ChemPubSoc Europe

DOI: 10.1002/chem.201403113

CHEMISTRY
A European Journal
Communication

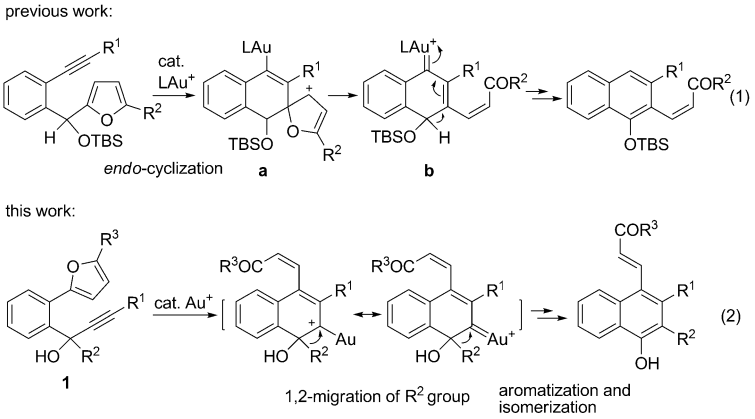
Synthetic Methods

Gold(I)-Catalyzed Furan-yne Cyclizations Involving 1,2-Rearrangement: Efficient Synthesis of Functionalized 1-Naphthols and Its Application to the Synthesis of Wailupemycin G

Yifeng Chen, Lu Wang, Ning Sun, Xin Xie, Xiaobo Zhou, Haoyi Chen, Yuxue Li,* and Yuanhong Liu*[a]

Abstract: Gold-catalyzed cascade cyclization/1,2-rearrangement of 1-(2-furanyl)phenyl propargyl alcohols has been developed, which provides a rapid and efficient access to multisubstituted 1-naphthols bearing an enal or enone moiety with high stereoselectivity. The (*Z*)- or (*E*)-stereochemistry can be easily controlled by choosing protected- or non-protected substrates. The utility of the methodology has been illustrated in the first total synthesis of wailupemycin G.

Rearrangement reactions, especially those proceed via 1,2-migration of a C–C or C–H bond driven by the vicinal electrophilic carbon center such as carbocations, are well-established reaction processes for the assembly of functionalized products.[1] Incorporation of a 1,2-rearrangement step into the transition-metal-catalyzed cascade reactions is highly attractive for the rapid construction of architecturally complex structures from easily available starting materials.[2] Recently, we have developed a series of gold-catalyzed cascade reactions of furan-ynes[3–5] via *endo*-type cyclizations leading to aromatic compounds such as benzenes, phenanthrenes and fulvenes containing enal or enone functionalities with excellent stereoselectivity.[3] For example, in the case of gold(I)-catalyzed cycloisomerization of furan-ynes to protected 1-naphthol derivatives [Scheme 1, Eq. (1)], the reaction proceeds via the formation of a cationic intermediate **a** followed by ring-opening of the furan ring and aromatization via elimination of a proton at the benzylic position to furnish the final products.[3d] We have now found that when furan-ynes bearing a propargylic alcohol moiety such as **1** were used as the substrates, the reaction could be terminated by a 1,2-rearrangement reaction, resulting in migration of R^2 group to vicinal carbon with simultaneous opening of the furan ring [Scheme 1, Eq. (2)].[6] In this paper, we report gold-catalyzed cycloisomerizations of 1-(2-furanyl)phenyl propargyl alcohols involving 1,2-rearrangement, which provide 1-naphthols bearing enal or enone functionalities with high levels of *E*-stereoselectivity. In the present reactions, there is no need to protect the hydroxy group in substrates **1**, thus providing a straightforward access to 1-naphthols. In addition, the use of its protected derivatives afforded the α,β-unsaturated carbonyl products with excellent *Z*-stereoselectivity. The methodology is also applied successfully to the first total synthesis of wailupemycin G.



Scheme 1. Transformations of furan-ynes in the presence of gold catalyst.

Our initial investigation focused on the cyclizations of 1-(2-(furan-2-yl)phenyl)-3-phenylprop-2-yn-1-ol **1a**, which was easily prepared in two steps from 2-bromobenzaldehyde via Stille coupling with 2-tributylstannylfuran followed by acetylide addition. To our delight, the desired cyclization occurred efficiently, and the best result was achieved by employing 2 mol% Johnphos(MeCN)$AuSbF_6$ (**A**) as the catalyst (for detailed optimization studies, see the Supporting Information). Thus, treatment of **1a** with 2 mol% of catalyst **A** in DCE at room temperature for 25 min produced 1-naphthol **2a** bearing an (*E*)-enal functionality in 93% yield as a single olefin isomer (Table 1).

[a] *Dr. Y. Chen, Dr. L. Wang, N. Sun, X. Xie, Dr. X. Zhou, H. Chen, Prof. Y. Li, Prof. Y. Liu*
State Key Laboratory of Organometallic Chemistry
Shanghai Institute of Organic Chemistry
Chinese Academy of Sciences
345 Lingling Lu, Shanghai 200032 (P.R. China)
Fax: (+86) 021-64166128
E-mail: yhliu@mail.sioc.ac.cn

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.201403113.

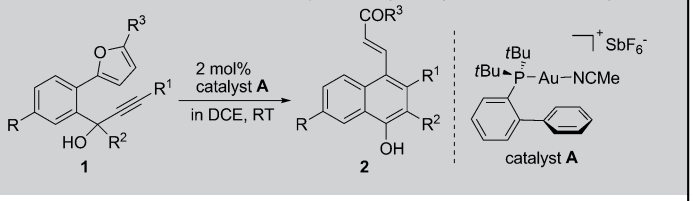
According to our previous study, the (*E*)-enal was formed through the double bond isomerization of the initially generated (*Z*)-enal, promoted by gold catalyst. High yields of **2a** (95–98%) were also obtained in solvents of DCM or toluene within 30 min. 1-Naphthol scaffolds are commonly occurring features in pharmaceuticals and natural products.[7,8] Our method allows the facile assembly of multisubstituted 1-naphthols under mild reaction conditions.

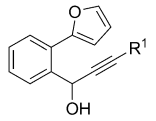
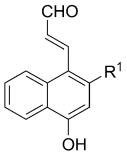
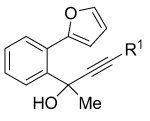
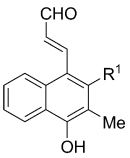
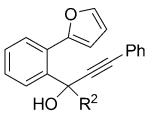
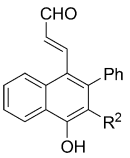
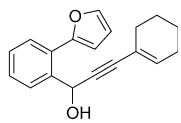
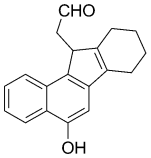
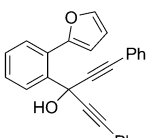
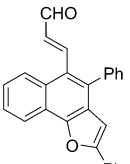
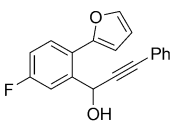
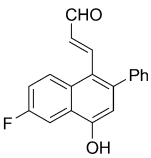
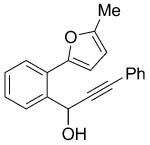
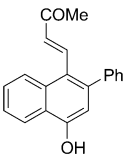
With the optimized reaction conditions in hand, we examined the scope of this rearrangement reaction using 2 mol% of catalyst **A** as the catalyst. As shown in Table 1, the method is applicable to a wide range of suitably substituted furan-ynes. The reaction proved to be quite general with respect to substituents at the alkyne terminus, since aryl, heteroaryl and alkyl groups were all compatible, leading to the desired 1-naphthols in generally excellent yields. For example, aryl alkynes with electron-withdrawing (*p*-Cl) or electron-donating (*p*-MeO) groups underwent the reaction smoothly, furnishing the expected products **2b** and **2c** in 88 and 98% yields, respectively. The presence of a bulky 1-naphthyl substituent does not interfere with the cyclization, and the desired **2d** was obtained in 95% yield. Thienyl group was well tolerated, producing **2e** in 96% yield. A range of alkyl-substituted alkynes such as *n*-butyl or cyclopropyl-substituted one were efficiently transformed into 1-naphthols **2f** and **2g** with excellent yields. Interestingly, a cyclohexenyl-substituted alkyne afforded a naphthyl-fused polycyclic compound **3** in 53% yield, indicating a further alkene-enal cyclization of the initially formed product occurred during the reaction process. Substitution of the parent phenyl ring with fluorine was also compatible for this transformation, providing the corresponding product **2i** in 95% yield.

These initial results encouraged us to investigate the possible 1,2-migration of various groups other than hydrogen, which would lead to an additional substitution at C-2 position of the 1-naphthol products. Thus a variety of tertiary propargylic alcohol substrates were prepared to probe the gold-catalyzed cycloisomerizations. To our delight, our method showed great efficiency for these 1,2-migrations. Methyl, phenyl and 2-furanyl groups all migrate smoothly, leading to multisubstituted 1-naphthols **2j**–**2p** in 81–94% yields. A thienyl group could also undergo the migration reaction, however, with a lower product yield of **2q** (59%). Interestingly, when the migrating group is an alkynyl group, the initially formed naphthol spontaneously cyclized via a tandem nucleophilic addition of the OH group, giving rise to naphtha[1,2-*b*]furan **4** in 71% yield. In this case, 5 mol% of the catalyst and higher reaction temperatures (70 °C) were required to achieve the full conversion. Substrate **1s** with a substituted furan ring was also suitable to deliver (*E*)-enone **2s** in 98% yield. The structures of compounds **2i**, **2k**, **3** and **4** were unambiguously confirmed by X-ray crystallographic analysis.[9]

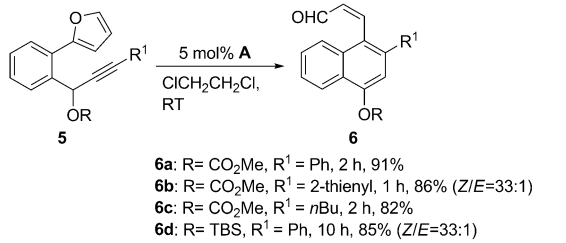
Recently we developed a gold-catalyzed cascade reaction of 1,6-diynyl carbonates, which is initiated by 3,3-rearrangement of the propargyl carbonate moiety.[10] We envisioned that a carbonate derivative of substrate **1** might produce different types of products via 3,3-rearrangement. However, we found that 1-naphthyl carbonates **6a**–**c** with a (*Z*)-enal moiety were formed from carbonates **5a**–**c** in 82–91% yield catalyzed by 5 mol% of catalyst **A** (Scheme 2). The result indicated that the furan-yne cyclization occurred more rapidly than 3,3-rearrangement of the propargyl carbonate moiety. Substrate **5d** protected by TBS group also afforded (*Z*)-enal **6d** as a major geometric isomer in 85% yield.[11] The above results indicated that the stereochemistry of the enal double bond can be easily controlled by choosing protected- or non-protected substrates.[12] Interestingly, treatment of **6d** (*Z*/*E* 50:1) with 5 mol% catalyst **A** in

Table 1. Formation of 1-naphthols via gold-catalyzed cyclizations of furan-ynes.



Substrate	Product[a]	Substrate	Product[a]
			
1a: R^1 = Ph	**2a**, 25 min, 93%	**1j**: R^1 = Ph	**2j**, 15 min, 94%
1b: R^1 = *p*-ClC_6H_4	**2b**, 20 min, 88%	**1k**: R^1 = *p*-ClC_6H_4	**2k**, 20 min, 92%
1c: R^1 = *p*-$OMeC_6H_4$	**2c**, 15 min, 98%	**1l**: R^1 = *p*-$OMeC_6H_4$	**2l**, 15 min, 91%
1d: R^1 = 1-naphthyl	**2d**, 25 min, 95%	**1m**: R^1 = 2-thienyl	**2m**, 30 min, 87%
1e: R^1 = 2-thienyl	**2e**, 15 min, 96%	**1n**: R^1 = cyclopropyl	**2n**, 25 min, 94%
1f: R^1 = nC_4H_9	**2f**, 15 min, 90%		
1g: R^1 = cyclopropyl	**2g**: 15 min, 92%	**1o**: R^2 = Ph **1p**: R^2 = 2-furanyl **1q**: R^2 = 2-thienyl	**2o**, 10 min, 81% **2p**, 20 min, 90% **2q**, 20 min, 59%
			
1h	**3**, 6 h, 53%	**1r**	**4**, 6 h, 71%[b]
			
1i	**2i**, 25 min, 95%	**1s**	**2s**, 15 min, 98%

[a] Yield of isolated product. [b] 5 mol% catalyst A, 70 °C. *E*/*Z* = 33:1.



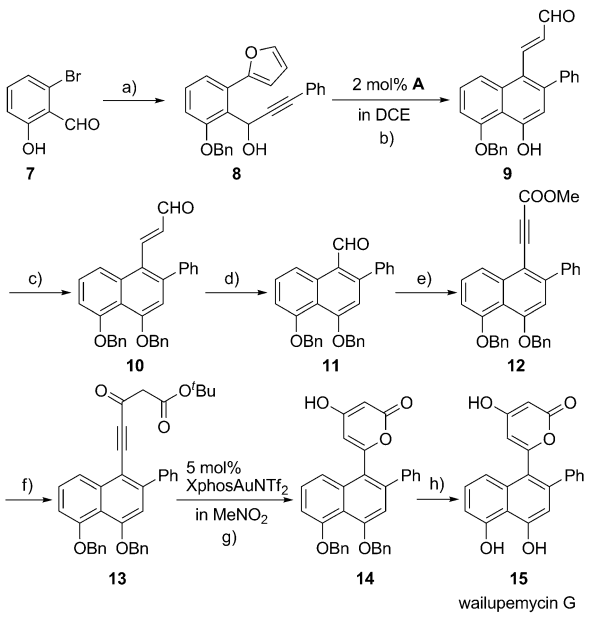
Scheme 2. Gold catalyzed cycloisomerizations of furan-ynes **5**.

DCE at 80 °C for 3 h resulted in *Z*/*E* isomerization to afford (*E*)-**6d** (*E*/*Z* 50:1) in 75% yield.[13] In the absence of gold catalyst, no isomerization occurred at 80 °C in DCE for 3 h. The results indicated that gold(I) was capable of catalyzing the isomerization reaction.

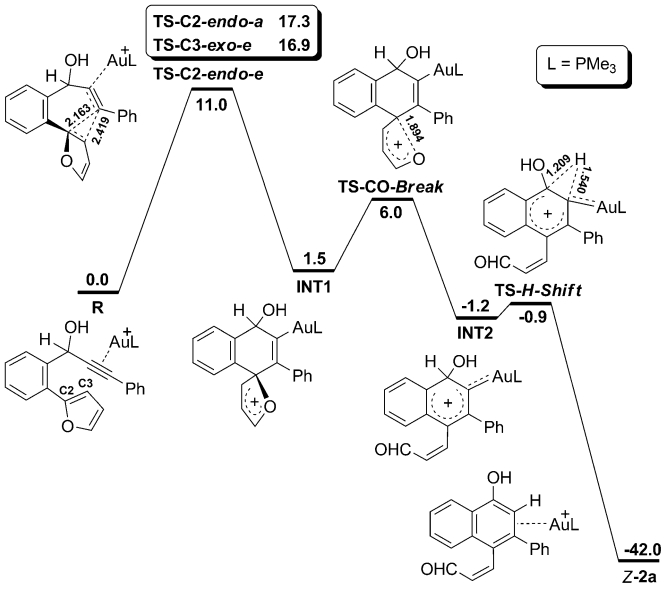
To demonstrate the synthetic utility of this new approach to diverse-oriented synthesis of 1-naphthols, total synthesis of wailupemycin G was performed. Waillupemycin G is an α-pyrone-containing metabolite produced by the marine bacterium *Streptomyces maritimus*,[14] which was first elucidated by Moore et al.[14a] during the study of the mutational analysis of the enterocin favorskii biosynthetic rearrangement. The bioactivity of this natural product has not been fully evaluated, possibly due to the limited availability. So far, no total synthesis of this natural product has been reported. As shown in Scheme 3, benzyl-protected phenol substrate **8** was first constructed from 2-bromo-6-hydroxybenzaldehyde **7** over three steps. Gratifyingly, exposure of furan-yne **8** to catalyst **A** in DCE at 80 °C furnished the desired product **9** in 81% yield with high stereoselectivity (*E*/*Z* 53:1). Protection of the naphthol OH group followed by oxidative cleavage of the double bond using $KMnO_4$/acetone afforded aldehyde **11** in 53% overall yield. Next, we need to construct an α-pyrone moiety. Inspired by the recent report of gold-catalyzed synthesis of 4-hydroxy-2-pyrones developed by Fürstner and co-workers[15] **11** was transferred to β-keto ester **13** via first conversion of **11** to acetylenic ester **12** followed by the reaction with (2-*tert*-butoxy-2-oxoethyl)lithium. Gold-catalyzed cyclization of **13** in the presence of 5 mol% $XphosAuNTf_2$ in $MeNO_2$ indeed afforded the desired pyrone **14** in 78% yield. Removal of the Bn protecting group in **14** delivered wailupemycin G, whose NMR data is consistent with that reported by Moore et al.[14a] The structure of wailupemycin G was further confirmed by X-ray crystal analysis.[9] The method presented here can be used for the assembly of a library of unnatural wailupemycin G analogues by tuning the substitution pattern of the starting furan-ynes **8**.[14d]

To disclose the reaction mechanism, density functional theory (DFT)[16] studies have been performed with GAUSSIAN09 program[17] using the PBE1PBE[18] method. For C, H, O and P, the 6-311 + G** basis set was used; and, for Au, the SDD basis set with Effective Core Potential (ECP)[19] was used. Geometry optimization was performed in dichloroethane using the SMD[20] method. Harmonic vibration frequency calculations were carried out and the optimized structures are all shown to be either minima (with no imaginary frequency) or transition states (with one imaginary frequency).

Firstly, in the cyclization step, the C2/C3 carbon atom of the furan ring attacks the triple bond. Several possible attacking modes were explored with substrate **1a** and the Me_3PAu^+ catalyst, three transition states for C2 and C3 attacking were located (Scheme 4 and Figure 1).[13] The most favorable transition



Scheme 3. Total synthesis of wailupemycin G. a) i) 2-tributylstannylfuran, cat. $[Pd_2(dba)_3]/PPh_3$, toluene, 94%; ii) BnBr, K_2CO_3, acetone, 85%; iii) (phenylethynyl)lithium, THF, 98%; b) 80 °C, 81%; *E*/*Z* 53:1; c) BnBr, K_2CO_3, NaI, acetone, 86%; *E*/*Z* 41:1; d) $KMnO_4$, acetone, 62%; e) i) CBr_4, PPh_3, CH_2Cl_2, 86%; ii) BuLi, THF, −78 °C then $ClCO_2Me$, 89%; f) LDA, *tert*-butyl acetate, THF, then **12**, 76%; **13** was a keto/enol mixture with a ratio of 3.7:1; g) 78%; h) cat. Pd/C, H_2, in EtOAc, 94%.



Scheme 4. Calculated reaction pathways for substrate **1a**. The selected bond lengths are in angstroms, and the relative free energies in dichloroethane (ΔG_{sol}) are in kcal mol^{-1}. Calculated at the PBE1PBE/6-311 + G**/SDD level.

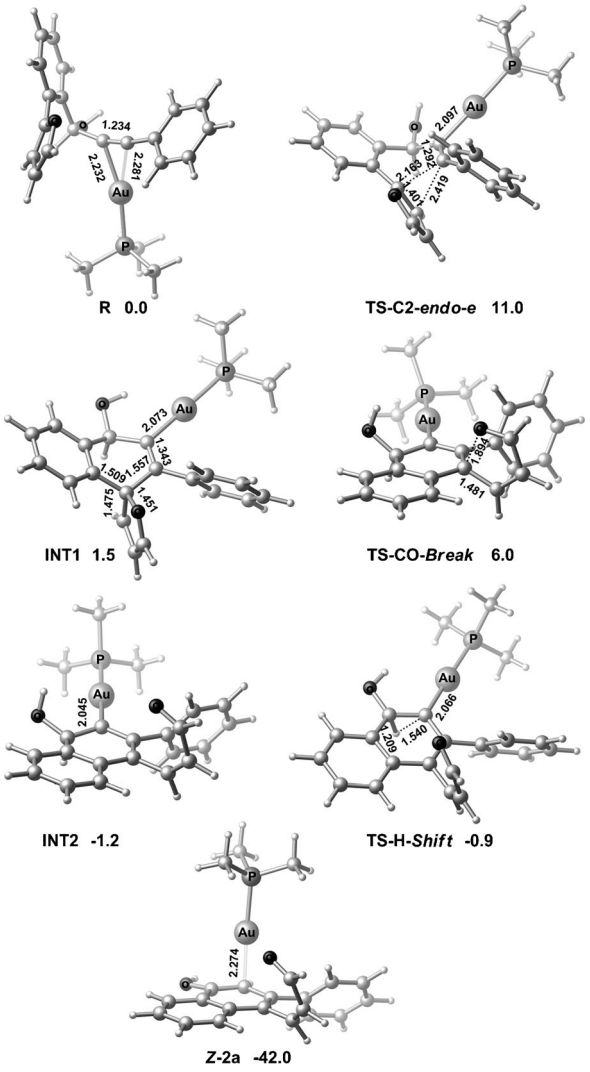


Figure 1. Optimized structures on the reaction pathways shown in Scheme 4. The selected bond lengths are in angstroms, and the relative free energies in dichloroethane (ΔG_{sol}) are in kcal mol^{-1}. Calculated at the PBE1PBE/6-311 + G**/SDD level.

state is the C2 *endo* attacking transition state **TS-C2-*endo*-*e***, in which the C–O bond of the furan ring is in the equatorial position (*e*) of the forming 6-membered ring. Ring opening of the furan ring in intermediate **INT1** leads to **INT2** over a barrier of 4.5 kcal mol^{-1}; and subsequent 1,2-H migration of **INT2** yields (*Z*)-**2a**. Isomerization of (*Z*)-**2a** affords the final product (*E*)-**2a**. The C–Au bond length in **INT1** is 2.073 Å, which decrease to 2.045 Å in **INT2**, indicating a stronger interaction between the carbocation and the Au atom, which can be ascribed to the π-donation of the 5d electrons of the Au atom.[21] The NBO charge on Au atom increase from +0.183 in **INT1** to +0.227 in **INT2**.[22] Therefore, **INT2** partially has gold carbene character. As shown in Scheme 4, the first step is the rate determining step in this reaction. **TS-C2-*endo*-*e*** is 5.9 kcal mol^{-1} lower in energy than the less favorable **TS-C3-*exo*-*e***, consistent well with the experimental observation that only product resulting from the C2 *endo* cyclization (i.e., **2a**) was observed.

In summary, we have developed a novel gold-catalyzed cyclization of furan-ynes bearing a propargylic alcohol moiety by incorporation of a 1,2-rearrangement step into the cascade. The reaction provides a rapid and efficient access to multisubstituted 1-naphthols bearing an enal or enone moiety at the C-4 position with high stereoselectivity. Notably, the stereochemistry can be controlled by choosing protected- or non-protected substrates. The utility of this method has been illustrated by the first total synthesis of wailupemycin G.

Acknowledgements

We thank the National Natural Science Foundation of China (Grant Nos. 21125210, 21121062, 21372244, 21172248), Chinese Academy of Science, and the Major State Basic Research Development Program (Grant No. 2011CB808700) for financial support.

Keywords: 1,2-migration · 1-naphthols · furans · gold · homogeneous catalysis

[1] a) T. J. Snape, *Chem. Soc. Rev.* **2007**, *36*, 1823; b) Z. L. Song, C. A. Fan, Y. Q. Tu, *Chem. Rev.* **2011**, *111*, 7523.

[2] For gold-catalyzed reactions involving 1,2-rearrangement, for a review, see: a) B. Crone, S. F. Kirsch, *Chem. Eur. J.* **2008**, *14*, 3514; For recent papers: b) V. Mamane, T. Gress, H. Krause, A. Fürstner, *J. Am. Chem. Soc.* **2004**, *126*, 8654; c) J. P. Markham, S. T. Staben, F. D. Toste, *J. Am. Chem. Soc.* **2005**, *127*, 9708; d) J. Sun, M. P. Conley, L. Zhang, S. A. Kozmin, *J. Am. Chem. Soc.* **2006**, *128*, 9705; e) E. Jiménez-Núñez, C. K. Claverie, C. Nieto-Oberhuber, A. M. Echavarren, *Angew. Chem.* **2006**, *118*, 5578; *Angew. Chem. Int. Ed.* **2006**, *45*, 5452; f) S. F. Kirsch, J. T. Binder, C. Liébert, H. Menz, *Angew. Chem.* **2006**, *118*, 6010; *Angew. Chem. Int. Ed.* **2006**, *45*, 5878; g) S. F. Kirsch, J. T. Binder, B. Crone, A. Duschek, T. T. Haug, C. Liébert, H. Menz, *Angew. Chem.* **2007**, *119*, 2360; *Angew. Chem. Int. Ed.* **2007**, *46*, 2310; h) J. T. Binder, B. Crone, S. F. Kirsch, C. Liébert, H. Menz, *Eur. J. Org. Chem.* **2007**, 1636; i) J. M. Tang, S. Bhunia, S. M. A. Sohel, M. Y. Lin, H. Y. Liao, S. Datta, A. Das, R. S. Liu, *J. Am. Chem. Soc.* **2007**, *129*, 15677; j) Y. Peng, M. Yu, L. Zhang, *Org. Lett.* **2008**, *10*, 5187; k) H. Yeom, Y. Lee, J. Jeong, E. So, S. Hwang, J. Lee, S. S. Lee, S. Shin, *Angew. Chem.* **2010**, *122*, 1655; *Angew. Chem. Int. Ed.* **2010**, *49*, 1611; l) T. M. Teng, A. Das, D. B. Huple, R. S. Liu, *J. Am. Chem. Soc.* **2010**, *132*, 12565; m) A. S. K. Hashmi, T. Wang, S. Shi, M. Rudolph, *J. Org. Chem.* **2012**, *77*, 7761; n) T. Lauterbach, S. Gatzweiler, P. Nösel, M. Rudolph, F. Rominger, A. S. K. Hashmi, *Adv. Synth. Catal.* **2013**, *355*, 2481. For gold or platinum-catalyzed reactions involving 1,2-rearrangement, see:o) K. D. Umland, A. Palisse, T. T. Haug, S. F. Kirsch, *Angew. Chem.* **2011**, *123*, 10140; *Angew. Chem. Int. Ed.* **2011**, *50*, 9965.

[3] a) Y. Chen, Y. Lu, G. Li, Y. Liu, *Org. Lett.* **2009**, *11*, 3838; b) Y. Chen, G. Li, Y. Liu, *Adv. Synth. Catal.* **2011**, *353*, 392; c) Y. Chen, Y. Liu, *J. Org. Chem.* **2011**, *76*, 5274; d) C. Wang, Y. Chen, X. Xie, J. Liu, Y. Liu, *J. Org. Chem.* **2012**, *77*, 1915.

[4] For gold-catalyzed cyclizations of furan-ynes via *exo*-cyclizations, see: a) A. S. K. Hashmi, T. M. Frost, J. W. Bats, *J. Am. Chem. Soc.* **2000**, *122*, 11553; b) A. S. K. Hashmi, T. M. Frost, J. W. Bats, *Org. Lett.* **2001**, *3*, 3769; c) A. S. K. Hashmi, L. Ding, P. Fischer, J. W. Bats, W. Frey, *Chem. Eur. J.* **2003**, *9*, 4339; d) A. S. K. Hashmi, J. P. Weyrauch, M. Rudolph, E. Kurpejović, *Angew. Chem.* **2004**, *116*, 6707; *Angew. Chem. Int. Ed.* **2004**, *43*, 6545; e) A. S. K. Hashmi, M. Rudolph, J. P. Weyrauch, M. Wölfle, W. Frey, J. W. Bats, *Angew. Chem.* **2005**, *117*, 2858; *Angew. Chem. Int. Ed.* **2005**, *44*, 2798; f) A. S. K. Hashmi, P. Haufe, C. Schmid, A. R. Nass, W. Frey, *Chem. Eur. J.* **2006**, *12*, 5376; g) A. S. K. Hashmi, M. C. Blanco, E. Kurpejović, W. Frey, J. W. Bats, *Adv. Synth. Catal.* **2006**, *348*, 709; h) A. S. K. Hashmi, M. Rudolph, J. W. Bats, W. Frey, F. Rominger, T. Oeser, *Chem. Eur. J.* **2008**, *14*, 6672; i) A. S. K. Hashmi, M. Rudolph, H. Siehl, M. Tanaka, J. W. Bats, W. Frey, *Chem. Eur. J.* **2008**, *14*, 3703; j) A. S. K. Hashmi, S. Pan-

kajakshan, M. Rudolph, E. Enns, T. Bander, F. Rominger, W. Frey, *Adv. Synth. Catal.* **2009**, *351*, 2855; k) A. S. K. Hashmi, M. Wölfle, F. Ata, W. Frey, F. Romingera, *Synthesis* **2010**, 2297. For *endo*-cyclizations, see: l) A. S. K. Hashmi, M. Rudolph, J. Huck, W. Frey, J. W. Bats, M. Hamzić, *Angew. Chem.* **2009**, *121*, 5962; *Angew. Chem. Int. Ed.* **2009**, *48*, 5848; m) A. S. K. Hashmi, W. Yang, F. Rominger, *Angew. Chem.* **2011**, *123*, 5882; *Angew. Chem. Int. Ed.* **2011**, *50*, 5762; n) A. S. K. Hashmi, W. Yang, F. Rominger, *Chem. Eur. J.* **2012**, *18*, 6576; o) Z. Dong, C. H. Liu, Y. Wang, M. Lin, Z. X. Yu, *Angew. Chem.* **2013**, *125*, 14407; *Angew. Chem. Int. Ed.* **2013**, *52*, 14157. For gold-catalyzed intermolecular reactions of furans with alkynes, see: p) M. T. Reetz, K. Sommer, *Eur. J. Org. Chem.* **2003**, 3485; q) N. Huguet, D. Leboeuf, A. M. Echavarren, *Chem. Eur. J.* **2013**, *19*, 6581, and ref. [4g].

[5] For Pt-catalyzed cyclizations of furan-ynes, see: B. Martín-Matute, C. Nevado, D. J. Cárdenas, A. M. Echavarren, *J. Am. Chem. Soc.* **2003**, *125*, 5757.

[6] For gold-catalyzed cyclizations of furan-ynes involving a Wagner–Meerwein rearrangement, see: ref. [4m,4n].

[7] a) K. P. Manfredi, J. W. Blunt, J. H. II Cardellina, J. B. McMahon, L. L. Pannell, G. M. Cragg, *J. Med. Chem.* **1991**, *34*, 3402; b) M. R. Boyd, Y. F. Hallock, J. H. II Cardellina, K. P. Manfredi, J. W. Blunt, J. B. McMahon, R. W. Buckheit, G. Bringmann, M. Schaffer, G. M. Cragg, D. W. Thomas, J. G. Jato, *J. Med. Chem.* **1994**, *37*, 1740; c) Y. F. Hallock, K. P. Manfredi, J. R. Dai, J. H. II Cardellina, R. J. Gulakowski, J. B. McMahon, M. Schaffer, M. Stahl, K. P. Gulden, G. Bringmann, G. Francois, M. R. Boyd, *J. Nat. Prod.* **1997**, *60*, 677; d) Y. F. Hallock, K. P. Manfredi, J. W. Blunt, J. H. II Cardellina, M. Schäffer, K. P. Gulden, G. Bringmann, A. Y. Lee, J. Clardy, G. François, M. R. Boyd, *J. Org. Chem.* **1994**, *59*, 6349; e) H. Itokawa, Z. Z. Ibraheim, Y. F. Qiao, K. Takeya, *Chem. Pharm. Bull.* **1993**, *41*, 1869; f) J. K. Son, S. J. Jung, J. H. Jung, Z. Fang, C. S. Lee, C. S. Seo, D. C. Moon, B. S. Min, M. R. Kim, M. H. Woo, *Chem. Pharm. Bull.* **2008**, *56*, 213; g) H. G. Floss, T. W. Yu, *Chem. Rev.* **2005**, *105*, 621; h) S. Boonsri, C. Karalai, C. Ponglimanont, S. Chantrapromma, A. Kanjana-opas *J. Nat. Prod.* **2008**, *71*, 1173.

[8] For the synthesis of 1-naphthols, see: a) M. Ballantine, M. L. Menard, W. Tam, *J. Org. Chem.* **2009**, *74*, 7570; b) C. Chen, S. F. Martin, *J. Org. Chem.* **2006**, *71*, 4810; c) S. Akai, T. Ikawa, S. Takayanagi, Y. Morikawa, S. Mohri, M. Tsubakiyama, M. Egi, Y. Wada, Y. Kita, *Angew. Chem.* **2008**, *120*, 7787; *Angew. Chem. Int. Ed.* **2008**, *47*, 7673; d) X. Huang, J. Xue, *J. Org. Chem.* **2007**, *72*, 3965; e) D. Mal, A. K. Jana, P. Mitra, K. Ghosh, *J. Org. Chem.* **2011**, *76*, 3392; f) G. Chai, Z. Lu, C. Fu, S. Ma, *Chem. Eur. J.* **2009**, *15*, 11083; g) H. Xu, S. Li, S. Liu, H. Fu, Y. Jiang, *Chem. Commun.* **2010**, *46*, 7617; h) H. Tsukamoto, Y. Kondo, *Org. Lett.* **2007**, *9*, 4227; i) A. G. Sergeev, T. Schulz, C. Torborg, A. Spannenberg, H. Neumann, M. Beller, *Angew. Chem.* **2009**, *121*, 7731; *Angew. Chem. Int. Ed.* **2009**, *48*, 7595.

[9] CCDC 981431(**2i**), 981432(**2k**), 981433(**3**), 981434(**4**) and 981435 (**15**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[10] a) Y. Chen, M. Chen, Y. Liu, *Angew. Chem.* **2012**, *124*, 6599; *Angew. Chem. Int. Ed.* **2012**, *51*, 6493. For related paper, see: b) M. Chen, J. Liu, L. Wang, X. Zhou, Y. Liu, *Chem. Commun.* **2013**, *49*, 8650.

[11] The *Z*/*E* ratio of **6d** changed to 10:1 when it was allowed to stand at room temperature overnight. We wondered that the *Z*/*E* isomerization might occur easier in its pure form than that in solution.

[12] We found that deprotection of **6a** by K_2CO_3/MeOH or **6d** by $(HF)_x$·Py resulted in double bond isomerization to give 1-naphthol (*E*)-**2a**. However, when **6a** was first reduced to alcohol by Luche reduction followed by deprotection, the (*Z*)-configuration could be retained to give a *Z*-olefin. For details, see supporting information.

[13] For details, see Supporting Information.

[14] a) L. Xiang, J. A. Kalaitzis, G. Nilsen, L. Chen, B. S. Moore, *Org. Lett.* **2002**, *4*, 957. For related biosynthesis of wailupemycins, see: b) J. Piel, K. Hoang, B. S. Moore, *J. Am. Chem. Soc.* **2000**, *122*, 5415; c) J. A. Kalaitzis, M. Izumikawa, L. Xiang, C. Hertweck, B. S. Moore, *J. Am. Chem. Soc.* **2003**, *125*, 9290; For biosynthesis of unnatural wailupemycin G analogues, see: d) J. A. Kalaitzis, Q. Cheng, P. M. Thomas, N. L. Kelleher, B. S. Moore, *J. Nat. Prod.* **2009**, *72*, 469. For total synthesis of wailupemycin A and B, see: e) S. Kirsch, T. Bach, *Angew. Chem.* **2003**, *115*, 4833; *Angew. Chem. Int. Ed.* **2003**, *42*, 4685; f) S. F. Kirsch, T. Bach, *Chem. Eur. J.* **2005**, *11*, 7007.

[15] W. Chaładaj, M. Corbet, A. Fürstner, *Angew. Chem.* **2012**, *124*, 7035; *Angew. Chem. Int. Ed.* **2012**, *51*, 6929.

[16] a) P. Hohenberg, W. Kohn, *Phys. Rev.* **1964**, *136*, B864; b) W. Kohn, L. J. Sham, *Phys. Rev.* **1965**, *140*, A1133.

[17] Gaussian 09, Revision A.02, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, A., Jr., Montgomery, J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. E. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, D. J. Fox, Gaussian, Inc., Wallingford, CT, **2009**.

[18] a) J. P. Perdew, K. Burke, M. Ernzerhof, *Phys. Rev. Lett.* **1996**, *77*, 3865; b) J. P. Perdew, K. Burke, M. Ernzerhof, *Phys. Rev. Lett.* **1997**, *78*, 1396.

[19] P. Fuentealba, H. Preuss, H. Stoll, L. Von Szentpály, *Chem. Phys. Lett.* **1982**, *89*, 418.

[20] A. V. Marenich, C. J. Cramer, D. G. Truhlar, *J. Phys. Chem.* **2009**, *113*, 6378.

[21] a) D. Benitez, N. D. Shapiro, E. Tkatchouk, Y. Wang, W. A. Goddard III, F. D. Toste, *Nat. Chem.* **2009**, *1*, 482; b) B. Lu, Y. Li, Y. Wang, D. H. Aue, Y. Luo, L. Zhang, *J. Am. Chem. Soc.* **2013**, *135*, 8512.

[22] A. E. Reed, R. B. Weinstock, F. Weinhold, *J. Chem. Phys.* **1985**, *83*, 735.

Received: April 16, 2014
Published online on July 30, 2014