Pozdniakova, S. V. Lindeman, A. A. Zhdanov, G. Pályi, *J. Mol. Catal. A* **1996**, *107*, 313; b) K. A. Andrianov, A. A. Zhdanov, *Dokl. Akad. Nauk SSSR* **1957**, *114*, 1005.

[11] a) A. Altomare, G. Cascarano, C. Giacovazzo and A. Guagliardi, *J. Appl. Crystallogr.* **1993**, *26*, 343; b) G. M. Sheldrick, SHELXL-97 (release 9F-2), Program for Crystal Structure Refinement, University of Göttingen, Göttingen (Germany), **1998**; c) L. J. Farrugia, *J. Appl. Crystallogr.* **1999**, *32*, 837; d) L. J. Farrugia, *J. Appl. Crystallogr.* **1997**, *30*, 565.

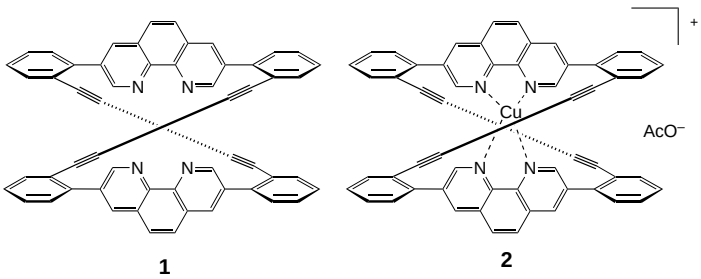


Figure 1. Phenanthrolenophane **1** and its copper(I) complex, **2**.

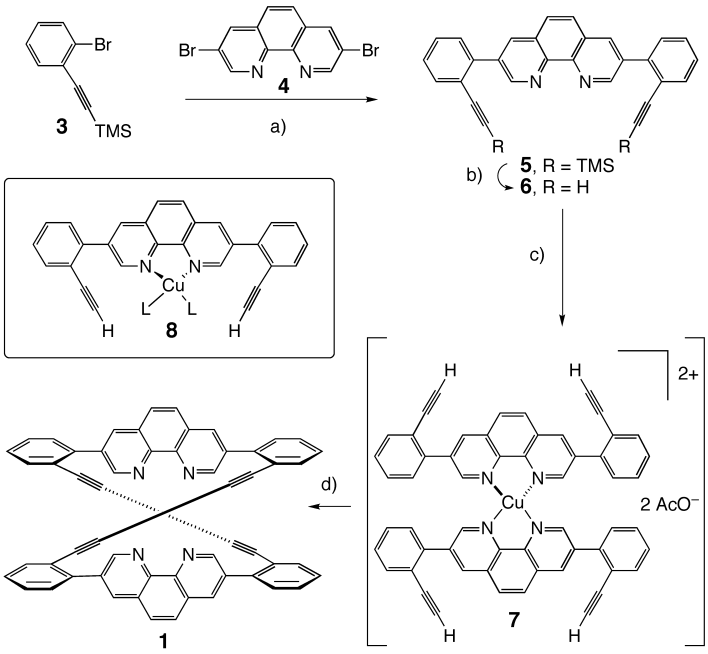
Template-Directed Synthesis of Helical Phenanthroline Cyclophanes**

Matthew A. Heuft and Alex G. Fallis*

Recently the synthesis and study of assorted carbocyclic cyclophanes and cage compounds[1] has been augmented by novel heterocyclic arrays. Representative examples include bis-2,2′-bipyridine units in twisted diyne dehydroannulenes for spectroscopic detection of metal ions,[2] butadiyne-bridged [4_4](2,6)pyridinophanes,[3] rigid cross-conjugated acetylenic macrocycles as a cyclic alternative for 4,4′-bipyridine functionalities for metal complexation,[4] and related thiophene-bridged macrocycles.[5]

Phenanthroline-based investigations involve studies of copper complex induced DNA cleavage,[6] the mechanism of strand scission,[7] enhancement of Diels–Alder reactions,[8] and applications of a cationic platinum–phenanthroline complex.[9] Substituted 1,10-phenanthrolines are highly fluorescent and the spectra are modulated by protonation or metal-ion complexation.[10] [2]Catenanes have been assembled by employing copper(I)–phenanthroline units,[11] and copper(I)–biphenanthrolines have provided scaffolds for molecular grids.[12]

We report here the synthesis of the helical 1,10-phenanthroline-capped cyclophanes **1** (Figure 1) and **11** (Scheme 2), which possess the potential for complexation with various metals, as illustrated by the insertion of copper(I) ions in **2** and **12**. Bromosilylacetylene **3** was converted into its organozincate[1e–g,13] by in situ halogen metal exchange with *n*BuLi, followed by transmetalation with $ZnBr_2$ (Scheme 1). Addition of [$Pd(PPh_3)_4$] and 3,8-dibromophenanthroline (**4**)[14] afforded **5** in 87% yield when DMF was used as a co-solvent.[15] Suzuki couplings also provide 3,8-diaryl-1,10-phenanthrolines.[14c,16] Deprotection of **5** with K_2CO_3 in MeOH/THF provided **6** in 85% yield.



Scheme 1. Synthesis of phenanthrolenophanes **1** and **2**. a) 1) *n*BuLi, THF, −78 °C; 2) $ZnBr_2$, 0 °C, 15 min; 3) **4**, [$Pd(PPh_3)_4$], THF/DMF (1/1), Δ, 72 h, 87%; b) K_2CO_3, CH_2Cl_2, MeOH, H_2O, 72 h, 85%; c) $Cu(OAc)_2$ (0.5 equiv), diethyl ether/py, 2 h; d) 1. $Cu(OAc)_2$ (5.5 equiv), diethyl ether/py, 18 h; 2. KCN (aq), CH_2Cl_2, 5 min, 70%.

We anticipated that controlled addition of copper(II) acetate to **6** (diethyl ether/pyridine) would initially generate the intermediate complex **7**. This "copper template" would then facilitate the desired coupling reaction and circumvent the competing formation of acetate **8** from direct coordination with $Cu(OAc)_2$.[17] The geometric environment of intermediate **8** will inhibit the desired reaction relative to that of **7** in which the terminal acetylene groups are suitably disposed for intermolecular coupling. In addition, polymerization pathways often observed in similar dimerizations should be diminished.[18]

Experimentally, addition of copper(II) acetate (initially 0.5 equiv) in a mixture of pyridine/diethyl ether initiated the reaction and allowed for the formation of **7**. Subsequent addition of excess reagent (5.5 equiv) completed the coupling and afforded the copper(I)-complexed cyclophane **2** in 84% yield (Scheme 1). Supporting evidence for this mechanism was provided by the observed color changes from yellow (**6**) to red (**7**) to green after an excess of $Cu(OAc)_2$ was added. Further confirmation of the importance of the copper

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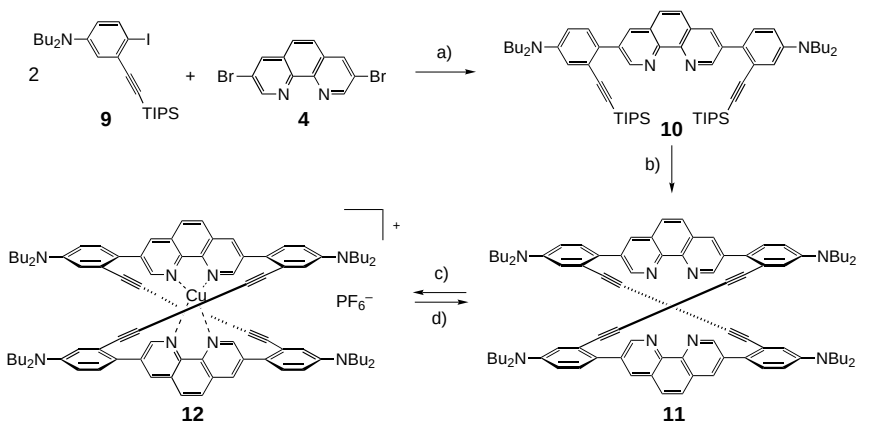
template in these oxidative couplings was revealed by the diminished yield of **2** (15%) when the reaction was conducted with direct exposure of **6** to $Cu(OAc)_2$ (6 equiv, pyridine/diethyl ether).[19]

The parent cyclophane **1**, was liberated from the copper(I)-coordinated phenanthroline cyclophane **2** upon treatment with aqueous potassium cyanide. Unfortunately, cyclophane **1** was only sparingly soluble in a range of organic solvents. The synthesis of the *N*,*N*-dibutylamine-substituted analogue **11** was investigated in an attempt to circumvent this difficulty and provide a substituted member of this series for comparison of the electronic properties. In addition, the butyl groups are diastereotopic in helical (chiral) cyclophane conformations and this should be reflected in the ^{13}C NMR spectrum, thus allowing the conformational behavior of the cyclophane to be probed.[20]



Scheme 2. Synthesis of phenanthrolenophanes **11** and **12**. a) 1. **9**, *n*BuLi, THF, −78°C; 2. $ZnBr_2$, 0°C, 15 min; 3. **4**, $[Pd(PPh_3)_4]$, THF/DMF (1/1), Δ, 72 h, 70%; b) 1. TBAF, diethyl ether/py, 15 min; 2. $Cu(OAc)_2$ (0.5 equiv), diethyl ether/py, 2 h; 3. $Cu(OAc)_2$ (5.5 equiv), diethyl ether/py, 2 h; 4. KCN (aq), 39%; c) $[Cu(MeCN)_4PF_6]$, CH_2Cl_2, 15 min, 97%; d) KCN (aq), CH_2Cl_2, 5 min, 97%. py = pyridine.

A very direct synthesis of **11** has been developed to improve the preparation of these compounds. Dibromide **4** was treated with known iodide **9**[18] through a parallel palladium coupling sequence to generate diacetylene **10** (Scheme 2). Compound **10** was transformed into the metal-free cyclophane **11** in a single reaction vessel by a sequential in situ desilylation/dimerization/decomplexation protocol related to the experiments we have developed recently.[21] These steps culminated in an aqueous potassium cyanide work-up to give **11** in 39% yield. Cyclophane **11** was soluble in a variety of chlorinated solvents.

Copper(I) complexes **2** and **12** were prepared independently as above, but crystals suitable for X-ray analysis were not obtained. However, molecular modeling studies (Figure 2) revealed the twisted nature and key features of the phenanthrolenophane copper complex **2** (Figure 1).[22] The heterocyclic rings displayed an orthogonal disposition with respect to each other and created a pseudotetrahedral coordination site for copper(I) or other electronically related metal ions. The helical nature of cyclophane **12** resulted from our synthetic protocol and the bridges selected.[1d–f]

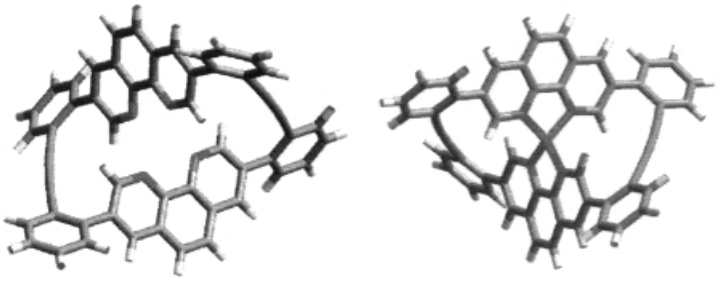


Figure 2. Molecular models of cyclophanes **1** and **2**.

Variable temperature ^{13}C NMR analysis of **12** indicated the helical isomerization barrier was 13.6 kcal mol^{-1}, an increase of approximately 4 kcal mol^{-1} relative to the uncomplexed cyclophane **11** (Figure 3). Different metals and substituent combinations may increase this barrier sufficiently to inhibit isomerization and facilitate resolution of the individual enantiomers.

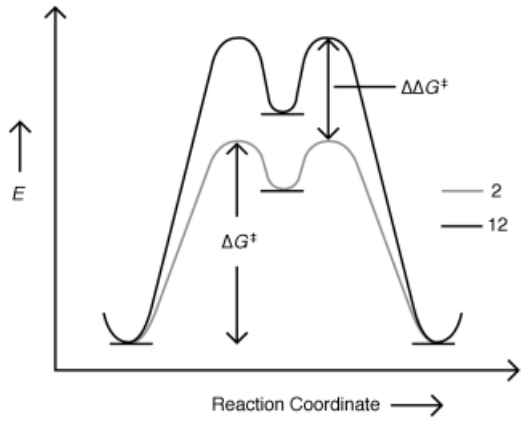


Figure 3. Potential energy diagram for the enantiomerization of cyclophanes **2** and **12**. $\Delta G_2^{\ddagger} < 9.4$ kcal mol^{-1}, $\Delta G_{12}^{\ddagger} = 13.6$ kcal mol^{-1}, $\Delta\Delta G^{\ddagger} > 4.2$ kcal mol^{-1}.

Electronic absorption (Figure 4) were obtained for cyclophanes **1**, **2**, **11**, and **12** and compared to related compounds (Table 1). Copper template **7** absorbed in the 600 to 700 nm range, which is indicative of copper(II) complexes. Emission spectra (Figure 5) of **1** and **11** were recorded but the metallocyclophanes (**2** and **12**) did not fluoresce.

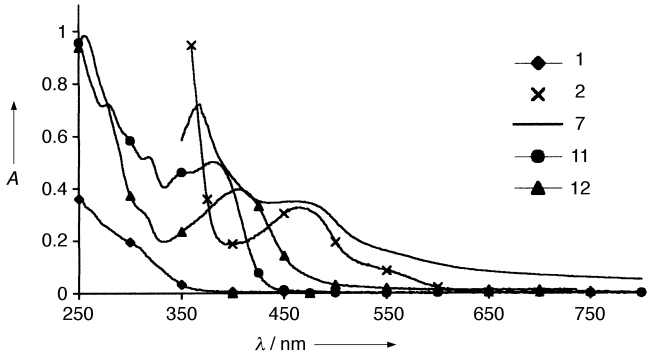


Figure 4. UV/Vis absorption spectra of **1**, **11**, and **12**.[23]

In summary, we have developed a short, efficient syntheses of a series of functionalized acetylenic phenanthroline cyclophanes by Pd- and Cu-mediated coupling reactions. Molecular modeling studies have established the nature of the

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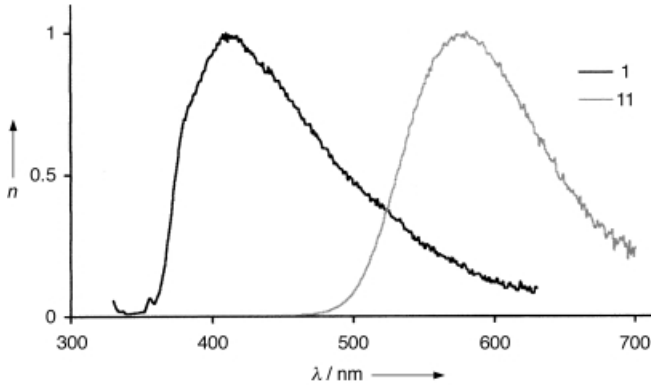
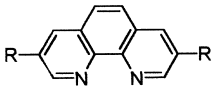


Figure 5. Normalized fluorescence spectra of **1** and **11** (*n*: counts).[24]

Table 1. UV/Vis absorption maxima of phenanthroline compounds and copper–phenanthrolic complexes.



13

Compound	λ_{max}(abs) [nm]	λ_{max}(em) [nm]
13 (R = H)[25]	440	
$[Cu(\mathbf{13})_2]^+$ (R = H)[26]	458	
13 (R = C≡C-Ph)[10]	346	376, 395
13 (R = C≡C-(*p*-PhNMe$_2$))[10]	410	523
1	307 (sh)	416
2 $[Cu(\mathbf{1})_2]^+$	473, 553 (sh)	
7 $[Cu(\mathbf{6})_2]^{2+}$	462	
11	383	584
12 $[Cu(\mathbf{11})_2]^+$	407	

copper-complexed core. In addition, resolution of the helical isomers may be feasible with additional ring substituents and metal complexation. The synthetic protocol above will facilitate the preparation of new derivatives that may possess unusual optical properties, while modification of the acetylene spacers offers some control of the helical conformation.

Experimental Section

Sequential in situ desilylation/dimerization/decomplexation procedure (**11**): A solution of tetrabutylammonium fluoride (TBAF) (1M in THF, 1.32 mL, 1.32 mmol, 2.5 equiv) was added in one portion to a stirred solution of **10** (500 mg, 0.53 mmol, 1 equiv) in pyridine/diethyl ether (3/1, 20 mL). After stirring the solution for 15 min, a solution of $Cu(OAc)_2$ (48 mg, 0.26 mmol, 0.5 equiv) in pyridine/diethyl ether (3/1, 20 mL) was added over 2.5 h by syringe pump. Once the addition was complete, additional $Cu(OAc)_2$ (530 mg, 2.92 mmol, 5.5 equiv) was added to the reaction and the solution turned green immediately. The reaction was stirred for 18 h at room temperature and partitioned between CH_2Cl_2 and water. The aqueous phase was extracted with CH_2Cl_2 (×3) and the combined extracts were washed with KCN (10%, aq) and water, filtered through celite, and concentrated. Following chromatography on silica gel (CH_2Cl_2/MeOH, 30/1), **11** was isolated as an orange solid (130 mg, 39%).

1: m.p. 150 °C slow decomp.; ^{1}H NMR (500 MHz, [D$_6$]DMSO, 25 °C, TMS): δ = 9.33 (brs, 4H), 8.87 (brs, 4H), 7.82–7.77 (m, 12H), 7.63 (brs, 4H), 7.40 ppm (brs, 4H); ^{13}C NMR (125 MHz, [D$_6$]DMSO, 25 °C, TMS): δ = 150.4 (d), 144.3 (s), 140.0 (s), 135.9 (d), 133.7 (s), 133.1 (d), 132.3 (d), 131.4 (d), 130.8 (d), 127.7 (s), 126.9 (d), 118.9 (s), 81.4 (s), 76.3 ppm (s); MS (ES) *m*/*z* (%): 757.0 (1), 579.1 (2), 279.0 (4), 141.9 (53).

2: m.p. > 260 °C; IR (CH_2Cl_2): $\tilde{\nu}$ = 3049.9, 1604.0, 1436.7, 1266.8, 1119.7 cm^{-1}; ^{1}H NMR (500 MHz, [D$_6$]DMSO, 25 °C, TMS): δ = 9.25 (brs, 4H), 8.84 (brs, 4H), 8.37 (brs, 4H), 7.65 (brs, 4H), 7.41 ppm (brs, 12H); ^{13}C NMR (125 MHz, [D$_6$]DMSO, 25 °C, TMS): δ = 149.2 (d), 141.6 (s), 139.8 (s), 136.7 (d), 136.4 (s), 133.5 (d), 130.8 (d), 129.8 (d), 129.0 (d), 128.7 (s), 127.7 (d), 118.9 (s), 81.3 (s), 76.0 ppm (s); MS (70 eV): *m*/*z* (%): 819.3 (100) [M^+], 136.0 (55).

11: m.p. 138–140 °C; IR (CH_2Cl_2): $\tilde{\nu}$ = 2960.9, 1596.2, 1369.8, 847.2 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): δ = 9.27 (s, 4H), 8.46 (s, 4H), 7.40 (d, *J* = 8.6 Hz, 4H), 7.03 (s, 4H), 6.91 (s, 4H), 6.75 (d, *J* = 6.9 Hz, 4H), 3.29 (t, *J* = 7.1 Hz, 16H), 1.62–1.53 (m, 16H), 1.41–1.32 (m, 16H), 0.96 ppm (t, *J* = 7.2 Hz, 24 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C, TMS): δ = 150.6 (d), 147.5 (s), 144.3 (s), 134.9 (d), 134.3 (s), 130.6 (d), 127.8 (s), 127.7 (s), 126.5 (d), 120.8 (s), 116.5 (d), 113.5 (d), 81.9 (s), 75.6 (s), 50.7 (t), 29.3 (t), 20.3 (t), 13.9 ppm (q); MS (ES) 1266.5 (1) [M^+], 579 (1.2), 279.0 (48), 186.1 (100).

12: m.p. > 250 °C (decomp); IR (CH_2Cl_2): $\tilde{\nu}$ = 2960.9, 1596.2, 1369.8, 847.2, 769.8 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, TMS): δ = 9.18 (brs, 4H), 8.30 (brs, 4H), 8.08 (brs, 4H), 7.19 (brs, 4H), 6.71 (s, 4H), 6.62 (brs, 4H), 3.21 (brs, 16H), 1.51 (brs, 16H), 1.32 (brs, 16H), 0.92 ppm (brs, 24 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C, TMS): δ = 150.0 (d), 148.1 (s), 141.6 (s), 137.8 (s), 134.8 (d), 130.5 (d), 128.9 (s), 127.3 (d), 126.6 (s), 120.5 (s), 115.4 (d), 113.7 (d), 81.9 (s), 75.4 (s), 50.6 (t), 29.6 (t), 20.2 (t), 13.9 ppm (q); MS (ES) 1328.5 (6) [M^+–PF_6], 342.1 (10), 186.2 (24).

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[1] a) G. J. Bodwell, *Angew. Chem.* **1996**, *108*, 2221–2224; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 2085–2088; b) A. de Meijere, B. Koenig, *Synlett* **1997**, 1221–1232; c) B. König, *Top. Curr. Chem.* **1998**, *196*, 92–136; d) S. K. Collins, G. P. A. Yap, A. G. Fallis, *Angew. Chem.* **2000**, *112*, 393–396; *Angew. Chem. Int. Ed.* **2000**, *39*, 385–388; e) S. K. Collins, G. P. A. Yap, A. G. Fallis, *Org. Lett.* **2000**, *2*, 3189–3192; f) S. K. Collins, G. P. A. Yap, A. G. Fallis, *Org. Lett.* **2002**, *4*, 11–14, and references therein.

[2] P. N. W. Baxter, *J. Org. Chem.* **2001**, *66*, 4170–4179.

[3] Y. Tobe, A. Nagano, K. Kawabata, M. Sonoda, K. Naemura, *Org. Lett.* **2000**, *2*, 3265–3268.

[4] K. Campbell, R. McDonald, N. R. Branda, R. R. Tykwinski, *Org. Lett.* **2001**, *3*, 1045–1048.

[5] M. J. Marsella, Z.-Q. Wang, R. J. Reid, K. Yoon, *Org. Lett.* **2001**, *3*, 885–887.

[6] D. R. McMillin, K. M. McNett, *Chem. Rev.* **1998**, *98*, 1201–1219.

[7] T. Oyoshi, H. Sugiyama, *J. Am. Chem. Soc.* **2000**, *122*, 6313–6314.

[8] S. Otto, J. B. F. N. Engberts, *J. Am. Chem. Soc.* **1999**, *121*, 6798–6806.

[9] a) J. W. Madine, X. Wang, R. A. Widenhoefer, *Org. Lett.* **2001**, *3*, 385–388; b) L. A. Goj, R. A. Widenhoefer, *J. Am. Chem. Soc.* **2001**, *123*, 11133–11147.

[10] H. S. Joshi, R. Jamshidi, Y. Tor, *Angew. Chem.* **1999**, *111*, 2888–2891; *Angew. Chem. Int. Ed.* **1999**, *38*, 2722–2725.

[11] F. Ibukuro, M. Fujita, K. Yamaguchi, J.-P. Sauvage, *J. Am. Chem. Soc.* **1999**, *121*, 11014–11015.

[12] a) S. Toyota, C. R. Woods, M. Benaglia, R. Haldimann, K. Warnmark, K. Hardcastle, J. S. Siegel, *Angew. Chem.* **2001**, *113*, 773–776; *Angew. Chem. Int. Ed.* **2001**, *40*, 751–754; b) J. C. Loren, J. S. Siegel, *Angew. Chem.* **2001**, *113*, 776–779; *Angew. Chem. Int. Ed.* **2001**, *40*, 754–757.

[13] a) S. Sengupta, V. Snieckus, *J. Org. Chem.* **1990**, *55*, 5680–5683; b) P. Knochel, D. Seebach, *Tetrahedron Lett.* **1982**, *23*, 3897–3900.

[14] a) D. Tzalis, Y. Tor, S. Failla, J. S. Siegel, *Tetrahedron Lett.* **1995**, *36*, 3489–3490; b) Y. Saitoh, T.-A. Koizumi, K. Osakada, T. Yamamoto, *Can. J. Chem.* **1997**, *75*, 1336–1339; c) C. Dietrich-Buchecker, M. C. Jimenez, J.-P. Sauvage, *Tetrahedron Lett.* **1999**, *40*, 3395–3396.

[15] M. Sjoegren, S. Hansson, P. O. Norrby, B. Aakermark, M. E. Cucciolito, A. Vitagliano, *Organometallics* **1992**, *11*, 3954–3964.

[16] M. Kimura, T. Shiba, T. Muto, K. Hanabusa, H. Shirai, *Tetrahedron Lett.* **2000**, *41*, 6809–6813.

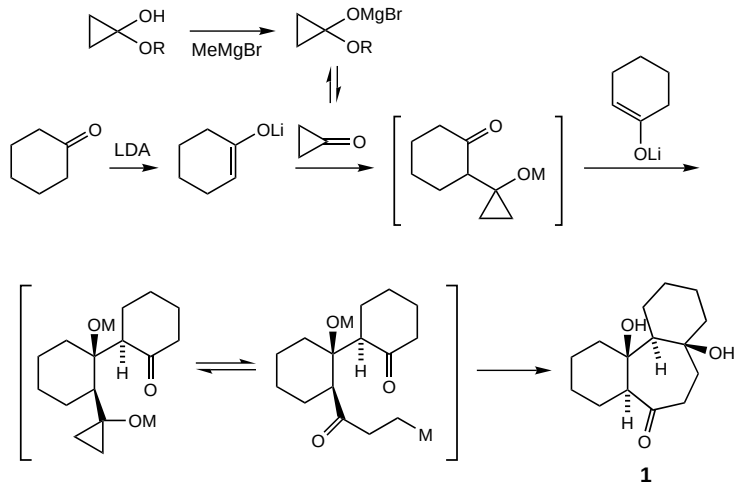
[17] a) *Templated Organic Synthesis* (Eds.: F. Diederich, P. J. Stang), Wiley-VCH, Weinheim, **2000**; b) C. Dietrich-Buchecker, J.-P. Sauvage, N. Geum, A. Hori, M. Fujita, S. Sakamoto, K. Yamaguchi, *Chem. Commun.* **2001**, 1182–1183.

[18] J. J. Pak, T. J. R. Weakley, M. M. Haley, *J. Am. Chem. Soc.* **1999**, *121*, 8182–8192.

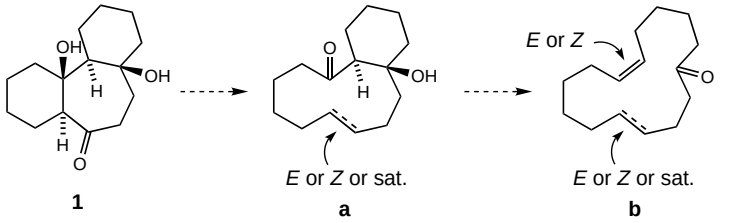
[19] a) R. Berscheid, F. Vögtle, *Synthesis* **1992**, 58–62; b) M. Brake, V. Enkelmann, U. H. F. Bunz, *J. Org. Chem.* **1996**, *61*, 1190–1191; c) P.

  0044-8249/02/4123-4522 $ 20.00+.50/0

Siemsen, R. C. Livingston, F. Diederich, *Angew. Chem.* **2000**, *112*, 2740 – 2767; *Angew. Chem. Int. Ed.* **2000**, *39*, 2632 – 2657; d) M. M. Haley, M. L. Bell, S. C. Brand, D. B. Kimball, J. J. Pak, W. B. Wan, *Tetrahedron Lett.* **1997**, *38*, 7483 – 7486.
[20] a) R. Boese, A. J. Matzger, K. P. C. Vollhardt, *J. Am. Chem. Soc.* **1997**, *119*, 2052 – 2053; b) A. R. Lim, B. M. Novak, *Solid State Commun.* **1999**, *112*, 459 – 464.
[21] M. A. Heuft, S. K. Collins, G. P. A. Yap, A. G. Fallis, *Org. Lett.* **2001**, *3*, 2883 – 2886.
[22] Density functional theory (DFT) calculations were obtained using a DN basis set with the Cerius^2-Dmol^3 molecular modeling suite from Molecular Simulations Inc. San Diego, 1999 (counterion in **2** not shown for clarity).
[23] Electronic absorption spectra λ_{max} nm^{-1} (CH_2Cl_2): **1**, 307 (sh); **11**, 383; **12**, 407.
[24] Emission spectra (CH_2Cl_2): **1**: $\lambda_{ex} = 320$ nm, $\lambda_{max} = 416$ nm; **11**: $\lambda_{ex} = 437$ nm, $\lambda_{max} = 584$ nm.
[25] C. T. Cunningham, K. L. H. Cunningham, J. F. Michalec, D. R. McMillin, *Inorg. Chem.* **1996**, *35*, 6406 – 6412.
[26] M. Ruthkosky, F. N. Castellano, G. J. Meyer, *Inorg. Chem.* **1996**, *35*, 6406 – 6412.



Scheme 1. Synthesis of ketone **1**.[5]



Scheme 2. Projected route to unsaturated C-15 macrocyclic ketones.

Access to C-15 Macrocyclic Ketones by Iterative Fragmentations of a Tricyclic System

Charles Fehr,* José Galindo, Olivier Etter, and Walter Thommen

In recent years, macrocyclic musks[1,2] have gained renewed interest for their excellent odor qualities (warm, sensual, animal, natural), and for their better biodegradability than benzenoid musks.[2,3]

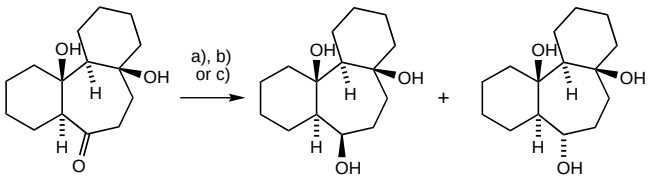
In particular, there is still a great need to find efficient syntheses for the construction of C-15 macrocyclic ketones possessing specific unsaturation. We herein report the first application of a new synthetic strategy in which the target compounds are obtained from an appropriately functionalized tricyclic system by two consecutive fragmentations. This approach is complementary to the metathesis-based annulations, which are often more direct but require high dilution and generally afford *E*/*Z* mixtures.[4]

Access to the targeted tricyclic fragmentation precursor was provided by the ready availability of the known dihydroxy ketone **1**, which was prepared in one pot from cyclohexanone and cyclopropanone (Scheme 1).[5] Despite a reported yield of 67%, it was only after modification of the experimental procedure that we were able to attain a reproducible yield of 44% (see Experimental Section).

The 1,3,5-functionalization of **1**, in which one oxygen atom is adjacent to a bridgehead and the two other oxygen atoms are situated at bridgehead positions, is ideally suited for cascade Grob fragmentations[6] and should allow, via intermediates **a**, ready access to new unsaturated C-15 macrocyclic ketones of type **b** (Scheme 2).

Reduction of **1** with $LiAlH_4$ afforded a 74:26 mixture of triols **2** and **3** (Scheme 3), whereas by using Red-Al® in THF at low temperature the all-*cis* triol **2** was obtained almost quantitatively in a highly diastereoselective manner (99:1). On the other hand, reduction with $BH_3{\cdot}SMe_2$ followed the opposite facial selectivity with an equally high diastereoselectivity (98:2), affording triol **3** in 81% yield (Scheme 3).[7]

For the conversion of alcohol **2** into tosylate **4**, whereas the application of classical conditions (TsCl, pyridine) gave rise to partial epimerization (by successive substitutions) and chloride formation, deprotonation of **2** with *n*BuLi followed by rapid treatment with TsCl gave the best results (Scheme 4).



a)	74	:	26	
b)	99	:	1	(98%)
c)	2	:	98	(81%)

Scheme 3. Diastereoselective reductions of ketone **1**. a) $LiAlH_4$ (1.15 equiv), THF, −70°C to −50°C; b) Red-Al® (3.0 equiv), THF, −70°C to room temperature; c) $BH_3{\cdot}SMe_2$ (0.71 equiv), THF, room temperature.

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