives with propargylic alcohols catalyzed by $Yb(OTf)_3$ has recently been reported: Huang, W.; Wang, J.; Shen, Q.; Zhou, X. *Tetrahedron* **2007**, *63*, 11636.

SCHEME 2. Synthesis of 6,7-Dihydro-5*H*-benzofuran-4-ones 7 from Alkynols and Dimedone



SCHEME 3. Synthesis of Compounds 10 and 11

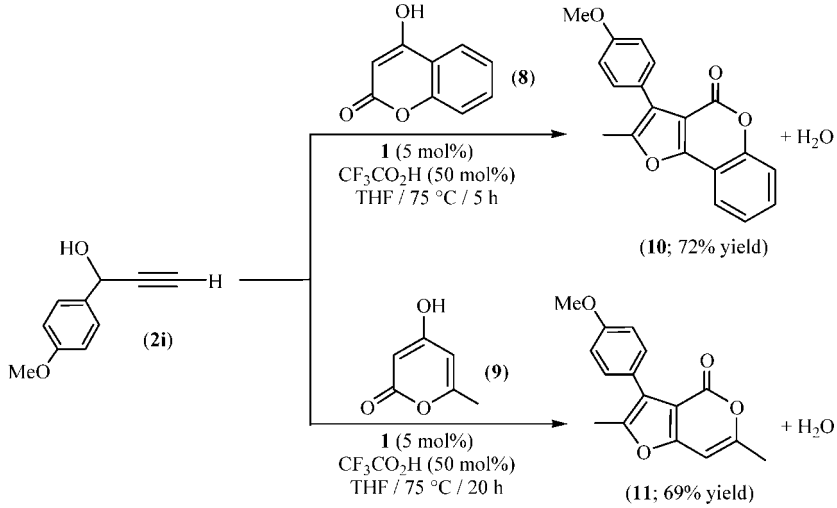
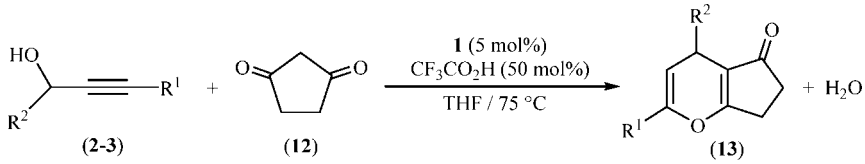


TABLE 2. Catalytic Synthesis of 6,7-Dihydro-4*H*-cyclopenta[*b*]pyran-5-ones from Propargylic Alcohols and 1,3-Cyclopentanedione[a]



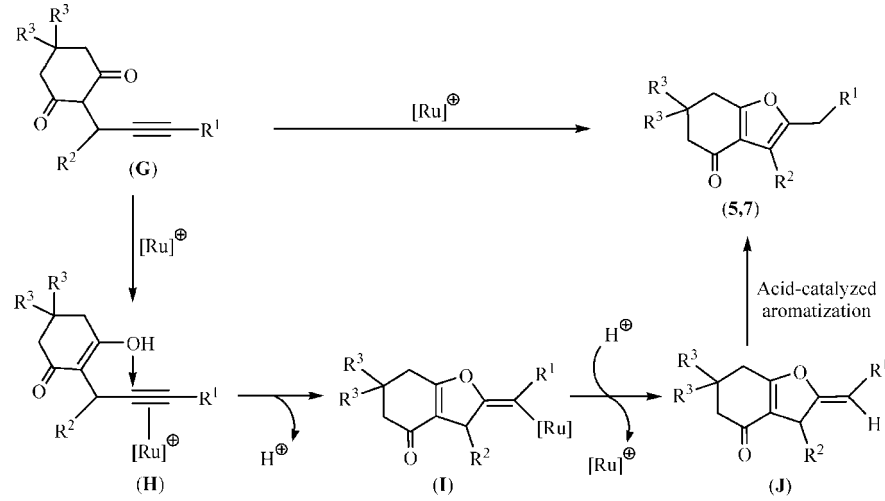
entry	propargylic alcohol	time (h)	yield (%)[b]
1	R^1 = H; R^2 = Ph (**2a**)	5	**13a**, 91
2	R^1 = H; R^2 = 1-naphthyl (**2b**)	2	**13b**, 89
3	R^1 = H; R^2 = 2-naphthyl (**2c**)	5	**13c**, 72
4	R^1 = H; R^2 = 2-C_6H_4Cl (**2d**)	12	**13d**, 82
5	R^1 = H; R^2 = 3-C_6H_4Cl (**2e**)	21	**13e**, 61
6	R^1 = H; R^2 = 4-C_6H_4Cl (**2f**)	5	**13f**, 87
7	R^1 = H; R^2 = 2-C_6H_4OMe (**2g**)	2	**13g**, 94
8	R^1 = H; R^2 = 3-C_6H_4OMe (**2h**)	5	**13h**, 85
9	R^1 = H; R^2 = 4-C_6H_4OMe (**2i**)	3	**13i**, 92
10	R^1 = H; R^2 = 2-thienyl (**2i**)	3	**13j**, 93
11	R^1 = Ph; R^2 = 2-C_6H_4OMe (**3a**)	4	**13k**, 91
12	R^1 = Me; R^2 = Ph (**3b**)	18	**13l**, 78
13	R^1 = Me; R^2 = 4-C_6H_4OMe (**3c**)	8	**13m**, 92

[a] All reactions between propargylic alcohols **2** and **3** (1 mmol) and 1,3-cyclopentanedione (**12**) (1 mmol) were carried out in the presence of complex **1** (0.05 mmol) and CF_3CO_2H (0.5 mmol), in THF (0.5 mL) at 75 °C (sealed tube), for the indicated time. [b] Isolated yield.

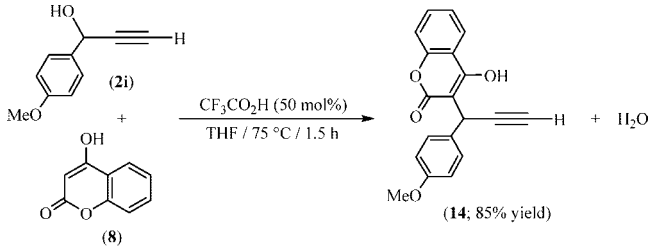
after appropriate chromatographic workup, was straightforward by following their analytical and spectroscopic data (details are given in the Supporting Information). Moreover, X-ray diffraction studies on compound **13j**, containing a thienyl substituent, unequivocally confirmed the formation of a six-membered pyran ring in these catalytic reactions (see Supporting Information).

Mechanistic Proposals. We assume that formation of 6,7-dihydro-5*H*-benzofuran-4-ones **5** and **7** (Table 1 and Scheme 2) follows the same reaction pathway previously proposed by us in the coupling of propargylic alcohols with acyclic 1,3-dicarbonyl compounds.[6] It involves the initial TFA-promoted propargylation of the 1,3-cyclohexanediones **4** and **6** with the alkynols to afford the corresponding γ-ketoalkyne intermediates,[8] which undergo a subsequent ruthenium-catalyzed cyclization to give the final reaction products (see Scheme 1). We note that, although not isolated, the γ-ketoalkynes **G** (Scheme 4) can be detected in the reaction media by monitoring the catalytic reactions by GC/MS. Transformation of intermediates **G** into the final 6,7-dihydro-5*H*-benzofuran-4-ones involves the initial activation of the C≡C bond of the alkyne, via π-coordination to ruthenium (intermediates **H**; see Scheme 4). Subsequent

SCHEME 4. Proposed Reaction Pathway for the Cyclization of γ-Ketoalkynes G into 6,7-Dihydro-5*H*-benzofuran-4-ones



SCHEME 5. TFA-Promoted Propargylation of 4-Hydroxycoumarin



intramolecular nucleophilic attack of the enolic form of the keto group at the C_2 position of the coordinated alkyne generates the alkenyl-ruthenium derivatives **I** (*exo* cyclization), which by protonolysis liberates the heterocycles **J**, regenerating the catalytically active ruthenium species. Final aromatization of **J**, promoted by the Brønsted acid TFA or the Lewis acid ruthenium species present in solution, leads to the final reaction products.[12]

Formation of furocoumarin **10** and the furo[3,2-c]pyran-4-one **11** (Scheme 3) most probably involves the same cyclization sequence. In order to unambiguously confirm that initial TFA-promoted propargylation of the carbonylic substrates is involved in the catalytic cycle, the reactivity of alkynol **2i** toward 4-hydroxycoumarin (**8**) using only CF_3CO_2H (50 mol %) in the absence of complex **1** was studied (Scheme 5). In accord with the proposed mechanism, the reaction affords the γ-ketoalkyne **14**, which is selectively formed after only 1.5 h. Chromatographic workup allowed the isolation (85%) and spectroscopic characterization of this functionalized alkyne (see Supporting Information). As expected, treatment of **14** with complex **1** and TFA, in THF at 75 °C, cleanly generates the furocoumarin **10**.

To the best of our knowledge, the synthesis of 6,7-dihydro-5*H*-benzofuran-4-ones through the direct coupling of propargylic alcohols with 1,3-cyclohexanedione derivatives has not being described to date.[13] The only related work is the cyclization of the terminal secondary alkynols **2** with 1,3-cyclohexanedione **4** to yield 4,6,7,8-tetrahydrochromen-5-ones, via a pyran-ring formation process, catalyzed by the thiolate-bridged diruthenium(III) complexes $[Cp^*RuCl(\mu^2\text{-}SR)_2RuCp^*Cl]$ (R = Me, ^{n}Pr, ^{i}Pr) (Scheme 6).[14] The reaction proceeds through the initial nucleophilic attack of the carbon atom of 1,3-cyclohexanedione (**4**) to the C_γ atom of the intermediate allenylidene complex **K**, generated by activation of the terminal propargylic alcohol.[15] The resulting vinylidene intermediate **L** evolves into the alkenyl complex **M** by intramolecular nucleophilic attack of the enolic hydroxyl group to the electrophilic α-carbon of the vinylidene chain. Final demetalation of **M** liberates the 4,6,7,8-tetrahydrochromen-5-ones and regenerates the catalytically active ruthenium species.[16]

The different outcome of our catalytic reaction is probably based on the reluctance of the π-alkyne intermediates **H** (when R^1 = H) to undergo tautomerization into the corresponding vinylidene isomers (analogous to **L**), which leads to the formation of five-membered furan rings instead of the six-membered pyrans obtained by Nishibayashi and co-workers. Moreover, the involvement of π-alkyne intermediates **H** instead of vinylidenes **L** is also in complete accord with the fact that internal alkynols, unable to form vinylidene species, also undergo the cyclization reaction to afford the corresponding 6,7-dihydro-5*H*-benzofuran-4-ones (entry 11 in Table 1), in marked contrast to Nishibayashi's case where internal alkynols are unreactive.

Concerning the synthesis of the 6,7-dihydro-4*H*-cyclopenta[*b*]pyran-5-ones **13** (Table 2), we propose that in this case an *endo*-cyclization of the initially formed γ-ketoalkynes **N** (also detected by GC/MS) takes place via intramolecular nucleophilic attack of the enol at the C_1 position of the

(12) We note that such a reaction pathway is proposed in the closely related metal-catalyzed cyclizations of (*Z*)-enynols into furans. See, for example: (a) Seiller, B.; Bruneau, C.; Dixneuf, P. H. *Tetrahedron* **1995**, *51*, 13089. (b) Gabriele, B.; Salerno, G.; Lauria, E. *J. Org. Chem.* **1999**, *64*, 7687.

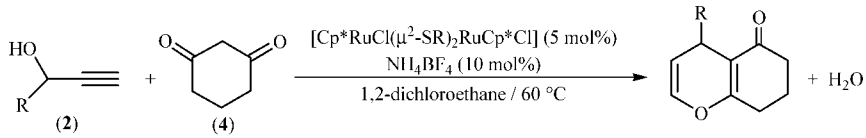
(13) No cyclizative C-C coupling reactions between alkynols and 1,3-cyclohexanediones have been reported. See, for example: (a) Gabbutt, C. D.; Hepworth, J. D.; Heron, B. M.; Partington, S. M.; Thomas, D. A. *Dyes Pigm.* **2001**, *49*, 65. (b) Nakatsuji, S.; Yahiro, T.; Nakashima, K.; Akiyama, S.; Nakazumi, H. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 1641.

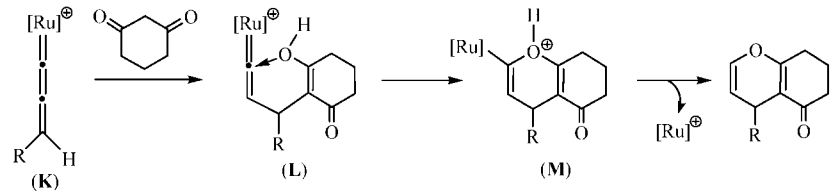
(14) Nishibayashi, Y.; Yoshikawa, M.; Inada, Y.; Hidai, M.; Uemura, S. *J. Org. Chem.* **2004**, *69*, 3408.

(15) Transformation of terminal propargylic alcohols into allenylidene ligands in the coordination sphere of transition metals is a well-known process. For reviews on this topic, see: (a) Bruce, M. I. *Chem. Rev.* **1998**, *98*, 2797. (b) Cadierno, V.; Gamasa, M. P.; Gimeno, J. *Eur. J. Inorg. Chem.* **2001**, 571. (d) King, R. B. Vinylidene, Allenylidene and Metallacumulene Complexes. *Coord. Chem. Rev.* **2004**, *248* (15−16), 1531–1703.

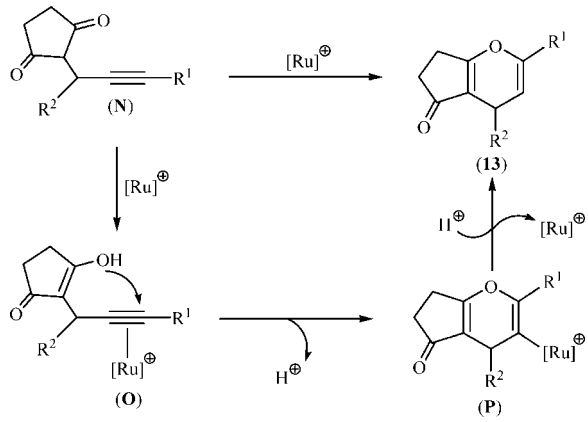
(16) Such a reaction pathway involving vinylidene intermediates is in complete accord with recent stoichiometric studies performed with mononuclear allenylidene-ruthenium(II) complexes containing the electron-rich fragment $[Cp^*Ru(dippe)]^+$: (a) Bustelo, E.; Jiménez-Tenorio, M.; Puerta, M. C.; Valerga, P. *Organometallics* **2007**, *26*, 4300.

SCHEME 6. Coupling of Terminal Alkynols with 1,3-Cyclohexanedione to Afford 4,6,7,8-Tetrahydrochromen-5-ones Catalyzed by Complexes [Cp*RuCl(μ^2-SR)$_2$RuCp*Cl][14]





SCHEME 7. Proposed Reaction Pathway for the Formation of 6,7-Dihydro-4*H*-cyclopenta[*b*]pyran-5-ones



coordinated alkyne (intermediate **O**; see Scheme 7). Final protonolysis of the resulting alkenyl species **P** liberates the 6,7-dihydro-4*H*-cyclopenta[*b*]pyran-5-ones. The preference shown by intermediates **O** to undergo the *endo* versus the expected *exo* cyclization probably arises from the higher ring strain in the hypothetical 5,6-dihydro-cyclopenta[*b*]furan-4-ones (**F** in Figure 1). We note that the coupling of alkynol **2a** with 1,3-cyclopentanedione **12** to afford **13a** was already described by Nishibayashi and co-workers using the dinuclear catalyst [Cp*RuCl(μ^2-SMe)$_2$RuCp*Cl].[14] As in the case of 1,3-cyclohexanedione (Scheme 6), they also proposed an intramolecular nucleophilic attack of the enolic hydroxyl group to the electrophilic α-carbon in the corresponding vinylidene intermediate as a key step in the catalytic cycle. Once again, the results obtained with the internal alkynols **3a**−**c** (entries 11−13 in Table 2) allow us to discard the involvement of vinylidene species in our catalytic reactions.

In summary, in this paper we have described a simple and highly efficient one-pot catalytic protocol for the preparation of 6,7-dihydro-5*H*-benzofuran-4-ones and 6,7-dihydro-4*H*-cyclopenta[*b*]pyran-5-ones. These synthetic routes, starting from readily accessible propargylic alcohols and commercially available cyclic 1,3-dicarbonyl compounds, represent appealing methodologies that are either scarcely documented, i.e., the synthesis of 6,7-dihydro-4*H*-cyclopenta[*b*]pyran-5-ones,[14] or unprecedented, i.e., the synthesis of 6,7-dihydro-5*H*-benzofuran-4-ones.

Experimental Section

General Procedure for the Catalytic Reactions. The corresponding propargylic alcohol (**2a**−**j** or **3a**−**c**; 1 mmol) and the appropriate 1,3-dicarbonyl compound or coumarin (**4**, **6**, **8**, **9**, or **12**; 1 mmol) were introduced into a sealed tube under nitrogen atmosphere. THF (0.5 mL), [Ru(η^3-2-C$_3$H$_4$Me)(CO)(dppf)][SbF$_6$] (**1**) (0.049 g, 0.05 mmol), and CF_3CO_2H (37 μL, 0.5 mmol) were then added at room temperature, and the resulting solution heated at 75 °C for the indicated time (see Tables 1 and 2 and Schemes 2 and 3; the course of the reaction was monitored by regular sampling and analysis by GC/MS). After removal of volatiles under vacuum, the residue was purified by column chromatography (silica gel) using a mixture EtOAc/hexanes (1:20) as eluent (a 1:50 mixture of EtOAc/hexanes was used for compounds **10** and **11**). Compounds 2-methyl-3-(1-naphthyl)-6,7-dihydro-5*H*-benzofuran-4-one (**5b**)[6] and 4-phenyl-6,7-dihydro-4*H*-cyclopenta[*b*]pyran-5-one (**13a**)[14] have been previously reported. Analytical and spectroscopic data for all new compounds are included in Supporting Information. Representative examples are:

2-Methyl-3-phenyl-6,7-dihydro-5*H*-benzofuran-4-one (5a). Colorless oil; IR (Nujol, cm^{-1}): ν 1575 (C═C), 1682 (C═O). ^{1}H NMR (300.1 MHz, $CDCl_3$): δ 2.14 (m, 2H), 2.31 (s, 3H), 2.46 (m, 2H), 2.88 (m, 2H), 7.26−7.34 (m, 5H) ppm; ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 11.9, 22.4, 23.6, 38.5, 119.6, 125.2, 126.9, 127.8, 129.7, 131.6, 148.7, 165.9, 194.4 ppm; MS (EI, 70 eV): *m*/*z* 226 (M$^+$, 100), 211 (5), 198 (90), 183 (5), 170 (50), 155 (15), 141 (10); HRMS (EI): *m*/*z* = 226.09839, $C_{15}H_{14}O_2$ requires 226.09883.

3-(4-Methoxyphenyl)-2-methyl-furo[3,2-*c*]chromen-4-one (10). White solid; IR (Nujol, cm^{-1}): ν 1594, 1615 and 1629 (C═C), 1738 (C═O). ^{1}H NMR (300.1 MHz, $CDCl_3$): δ 2.52 (s, 3H), 3.86 (s, 3H), 6.99 (d, 2H, *J* = 8.5 Hz), 7.26−7.49 (m, 5H), 7.87 (d, 1H, *J* = 7.4 Hz) ppm; ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 12.5, 55.2, 109.7, 112.8, 113.7, 117.0, 120.0, 120.5, 122.1, 124.2, 130.1, 131.0, 151.2, 152.2, 156.1, 157.8, 159.1 ppm; MS (EI, 70 eV): *m*/*z* 306 (M$^+$, 100), 291 (10), 263 (5); HRMS (EI): *m*/*z* = 306.08786, $C_{19}H_{14}O_4$ requires 306.08866.

3-(4-Methoxyphenyl)-2,6-dimethyl-furo[3,2-*c*]pyran-4-one (11). White solid; IR (Nujol, cm^{-1}): ν 1574, 1601 and 1615 (C═C), 1738 (C═O). ^{1}H NMR (300.1 MHz, $CDCl_3$): δ 2.33 (s, 3H), 2.42 (s, 3H), 3.84 (s, 3H), 6.37 (s, 1H), 6.97 (m, 2H), 7.41 (m, 2H) ppm; ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 12.4, 20.1, 55.2, 95.4, 107.5, 113.6, 118.6, 122.4, 130.9, 142.6, 149.4, 158.9, 159.1, 160.6 ppm; MS (EI, 70 eV): *m*/*z* 270 (M$^+$, 100), 255 (10), 227 (10); HRMS (EI): *m*/*z* = 270.08836, $C_{16}H_{14}O_4$ requires 270.08866.

4-(1-Naphthyl)-6,7-dihydro-4*H*-cyclopenta[*b*]pyran-5-one (13b). Orange solid; IR (Nujol, cm^{-1}): ν 1614 and 1666 (C═C), 1698 (C═O). ^{1}H NMR (300.1 MHz, $CDCl_3$): δ 2.52 (m, 2H), 2.68−2.88 (m, 2H), 5.12 (br, 1H), 5.30 (dd, 1H, *J* = 6.0 and 3.7 Hz), 6.54 (dd, 1H, *J* = 6.0 and 1.7 Hz), 7.22−7.89 (m, 6H), 8.20 (d, 1H, *J* = 8.5 Hz) ppm; ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 25.7, 30.2, 32.9, 108.9, 116.7, 122.8, 125.5, 125.6, 125.8, 126.2, 127.5, 128.9, 130.7,

134.0, 138.3, 138.7, 180.1, 203.7 ppm; MS (EI, 70 eV): *m*/*z* 262 (M^+, 100), 245 (80), 135 (80); Anal. Calcd for $C_{18}H_{14}O_2$: C, 82.42; H, 5.38. Found: C, 82.25; H, 5.40.

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Supporting Information Available: General experimental methods, characterization data and copies of the ^1H and ^{13}C NMR spectra of all new compounds (**5a**, **5c**−**k**, **7a**, **7i**, **7j**, **10**, **11**, **13b**−**m**, and **14**), and a CIF file giving crystallographic data for compounds **10** and **13j**. This material is available free of charge via the Internet at http://pubs.acs.org.

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