ORGANIC LETTERS

2006
Vol. 8, No. 3
515−518

Gold(I)-Catalyzed Formation of 4-Alkylidene-1,3-dioxolan-2-ones from Propargylic *tert*-Butyl Carbonates

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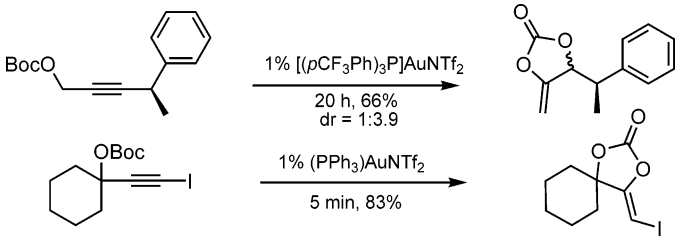
Received December 21, 2005

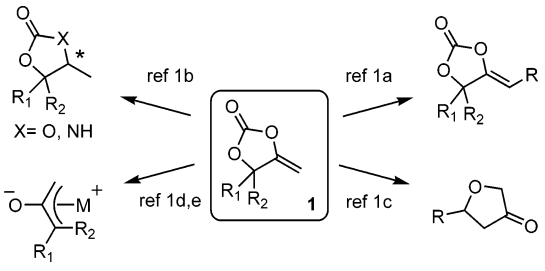
ABSTRACT



A study concerning the gold(I)-catalyzed rearrangement of propargylic *tert*-butyl carbonates into 4-alkylidene-1,3-dioxolan-2-ones is described. The mild reaction conditions employed allow the efficient synthesis of a variety of cyclic carbonates that would be less conveniently obtained using reported methods. Variability in the structure of the final product has been observed and is significantly dependent on the nature of the substituent attached to the alkyne moiety.

Derivatives of 4-methylene-1,3-dioxolan-2-ones **1** are attractive building blocks for organic synthesis because they represent a useful source of masked hydroxyketones, which can be further transformed into a range of more elaborated structures (Scheme 1).[1] However, their use in synthesis remains largely unexplored due to a lack of efficient and general methods to access them.[2]

Scheme 1. Possible Transformations of 4-Methylene-1,3-dioxolan-2-ones **1**



Following the recent developments in the field of gold-catalyzed nucleophilic additions onto alkynes,[3] we surmised that a suitably selected propargylic carbonate **2** might be a

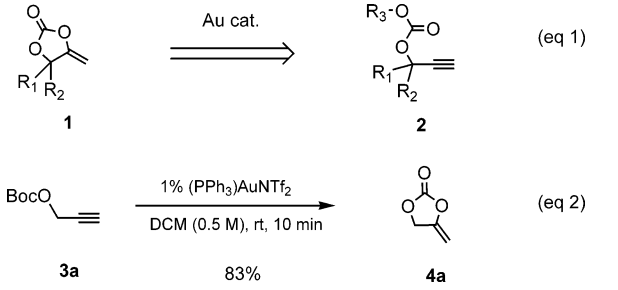
(1) (a) Toullec, C.; Martin, A. C.; Gio-Batta, M.; Bruneau, C. Dixneuf, P. H. *Tetrahedron Lett.* **2000**, *41*, 5527−5531. (b) Le Gendre, P.; Thominot, P.; Bruneau, C.; Dixneuf, P. H. *J. Org. Chem.* **1998**, *63*, 1806−1809; **1996**, *61*, 8453−8455. (c) Inoue, Y.; Matsushita, K. Yen, I−F.; Imaizumi, S. *Chem. Lett.* **1991**, 1377−1378. (d) Ohe, K.; Matsuda, H.; Ishihara, T.; Ogoshi, S.; Chatani, N.; Murai, S. *J. Org. Chem.* **1993**, *58*, 1173−1177. (e) Ohe, K.; Matsuda, H.; Morimoto, T.; Ogoshi, S.; Chatani, N.; Murai, S. *J. Am. Chem. Soc.* **1994**, *116*, 4125−4126.

(2) 4-Methylene-1,3-dioxolan-2-ones are typically synthesized using propargylic alcohols under CO_2 pressure and in the presence of a catalyst. The great majority of these methods are limited to the use of tertiary propargylic alcohols. (a) Ru: Sazaki, Y. *Tetrahedron Lett.* **1986**, *27*, 1573−1574. (b) Co: Inoue, Y.; Ishikawa, J.; Taniguchi, M.; Hashimoto, H. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 1204−1206. (c) Cu: Gu, Y.; Shi, F.; Deng, Y. *J. Org. Chem.* **2004**, *69*, 391−394. Laas, H.; Nissen, A.; Nürrenbach, A. *Synthesis* **1981**, 958−959. (d) PBu_3: Joumier, J. M.; Bruneau, C.; Dixneuf, P. H. *Synlett* **1992**, 453−454. Joumier, J. M.; Fournier, J.; Bruneau, C.; Dixneuf, P. H. *J. Chem. Soc., Perkin. Trans. 1*, **1991**, 3271−3274. Fournier, J.; Bruneau, C.; Dixneuf, P. H. *Tetrahedron Lett.* **1989**, *30*, 3981−3982. (e) Pd: Jiang, Z.-X.; Qing, F.-L. *J. Fluorine Chem.* **2003**, *123*, 57−60. Uemura, K., Kawaguchi, T.; Takayama, H. Nakamura, A. Inoue, Y. *J. Mol. Catal. A: Chem.* **1999**, *139*, 1−9. Iritani, K.; Yanagihara, N.; Utimoto, K. *J. Org. Chem.* **1986**, 51, 5499−5501. (f) Inorganic base: see ref 2e.

10.1021/ol053100o CCC: $33.50
Published on Web 01/12/2006

valuable precursor for the gold-catalyzed synthesis of **1** (Scheme 2, eq 1). Compound **3a** was first chosen as a model

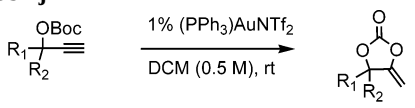
Scheme 2. Synthetic Approach to 4-Methylene-1,3-dioxolan-2-ones from Propargylic Carbonates



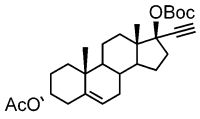
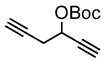
substrate to validate this approach (Scheme 2, eq 2).[4] We were pleased to observe that the rearrangement of **3a**, catalyzed by 1% of $(Ph_3P)AuNTf_2$[5] in dichloromethane, afforded the desired carbonate **4a** in 83% yield.

The reaction proved to be quite general and various substituted terminal alkynes reacted under the same conditions to furnish the corresponding cyclic carbonates in yields ranging from 40% to 98% (Table 1). The time required to reach completion is generally less than 1 h with the exception of tertiary *tert*-butyloxycarbonyl substrates **3f**, **3j**, and **3i**, which were less reactive. The reaction of androstene derivative **3h** was exceptionally efficient and gave the corresponding pure spirocyclic carbonate **4h** in 90% yield after a simple filtration of the crude reaction mixture. The moderate yield obtained in the case of substrate **3i** may be attributed to its poor stability in acidic medium. Interestingly, the reaction of diyne **3j** selectively furnished **4j** without formation of the six-membered cyclic carbonate resulting from a 6-*exo* cyclization. We next focused our attention on the reactivity of internal alkynes. As attested by the results compiled in Table 2, these were also reactive. Substrates **3k**−**n** gave exclusively the *E*-isomers of the corresponding cyclic carbonates **4k**−**n** in good yields. The valuable vinylbromide **4k** was formed in 87% yield in 1 h, whereas masked ketoester **4l** was obtained in the same yield after 2 h of reaction time.

Table 1. Au(I)-Catalyzed Transformations of Terminal Alkynes **3b**−**j**



3b-j **4b-j**

entry		substrate	product	time	yield [a]
1	**3b**	R_1=Me, R_2=H	**4b**	15 min	94%
2	**3c**	R_1=R_2=Me	**4c**	5 min	85%
3	**3d**	R_1=Me,R_2=Et	**4d**	5 min	98%
4	**3e**	R_1-R_2= -$(CH_2)_5$ -	**4e**	30 min	96%
5	**3f**	R_1=Ph, R_2=H	**4f**	10 h	74%
6	**3g**	R_1=Ph,R_2=Me	**4g**	17 h	76%
7	**3h**		**4h**	10 min	90%
8	**3i**		**4i**	18 h	40 %
9	**3j**		**4j**	5 min	95%

[a] Isolated yields.

Interestingly, unsymmetrical substrate **3n** selectively furnished **4n** in 77% yield as the result of a faster cyclization of the more substituted *tert*-butyloxycarbonyl group.[6] Curiously, alkynes **3p**−**s** were inert when $(Ph_3P)AuNTf_2$ was used as the catalyst. Pleasingly, the more electrophilic catalyst $[(pCF_3Ph)_3P]AuNTf_2$ allowed the conversion of the substrates into mainly the *exo*-methylene compounds **4p**−**s** in moderate to good yield.[7,8]

Surprisingly, in the case of substrates **3o**−**s**, the cyclic carbonate moiety was shifted by one carbon in comparison with the structures of the products previously obtained. Thus, *N*-alkynyl oxazolidinone **3o** rapidly furnished **4o** in 94% yield. Alkyl substituted alkynes **3p**−**s** reacted more slowly to give the corresponding cyclic carbonates in approximately 60% yield. Alkynes **3r** and **3s** possessing an asymmetric center at the propagylic position were slowly transformed into a mixture of two isomers with a diastereoisomeric ratio reaching 1:3.9 in the case of **3s**.[9]

To account for these observations, a mechanistic manifold for the formation of the cyclic carbonates is proposed in Scheme 3.[10] Gold(I) activation of the triple bond in propargylic *tert*-butyl carbonate **5** promotes the formation of

(3) Selection of recent developments: (a)Antoniotti, S.; Genin, E.; Michelet, V.; Genêt, J.-P. *J. Am. Chem. Soc.* **2005**, *127*, 9976−9977. (b) Casado, R.; Contel, M.; Laguna, M.; Romero, P.; Sanz, S. *J. Am. Chem. Soc.* **2003**, *125*, 11925−11935. (c) Asao, N.; Sato, K.; Yamamoto, Y. *J. Org. Chem.* **2005**, *70*, 3682−3685. (d) Hashmi, A. S. K.; Weyrauch, J. P.; Frey, W.; Bats, J. W. *Org. Lett.* **2004**, *6*, 4391−4394. (e) Gorin, D. J.; Davis, N. R.; Toste, F. D. *J. Am. Chem. Soc.* **2005**, *127*, 11260−11261. (f) Nieto-Oberhuber, C.; Lopez, S.; Echavarren, A. M. *J. Am. Chem. Soc.* **2005**, *127*, 6178−6179. (g) Zhang, L.; Kozmin, S. A. *J. Am. Chem. Soc.* **2005**, *127*, 6962−6963. (h) Shi, X.; Gorin, D. J.; Toste, F. D. *J. Am. Chem. Soc.* **2005**, *127*, 5802−5803. (i) Mamane, V.; Gress, T.; Krause, H.; Fürstner, A. *J. Am. Chem. Soc.* **2004**, *126*, 8654−8655. (j) Nieto-Oberhuber, C.; Muñoz, M.; Buñuel, E.; Nevado, C.; Cárdenas, D. J.; Echavarren, A. M. *Angew. Chem., Int. Ed.* **2004**, *43*, 2402−2406.

(4) By analogy with the well-documented iodine-mediated cyclization of allylic and homoallylic *tert*-butyl carbonate. See: Duan, J.; Smith, A. B., III *J. Org. Chem.* **1993**, *58*, 3703−3711. Madness, M. L.; Lautens, M. *Synthesis* **2004**, 1399−1408. No example of iodine-mediated cyclization of propargylic *tert*-butyl carbonate has been reported.

(5) Mezailles, N.; Ricard, L.; Gagosz, F. *Org. Lett.* **2005**, *7*, 4133−4136.

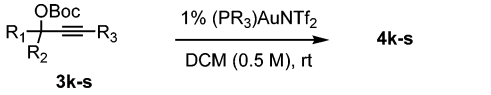
(6) The observed selectivity may be the result of a Thorpe−Ingold effect favoring the cyclisation of the more substituted Boc group.

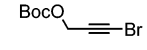
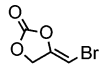
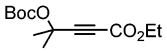
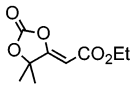
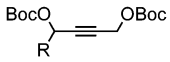
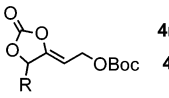
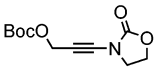
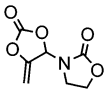
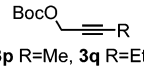
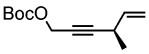
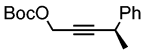
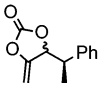
(7) Around 10% of cyclic carbonates formed following path A (see Scheme 3) was also observed.

(8) $[(pCF_3Ph)_3P]AuNTf_2$ was also effective for the described transformation of substrates **3a**−**o**.

(9) Studies towards the identification of the major isomer and diastereoselectivity rational are underway.

Table 2. Au(I)-Catalyzed Transformations of Alkynes **3k**−**s**

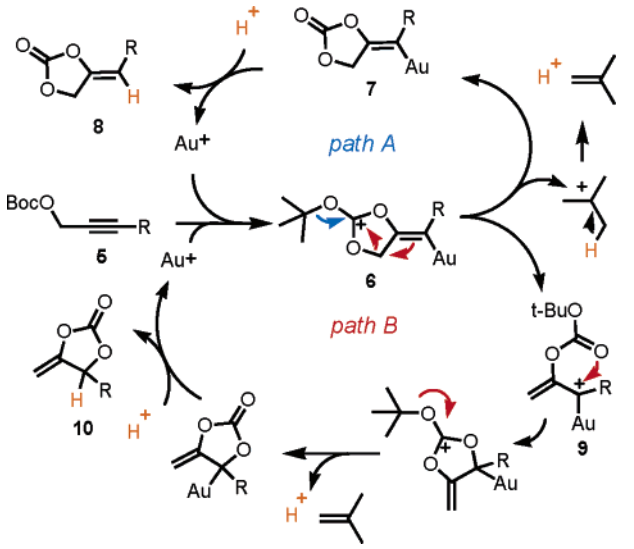


entry	substrate	product	time	yield [a]
1 [b]	**3k** 	**4k** 	1 h	87%
2 [b]	**3l** 	**4l** 	2 h	87%
3 [b]	 **3m** R=H,**3n** R=Me		**4m** 50 min **4n** 30 min	62% 77%
5 [b]	**3o** 	**4o** 	30 min	94%
6 [c]	 **3p** R=Me, **3q** R=Et		**4p**=**4b** 24 h **4q** 24 h	62% 60%
7 [c]	**3r** 	**4r** 	20 h dr = 1:1.6 [d]	68%
8 [c]	**3s** 	**4s** 	20 h dr = 1:3.9 [d]	66%

[a] Isolated yields. [b] With $(Ph_3P)AuNTf_2$. [c] With $[(pCF_3Ph)_3P]AuNTf_2$. [d] Ratio determined by ^1H NMR.

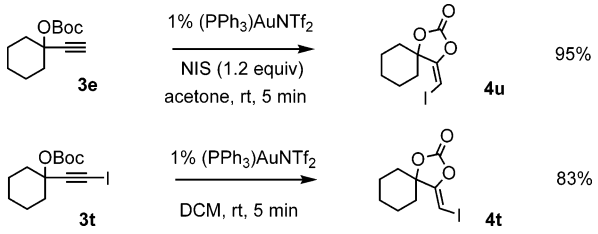
the stabilized cationic species **6**.[11] The latter may follow two distinct reaction pathways depending on the nature of the alkyne substituent R. Fragmentation of the C−O bond of the *tert*-butyloxy group in **6** can lead to the formation of the neutral vinyl-gold species **7**, which is subsequently protonated to finally furnish cyclic carbonate **8** (path A).[12] This pathway seems to be favored in the case of terminal alkynes (R = H) or alkynes bearing electron-withdrawing groups (R = ester, halogen). The internal allylic C−O bond in intermediate **6** can alternatively fragment to give the stabilized allylic cation **9** (path B). Cyclization of the *tert*-butyloxycarbonyl group, followed by fragmentation and protonation finally affords cyclic carbonate **10**. This pathway appears to be favored in the case of internal alkynes (R ≠ H) and more especially in the presence of electron-rich groups (R = alkyl).[13]

Scheme 3. Proposed Mechanism for the Formations of Cyclic Carbonates



To further highlight the potential of this new process, we attempted to trap the intermediate vinyl-gold species **7** by a source of electrophilic iodine prior to protonation. Such a transformation would be of high synthetic interest since it would lead to vinyl iodides. To this end, alkyne **3e** was treated with 1% $(Ph_3P)AuNTf_2$ and a slight excess of NIS in acetone (Scheme 4). We were pleased to observe the rapid

Scheme 4. Au(I)-Catalyzed Formations of Vinyl Iodides **4u** and **4t**

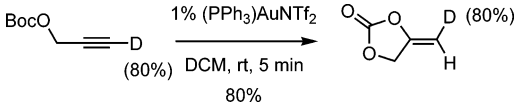


and exclusive formation of *Z*-vinyliodide **4u**, which was isolated in 95% yield.[14,15] Interestingly, the corresponding *E*-isomer **4t** was obtained in 83% yield when iodoalkyne **3t** was treated with the same quantity of catalyst in dichloromethane.

(10) For related Pt(II)-catalyzed cyclisation-fragmentation processes, see: Davies, P. W.; Fürstner, A. *J. Am. Chem. Soc.* **2005**, *127*, 15024−15025. Nakamura, I.; Mizushima, Y.; Yamamoto, Y. *J. Am. Chem. Soc.* **2005**, *127*, 15022−15023.

(11) A similar intermediate was recently proposed by Toste and co-workers for the gold(I)-catalyzed conversion of 1-ethynyl-2-propenyl acetates into cyclopentenones (*see* ref 3h).

(12) Reaction of 80% deuterated **3a** is in agreement with this mechanism.



(13) Curiously, internal alkynes **3m** and **3n** are reacting following path A. The reason for such a selectivity is still unclear, and studies to rationalize this result are underway.

(14) Reaction in a less polar solvent such as dichloromethane furnished a 1:1 mixture of **4e** and **4u** as the result of a less efficient trapping.

(15) Treatment of **3e** with a 2-fold excess of NIS and without Au+ catalyst slowly furnished **4u**: 5% conversion after 3 h, 82% isolated yield after 48 h.

In summary, we have shown that highly active phosphine gold(I) complexes we described recently[5] efficiently catalyze the formation of various 4-alkylidene-1,3-dioxolan-2-ones from readily available propargylic *tert*-butyl carbonates. Further studies relating to the use of this gold(I)-catalyzed cyclization-fragmentation process to the synthesis of other valuable synthons are underway and will be reported in due course.

Acknowledgment. The author wishes to thank Prof. S. Z. Zard, Dr. B. Quiclet-Sire, and Dr. I. Hanna for helpful discussions and Rhodia Chimie Fine for a donation of $HNTf_2$.

Supporting Information Available: Experimental procedures and spectral data for new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

OL053100O