Fluxional Molecules

International Edition: DOI: 10.1002/anie.201606101
German Edition: DOI: 10.1002/ange.201606101

Synthesis of Barbaralones and Bullvalenes Made Easy by Gold Catalysis

*Sofia Ferrer and Antonio M. Echavarren**

Abstract: *The gold(I)-catalyzed oxidative cyclization of 7-ethynyl-1,3,5-cycloheptatrienes gives 1-substituted barbaralones in a general manner, which simplifies the access to other fluxional molecules. As an example, we report the shortest syntheses of bullvalene, phenylbullvalene, and disubstituted bullvalenes, and a readily accessible route to complex cage-type structures by further gold(I)-catalyzed reactions.*

Fluxional molecules, such as barbaralone (**1a**), bullvalone (**2a**), and bullvalene (**3a**) have been central to the understanding of the phenomena of valence tautomerism (see Figure 1).[1,2] These molecules undergo low energy [3.3]-sigmatropic rearrangements, which in the case of bullvalene

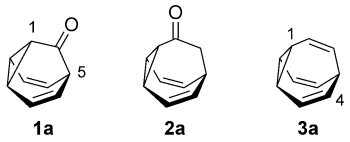
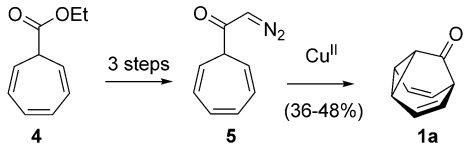


Figure 1. Barbaralone (**1a**), bullvalone (**2a**), and bullvalene (**3a**).

lead to 1209600 degenerate tautomers,[3–5] whereas a lower number of constitutional isomers are possible for substituted bullvalenes[6–8] and only two exist for barbaralone (**1a**).[9]

Syntheses of these fluxional molecules requires multistep procedures that proceed with low overall yield, often using explosive and toxic diazomethane. Thus, the optimized synthesis of barbaralone (**1a**), en route to bullvalene (**3a**),[10] starts with the Büchner reaction of ethyl diazoacetate with benzene to form **4**,[11,12] which is converted into **1a** in four steps via diazomethyl ketone **5** (Scheme 1).[10] Bullvalene (**3a**)



Scheme 1. Synthesis of barbaralone (**1a**) from ethyl cyclohepta-2,4,6-triene-1-carboxylate (**4**).

can be prepared from **1a** in four additional steps by two different procedures by homologation of **1a** to bullvalone (**2a**) with diazomethane.[2,10] Barbaralone (**1a**) has also been prepared from (cyclooctatetraene)tricarbonyliron in two steps in approximately 36% yield.[13]

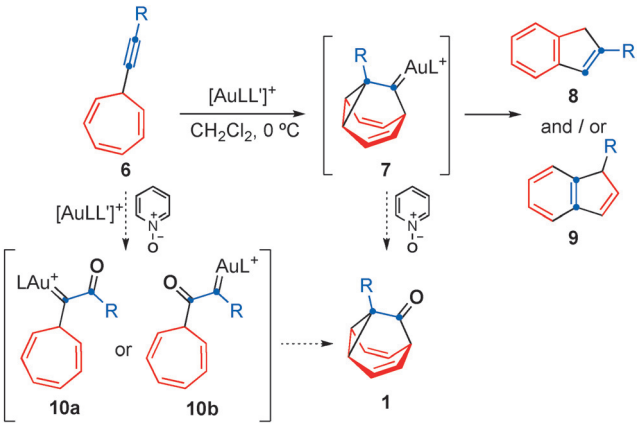
1-Methylbarbaralone (**1w**) was prepared by a procedure similar to that shown in Scheme 1 using ethyldiazomethane in the reaction with cycloheptatriene carbamoyl chloride to form the homologue of **5**.[9b] Although some ingenious syntheses of highly substituted bullvalenes have been designed,[8] most bullvalenes have been prepared from parent **3a**. Thus, for example, phenylbullvalene (**3b**) was obtained in three steps (26% yield) from **3a** by dibromination, dehydrobromination with KO*t*Bu, and reaction of the resulting bromobullvalene with Ph_2CuLi.[7d]

Current synthetic art does not allow preparation of substituted barbaralones in a general way,[14] which limits the access to fluxional homologues and other theoretically interesting molecules.[12,15] We have recently found that 7-aryl-1,3,5-cycloheptatrienes undergo a gold(I)-catalyzed retro-Büchner reaction to form highly reactive aryl gold(I) carbenes (a decarbenation reaction).[16] However, 7-ethynyl-1,3,5-cycloheptatrienes (**6**) react differently to form fluxional barbaralyl gold(I) intermediates **7**; after a series of complex rearrangements **7** finally leads to indenes **8** and/or **9**, depending on the gold catalyst (Scheme 2).[17] Since the gold-catalyzed oxidation of alkynes has been shown to take place readily with oxidants such as sulfoxides, or amine-*N*-oxides to form α-oxo gold(I) carbenes,[18,19] we envisioned that the oxidation of intermediates **7** could lead to 1-substituted barbaralones **1** (Scheme 2). However, if the oxidation takes place directly on 7-ethynyl-1,3,5-cycloheptatrienes (**6**), the two regioisomeric α-oxo gold(I) carbenes **10a** and **10b** would be formed,[18] of which only **10b** would lead to barbaralones **1** by intramolecular cyclopropanation.

Herein, we report a general and straightforward synthesis of 1-substituted barbaralones **1** from alkynes and commercially available tropylium tetrafluoroborate in just two steps by oxidative cyclization of 7-ethynyl-1,3,5-cycloheptatrienes.

We first studied the reaction of 7-(phenylethynyl)cyclohepta-1,3,5-triene (**6b**) with different gold(I) catalysts in the

[*] S. Ferrer, Prof. A. M. Echavarren
Institute of Chemical Research of Catalonia (ICIQ)
Barcelona Institute of Science and Technology
Av. Països Catalans 16, 43007 Tarragona (Spain)
E-mail: aechavarren@iciq.es
Prof. A. M. Echavarren
Departament de Química Analítica i Química Orgànica
Universitat Rovira i Virgili
C/ Marcel·li Domingo s/n, 43007 Tarragona (Spain)
Supporting information and the ORCID identification number(s) for the author(s) of this article can be found under http://dx.doi.org/10.1002/anie.201606101.

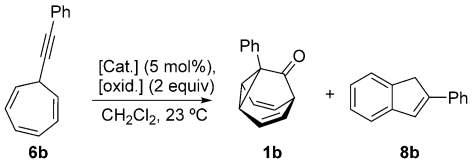


Scheme 2. Two different pathways for the formation of barbaralones **1** by gold(I)-catalyzed oxidative cyclization of 7-ethynyl-1,3,5-cycloheptatrienes (**6**).

presence of diphenylsulfoxide (**Ox_1**), and the *N*-oxides of pyridine (**Ox_2**), 3,5-dichloropyridine (**Ox_3**), or 8-methylquinoline (**Ox_4**) as oxidants (Table 1). Using Johnphos gold(I) complex **A** in combination with **Ox_3**, 1-phenylbarbaralone (**1b**) was obtained in 50% yield, together with 2-phenyl-1*H*-indene (**8b**; Table 1, entry 3). Related gold(I) complexes **B** and **C** led to **1b** in lower yields in the presence of **Ox_3** (Table 1, entries 5 and 6). The best yields of **1b** were obtained using [IPrAu(MeCN)][SbF_6] (**D**) and either **Ox_1** or **Ox_3** (Table 1, respectively entries 7 and 9). Oxidants **Ox_2** and **Ox_4** led to very poor results (Table 1, respectively entries 8 and 10). Interestingly, whereas phosphite gold(I) complex **E** afforded low yields (Table 1, entries 11 and 12), pycolinate gold(III) complex provided **1b** in a similar yield in the presence of **Ox_3** (Table 1, entry 14). Reactions of alkynes with pyridine-*N*-oxides can also be performed with Brønsted acids[20] or Zn^{II} catalysts.[21] However, in our system, a complex reaction mixture was obtained in the presence of methanesulfonic acid (Table 1, entry 15) and starting material was recovered when $Zn(OTf)_2$ was used as the catalyst (Table 1, entry 16).

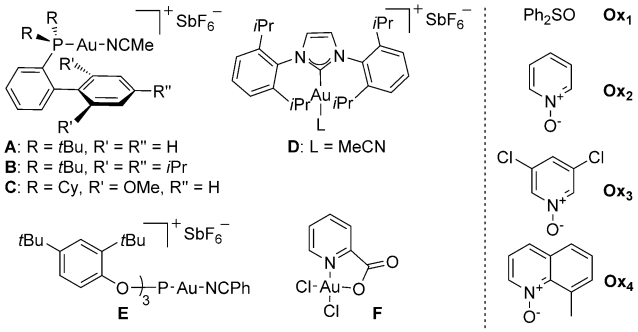
To assess the generality of this oxidative cyclization, various 7-ethynyl-1,3,5-cycloheptatrienes (**6a–v**) were prepared[17] and the combinations of catalyst and oxidant that provided the best results in the preliminary studies (conditions: A) cat. **D**, **Ox_1**; B) cat. **D**, **Ox_3**; C) cat. **A**, **Ox_3**) were tested on these substrates (Table 2). The most simple substrate, 7-ethynyl-1,3,5-cycloheptatriene (**6a**), produced barbaralone (**1a**) in 97% yield. The reaction was compatible with 7-(arylethynyl)-1,3,5-cycloheptatrienes **6c–o** bearing different *o*-, *m*-, or *p*- substituents on the phenyl ring, such as methyl-, *tert*-butyl-, fluorine-, chlorine-, methoxy-, or trifluoromethyl-, affording the corresponding 1-substituted barbaralones (**1c–o**) in moderate to good yields. Substrates **6p–q**, possessing a naphthyl or a thiophenyl substituent, gave barbaralones **1p–q** in yields up to 88%. This catalytic procedure was extendible to alkynyl cycloheptatrienes with aliphatic or alkyl groups (**6s–v**), including *n*-butyl, *n*-hexyl, 2-phenylethyl, and cyclopropyl, giving the desired barbaralones **1s–v** in moderate to excellent yields. The reaction was also applicable to a substrate containing two alkynes (**6r**),

Table 1: Gold(I)-catalyzed oxidative reaction of **6b** to give 1-phenylbarbaralone (**1b**).



Entry	[Cat.]	Oxid.	Time [h]	**1b** Yield [%][a]	**8b** Yield [%][a]
1	**A**	**Ox_1**	2.5	12	58
2	**A**	**Ox_2**	16	5	–
3	**A**	**Ox_3**	2.5	50 (50)[b]	28
4	**A**	**Ox_4**	16	23	–
5	**B**	**Ox_3**	3	30	36
6	**C**	**Ox_3**	3	32	42
7	**D**	**Ox_1**	3	(83)[b]	–
8	**D**	**Ox_2**	24	2	–
9	**D**	**Ox_3**	3	64	–
10	**D**	**Ox_4**	3	7	–
11	**E**	**Ox_1**	2.5	20	–
12	**E**	**Ox_3**	2.5	30	–
13	**F**	**Ox_1**	5	14	61
14	**F**	**Ox_3**	5	61	–
15	$MeSO_3H$[c]	**Ox_3**	2.5	complex mixture	
16	$Zn(OTf)_2$[d]	**Ox_3**	24	starting material	

[a] Yields determined by ^1H NMR using mesitylene as an internal standard. [b] Yield of isolated products. [c] 4 equiv [d] 10 mol%. Catalyst (cat.), oxidant (oxid.).

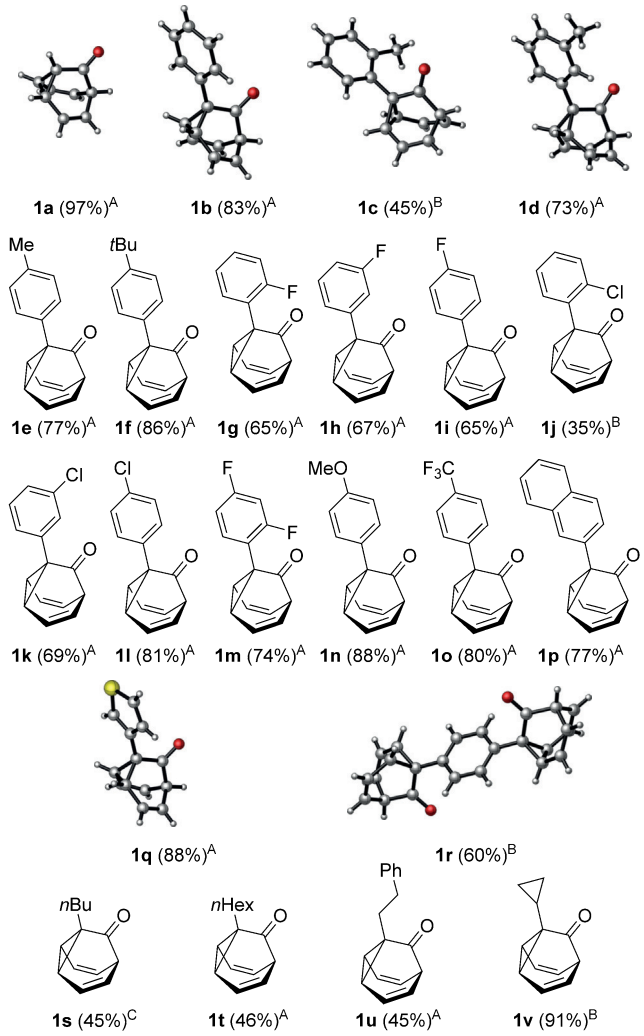


affording dibarbaralone **1r** in 60% yield. The process was efficiently scalable, providing up to 850 mg of barbaralone (**1a**) in one run in 96% yield. Mechanistically, the formation of aryl substituted barbaralones **1b–r** strongly suggests that the oxidation takes place on barbaralyl gold(I) intermediates **7** (Scheme 2), rather than on the alkyne, which would favor formation of unproductive intermediate **10a** by benzylic oxidation.[18]

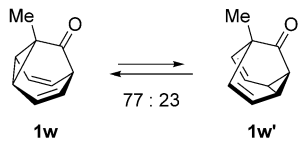
The introduction of a methyl substituent was found to shift the sigmatropic equilibrium toward the 1-substituted isomer (Scheme 3).[6c,9b] Our NMR data show that 1-substituted barbaralones are in all cases the most stable tautomers, as confirmed by the X-ray diffraction structures of **1a–d**, **1q**, and **1r** (Table 2).[22]

With the synthesis of barbaralones (**1**) in hand, and the preparation of bullvalenes (**3**) in mind, we examined the applicability of this oxidative cyclization for the synthesis of bullvalone (**2a**) using propargyl cycloheptatriene as substrate

Table 2: Gold(I)-catalyzed oxidative synthesis of barbaralones **1a–v**.



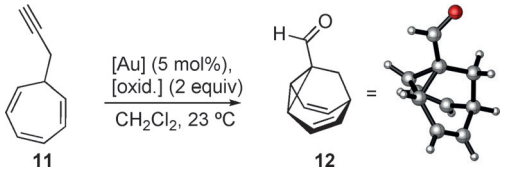
Conditions: A) cat. **D**, $\mathbf{Ox_1}$; B) cat. **D**, $\mathbf{Ox_3}$; C) cat. **A**, $\mathbf{Ox_3}$.



Scheme 3. Equilibrium between 1-methyl- and 5-methylbarbaralones.[9b]

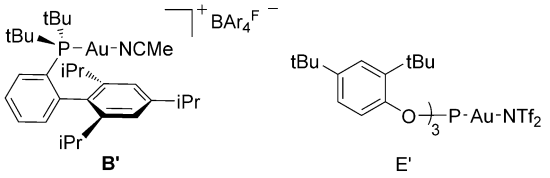
(**11**). Thus, the reaction of propargyl cycloheptatriene (**11**) with different gold(I) catalysts in the presence of the previously employed oxidants was investigated (Table 3). However, instead of the desired bullvalone, arising from a 5-*endo-dig* oxidative cyclization, in all cases we observed the recovered starting material or formation of 1-formylbarbaralane (**12**),[22] the product of a 5-*exo-dig* process. While Johnphos gold(I) complex **A** gave poor results regardless of the oxidant used (Table 3, entries 1–4), good yields were obtained with *t*BuXPhos gold(I) catalyst (**B′**) and [IPrAu(MeCN)]SbF_6 (**D**) with $\mathbf{Ox_1}$ (Table 3, entries 5 and 8). A

Table 3: Gold(I)-catalyzed oxidative reaction of propargyl cycloheptatriene (**11**) to give 1-formylbarbaralane (**12**).



Entry	[Au]	Oxid.	Time [h]	**12** Yield [%][a]
1	**A**	$\mathbf{Ox_1}$	18	27
2	**A**	$\mathbf{Ox_2}$	15	–
3	**A**	$\mathbf{Ox_3}$	18	5
4	**A**	$\mathbf{Ox_4}$	15	–
5	**B′**	$\mathbf{Ox_1}$	17	91 (87)[b]
6	**B′**	$\mathbf{Ox_3}$	17	7
8	**D**	$\mathbf{Ox_1}$	4	90 (87)[b]
9	**D**	$\mathbf{Ox_3}$	18	8
10	**E′**	$\mathbf{Ox_1}$	6	92
11	**E′**	$\mathbf{Ox_3}$	24	–

[a] Yields determined by ^{1}H NMR spectroscopy using mesitylene as an internal standard. [b] Yield of isolated products.

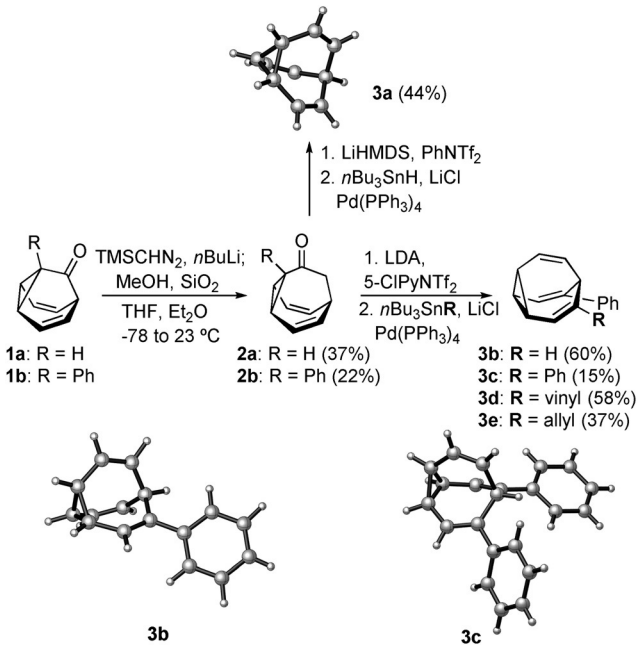


better yield of aldehyde **12** was obtained using phosphite gold(I) complex **E′** and $\mathbf{Ox_1}$ (Table 3, entry 10).

At this stage we considered accessing bullvalones (**2**) via barbaralones (**1**) en route to bullvalenes (**3**). Homologation of **1a** with diazomethane has been reported to give bullvalone (**2a**) in 24% yield along with an isomeric aldehyde (34%).[2,10] Reduction of **2a** followed by acetylation led to the corresponding acetate (40%, two steps), which was pyrolyzed at 345 °C to give a 1:1 ratio of bullvalene (**3a**) and *cis*-9,10-dihydronaphthalene.[2,23] An improved procedure was reported via bullvalone tosylhydrazone, providing bullvalene (**3a**) in approximately 5% yield from **2a** in four steps.[10,24]

In our new approach, bullvalene (**3a**) and phenylbullvalene (**3b**) were prepared from barbaralones **1a–b** by a three-step procedure. A homologation reaction of **1a** and **1b** with the lithium anion of (trimethylsilyl)diazomethane[25] gave bullvalones **2a** and **2b** in 37 and 22% yield, respectively (Scheme 4). Formation of the corresponding enol triflates using LDA and Comins' reagent, or LiHMDS and $PhNTf_2$ followed by immediate reduction with n-Bu_3SnH and $Pd(PPh_3)_4$ as catalyst,[26] afforded **3a** and **3b**[27] in 44% and 60% yield, respectively, whose structures were confirmed by X-ray diffraction.[22] This new synthesis of bullvalene (**3a**) is the most efficient to date as it requires a total of five steps (10% overall yield) from commercially available tropylium tetrafluoroborate and ethynyl magnesium bromide.

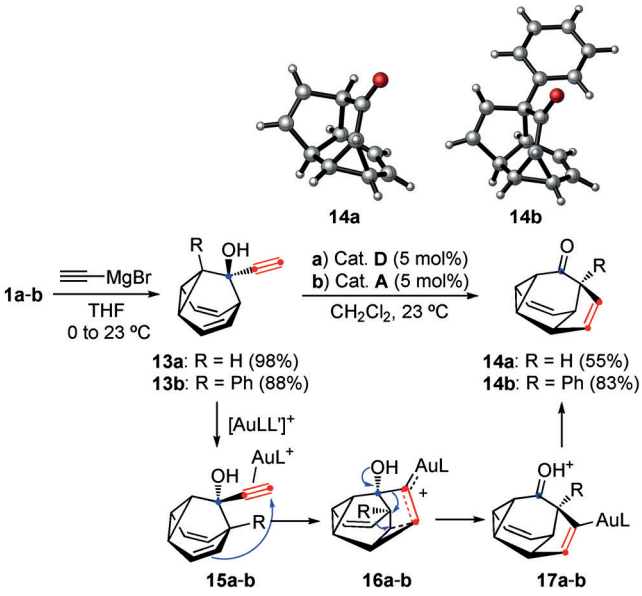
Various disubstituted bullvalenes **3c–e** were also prepared from phenyl bullvalone (**2b**) through sequential formation of the enol triflate followed by Stille couplings (Scheme 4).[28]



Scheme 4. Synthesis of bullvalene (**3a**), phenylbullvalene (**3b**), and disubstituted bullvalenes **3c–e**.

The molecular structure of diphenyl bullvalene **3c** was determined by X-ray diffraction.[22] Bullvalenes **3c–e** were in equilibrium with the 3,6- and 3,7-disubstituted isomers at −40 °C; the observed ratios of the respective compounds was 7.6:5.7:1, 5.2:1.5:1, and 3.8:2.3:1.[7d]

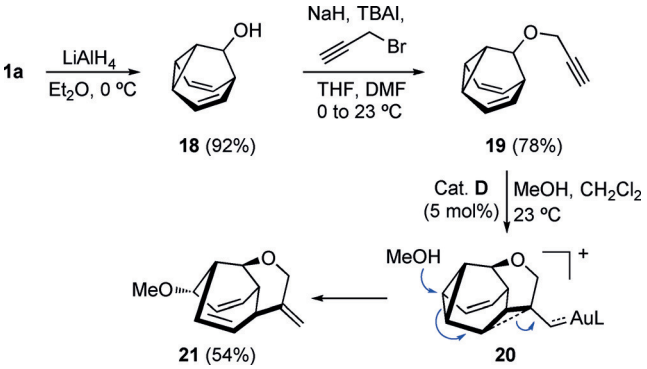
Barbaralones **1a** and **1b** were converted into **14a** and **14b** in two steps by the addition of ethynyl magnesium bromide and subsequent gold(I)-catalyzed reaction of the corresponding alcohols **13a** and **13b**, which proceeded by a new type of cyclization/rearrangement (Scheme 5). Structures **14a** and **14b** were confirmed by X-ray diffraction.[22]



Scheme 5. Preparation of highly fused tetracyclic molecules **14a** and **14b**.

Unprecedented tetracyclic cages **14a** and **14b** are probably formed by coordination of gold(I) of the alkyne of the minor tautomer of **13a** and **13b** to give **15a** and **15b**, followed by intramolecular attack of the alkene to form delocalized intermediates **16a** and **16b**[29,30] and semipinacol-type rearrangement to give **17a** and **17b** (Scheme 5). To the best of our knowledge, and despite the many different types of gold(I)-catalyzed cycloisomerizations,[30] this formation of a five-membered ring by cyclization-rearrangement is unprecedented.

Furthermore, alkylation of barbaralol **18**[22] with propargyl bromide gives 1,7-enyne **19**, which undergoes an *exo-dig* cyclization with gold(I) catalyst **D** to form intermediate **20**,[30] which then reacts with methanol as a nucleophile to form tricyclic system **21** (Scheme 6).



Scheme 6. Formation of tricyclic derivative **21** from barbaralol (**18**).

In summary, we have developed an efficient synthesis of 1-substituted barbaralones by gold(I)-catalyzed oxidative cyclization of 7-(substituted ethynyl)-1,3,5-cycloheptatrienes. This method has allowed accomplishment of the shortest syntheses of bullvalene and other substituted bullvalenes. Thus, parent bullvalene (**3a**) is obtained in five steps from commercially available starting materials in 10% overall yield, which compares favorably with previous procedures that require nine or more steps and proceeded with very low overall efficiency. The straightforward access to barbaralones opens a way to obtain complex cage systems with unprecedented molecular architectures.

Acknowledgements

We thank MINECO (Severo Ochoa Excellence Accreditation 2014–2018 (SEV-2013-0319) CTQ2013-42106-P), the MEC (FPU fellowship to SF), the European Research Council (Advanced Grant No. 321066), the AGAUR (2014 SGR 818), and the ICIQ Foundation. We also thank the ICIQ X-ray diffraction unit and Dr. Michael E. Muratore for helpful discussions.

Keywords: barbaralones · bullvalenes · cyclization reactions · gold · valence tautomerism

How to cite: *Angew. Chem. Int. Ed.* **2016**, *55*, 11178–11182
Angew. Chem. **2016**, *128*, 11344–11348

[1] a) W. v. E. Doering, W. R. Roth, *Angew. Chem. Int. Ed. Engl.* **1963**, *2*, 115–122; *Angew. Chem.* **1963**, *75*, 27–35; b) R. V. Williams, *Chem. Rev.* **2001**, *101*, 1185–1204; c) D. A. Hrovat, E. C. Brown, R. V. Williams, H. Quast, W. T. Borden, *J. Org. Chem.* **2005**, *70*, 2627–2632; d) M. He, J. W. Bode, *Proc. Natl. Acad. Sci. USA* **2011**, *108*, 14752–14756.

[2] a) W. v. E. Doering, W. R. Roth, *Tetrahedron* **1963**, *19*, 715–737; b) W. V. E. Doering, B. M. Ferrier, E. T. Fossel, J. H. Hatenstein, M. Jones, Jr., G. Klumpp, R. M. Rubin, M. Saunders, *Tetrahedron* **1967**, *23*, 3943–3963.

[3] a) G. Schröder, *Angew. Chem. Int. Ed. Engl.* **1963**, *2*, 481; *Angew. Chem.* **1963**, *75*, 722; b) G. Schröder, *Chem. Ber.* **1964**, *97*, 3140–3149; c) R. Merényi, J. F. M. Oth, G. Schröder, *Chem. Ber.* **1964**, *97*, 3150–3161; d) G. Schröder, J. F. M. Oth, R. Merényi, *Angew. Chem. Int. Ed. Engl.* **1965**, *4*, 752–761; *Angew. Chem.* **1965**, *77*, 774–784; e) J. F. M. Oth, K. Müllen, J.-M. Gilles, G. Schröder, *Helv. Chim. Acta* **1974**, *57*, 1415–1433.

[4] M. Saunders, *Tetrahedron Lett.* **1963**, *4*, 1699–1702.

[5] a) R. Poupko, H. Zimmermann, Z. Luz, *J. Am. Chem. Soc.* **1984**, *106*, 5391–5394; b) B. H. Meier, W. L. Earl, *J. Am. Chem. Soc.* **1985**, *107*, 5553–5555; c) P. Luger, K. Roth, *J. Chem. Soc. Perkin Trans. 2* **1989**, 649–655; d) J. J. Titman, Z. Luz, H. W. Spiess, *J. Am. Chem. Soc.* **1992**, *114*, 3765–3771; e) S. Schlick, Z. Luz, R. Poupko, *J. Am. Chem. Soc.* **1992**, *114*, 4315–4320.

[6] a) R. Poupko, H. Zimmermann, K. Müller, Z. Luz, *J. Am. Chem. Soc.* **1996**, *118*, 7995–8005; b) K. Müller, H. Zimmermann, C. Krieger, R. Poupko, Z. Luz, *J. Am. Chem. Soc.* **1996**, *118*, 8006–8014; c) R. Poupko, K. Müller, C. Krieger, H. Zimmermann, Z. Luz, *J. Am. Chem. Soc.* **1996**, *118*, 8015–8023; d) Z. Luz, L. Olivier, R. Poupko, K. Müller, C. Krieger, H. Zimmermann, *J. Am. Chem. Soc.* **1998**, *120*, 5526–5538.

[7] a) B. Volkmann, G. Schröder, *Chem. Ber.* **1984**, *117*, 2226–2232; b) K. Rebsamen, G. Schröder, *Chem. Ber.* **1993**, *126*, 1419–1423; c) K. Rebsamen, G. Schröder, *Chem. Ber.* **1993**, *126*, 1425–1427; d) K. Rebsamen, H. Röttele, G. Schröder, *Chem. Ber.* **1993**, *126*, 1429–1433.

[8] a) A. R. Lippert, J. Kaeobamrung, J. W. Bode, *J. Am. Chem. Soc.* **2006**, *128*, 14738–14739; b) A. R. Lippert, V. L. Keleshian, J. W. Bode, *Org. Biomol. Chem.* **2009**, *7*, 1529–1532; c) A. R. Lippert, A. Naganawa, V. L. Keleshian, J. W. Bode, *J. Am. Chem. Soc.* **2010**, *132*, 15790–15799; d) K. K. Larson, M. He, J. F. Teichert, A. Naganawa, J. W. Bode, *Chem. Sci.* **2012**, *3*, 1825–1828; e) M. He, J. W. Bode, *Org. Biomol. Chem.* **2013**, *11*, 1306–1317; f) J. F. Teichert, D. Mazunin, J. W. Bode, *J. Am. Chem. Soc.* **2013**, *135*, 11314–11321.

[9] a) J. B. Lambert, *Tetrahedron Lett.* **1963**, *4*, 1901–1906; b) J. C. Barborak, S. Chari, P. v. R. Schleyer, *J. Am. Chem. Soc.* **1971**, *93*, 5275–5277; c) H. Nakanishi, O. Yamamoto, *Chem. Lett.* **1975**, 513–516; d) C. Engdahl, P. Ahlberg, *J. Am. Chem. Soc.* **1979**, *101*, 3940–3946; e) E. R. Johnston, J. S. Barber, M. Jacomet, J. C. Barborak, *J. Am. Chem. Soc.* **1998**, *120*, 1489–1493.

[10] J. Casas, F. Serratosa, *An. Quím.* **1977**, *73*, 300–302.

[11] M. J. S. Dewar, R. Pettit, *J. Chem. Soc.* **1956**, 2021–2025.

[12] For two alternative procedures, see: E. Vedejs, R. A. Gabel, P. D. Weeks, *J. Am. Chem. Soc.* **1972**, *94*, 5842–5845.

[13] V. Heil, B. F. G. Johnson, J. Lewis, D. J. Thompson, *J. Chem. Soc. Chem. Commun.* **1974**, 270–271.

[14] For cyclopentannulated barbaralones by photocycloaddition of 2-(pent-4-yn-1-yl)tropones, see: K. S. Feldman, J. H. Come, G. J. Fegley, B. D. Smith, M. Parvez, *Tetrahedron Lett.* **1987**, *28*, 607–610.

[15] S. Kirchmeyer, A. de Meijere, *Helv. Chim. Acta* **1990**, *73*, 1182–1196.

[16] a) C. R. Solorio-Alvarado, Y. Wang, A. M. Echavarren, *J. Am. Chem. Soc.* **2011**, *133*, 11952–11955; b) Y. Wang, P. McGonigal, B. Herlé, M. Besora, A. M. Echavarren, *J. Am. Chem. Soc.* **2014**, *136*, 801–809.

[17] P. R. McGonigal, C. de León, Y. Wang, A. Homs, C. R. Solorio-Alvarado, A. M. Echavarren, *Angew. Chem. Int. Ed.* **2012**, *51*, 13093–13096; *Angew. Chem.* **2012**, *124*, 13270–13273.

[18] a) L. Zhang, *Acc. Chem. Res.* **2014**, *47*, 877–888; b) Z. Zheng, Z. Wang, Y. Wang, L. Zhang, *Chem. Soc. Rev.* **2016**, DOI: 10.1039/c5cs00887e.

[19] a) D. Vasu, H.-H. Hung, S. Bhunia, S. A. Gawade, A. Das, R.-S. Liu, *Angew. Chem. Int. Ed.* **2011**, *50*, 6911–6914; *Angew. Chem.* **2011**, *123*, 7043–7046; b) D. B. Huple, S. Ghorpade, R.-S. Liu, *Adv. Synth. Catal.* **2016**, *358*, 1348–1367; c) J. Schulz, J. Jasik, A. Gray, J. Roithová, *Chem. Eur. J.* **2016**, *22*, DOI: 10.1002/chem.201601634, and references therein.

[20] D.-F. Chen, Z.-Y. Han, Y.-P. He, J. Yu, L.-Z. Gong, *Angew. Chem. Int. Ed.* **2012**, *51*, 12307–12310; *Angew. Chem.* **2012**, *124*, 12473–12476.

[21] L. Li, B. Zhou, Y.-H. Wang, C. Shu, Y.-F. Pan, X. Lu, L.-W. Ye, *Angew. Chem. Int. Ed.* **2015**, *54*, 8245–8249; *Angew. Chem.* **2015**, *127*, 8363–8367.

[22] CCDC 1487016 (**1a**), CCDC 1487017 (**1b**), CCDC 1487018 (**1c**), CCDC 1487019 (**1d**), CCDC 1487020 (**1q**), CCDC 1487021 (**1r**), CCDC 1487022 (**2b**), CCDC 1487023 (**3a**), CCDC 1487024 (**3b**), CCDC 1487025 (**3c**), CCDC 1487026 (**12**), CCDC 1487027 (**14a**), and CCDC 1487028 (**14b**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.

[23] The yield for the last step was not provided in the original report.[2b]

[24] a) F. Serratosa, F. López, J. Font, *Tetrahedron Lett.* **1972**, 2589–2590; b) F. Serratosa, F. López, J. Font, *An. Quím.* **1974**, *70*, 893–899.

[25] H. Liu, C. Sun, N.-K. Lee, R. F. Henry, D. Lee, *Chem. Eur. J.* **2012**, *18*, 11889–11893.

[26] W. J. Scott, J. K. Stille, *J. Am. Chem. Soc.* **1986**, *108*, 3033–3040.

[27] Phenylbullvalene **3b** has been shown to be in a 3:1 equilibrium with the 3-substituted isomer at −40 °C.[7d] We have confirmed this result and have observed that the equilibrium can be shifted to 5.6:1 at −90 °C.

[28] W. J. Scott, G. T. Crisp, J. K. Stille, *J. Am. Chem. Soc.* **1984**, *106*, 4630–4632.

[29] V. López-Carrillo, N. Huguet, Á. Mosquera, A. M. Echavarren, *Chem. Eur. J.* **2011**, *17*, 10972–10978.

[30] a) E. Jiménez-Núñez, A. M. Echavarren, *Chem. Rev.* **2008**, *108*, 3326–3350; b) R. Dorel, A. Echavarren, *Chem. Rev.* **2015**, *115*, 9028–9072; c) R. Dorel, A. M. Echavarren, *J. Org. Chem.* **2015**, *80*, 7321–7332.

Received: June 23, 2016
Published online: August 22, 2016

