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Synthesis and Characterization of Oxygen-Substituted Pericyclynes

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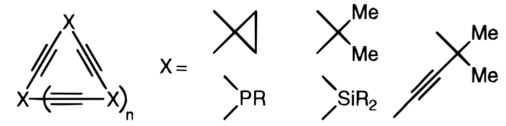
Pericyclynes, homoconjugated macrocycles in which alkynes and saturated fragments (X) are connected in alternation (**1**), were first studied by Scott[1] and his group. Pericyclynes fascinate due to their aesthetically pleasing structures, representing "exploded" versions of cycloalkanes which arouse interest for the study of cyclic homoconjugation in neutral systems.



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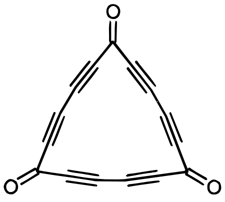

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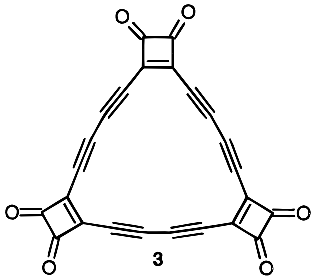

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On the other hand, Diederich and Rubin[2] have described the synthesis of higher carbon oxides of the structure **3** by a synthesis involving a Hay[3] type coupling. As a conceivable hybrid between these two structures, polyketones **2** can be envisaged as a novel type of carbon oxide and a class of unusual hydrogen-free organic compounds: we wish to describe the synthesis of several protected precursors of **2**, the cycles **4**−**8** (Chart 1), the first pericyclynes persubstituted by ether functions.

Ketalization of **9a**,**b**[4] with 2,2-dimethylpropanediol in boiling benzene under the influence of *p*-toluenesulfonic acid afforded a 72% yield of **10a** and 87% of **10b**. These bisalkynes were isolated after aqueous workup and distillation (oil pump vacuum) as a stable colorless powder (**10a**) and a stable colorless oil (**10b**). Reaction of **10a**,**b** with potassium carbonate in methanol (21 °C, 90 min) led to the deprotected and the half-deprotected alkynyls **11a**,**b**.[5]

Diethynyl **11a** (mp 79 °C) was cyclized by dissolving in a slurry of $Cu(OAc)_2$ in acetonitrile (10 mM solution of **11a**) and heating the solution to 65 °C for 3.5 h (Vögtle conditions[6]). Aqueous workup and separation of the oligomers by preparative gel permeation chromatography (GPC) furnished 19 mg (5.8%, decomp > 190 °C) of **4**, 41 mg (12.6%, decomp > 152 °C) of **5**, 30 mg (9.2%, decomp > 120 °C) of **6**, and 10 mg (3.1%, decomp > 115 °C) of **7** as colorless powders. For a more controlled access to the even-membered cycles, **11b** was subjected to the Vögtle variant of the Eglington coupling,[6] affording **12** after deprotection with Bu_4NF in 68% (Scheme 1).[7] The diyne **12** was coupled (*vide supra*, 6.1 mM concentration of **12**) yielding 26 mg (9.3%) of **4**, 91 mg (32.7%) of **6**, and 50 mg (18.0%, decomp > 123 °C) of octamer **8** after standard workup.[8]

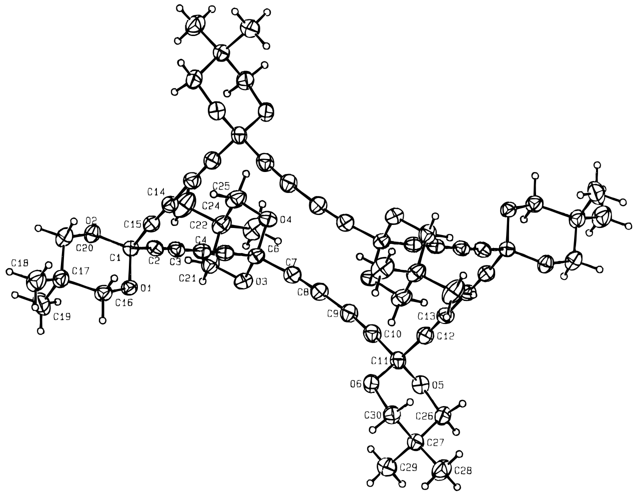
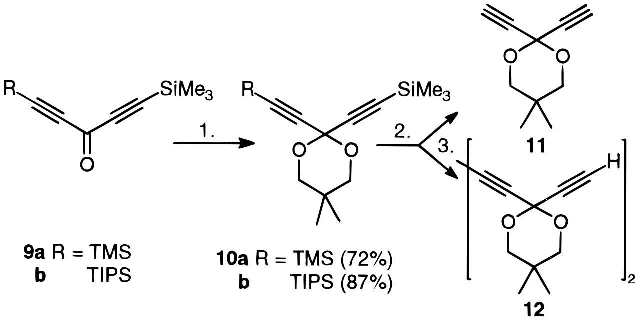


Figure 1.

Scheme 1



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[1] Scott, L. T.; Cooney, M. J. In *Modern Acetylene Chemistry;* Stang, P. J., Diederich, F., Eds; VCH: Weinheim, 1995; p 321, and therein cited references. Scott, L. T.; Cooney, M. J.; Johnels, D. J. *J. Am. Chem. Soc.* **1990**, *112*, 4054.

[2] Rubin, Y.; Kahr, M.; Knobler, C. B.; Wilkins, L. *J. Am. Chem. Soc.* **1991**, *113*, 495. (b) Diederich, F. In *Modern Acetylene Chemistry;* Stang, P. J., Diederich, F., Eds; VCH: Weinheim, 1995; p 444 and therein cited references. (c) Bunz, U. H. F. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1073.

[3] (a) Hay, A. S. *J. Org. Chem.* **1962**, *27*, 3320. (b) Glaser, C. *Chem. Ber.* **1869**, *2*, 422. (c) Kevelam, H. J.; Jong, K. L.; Meinders, H. C.; Challa, G. *Makromol. Chem.* **1975**, *176*, 1369.

[4] (a) Hauptmann, H. *Tetrahedron Lett.* **1975**, 1931. Hauptmann, H. *Tetrahedron* **1976**, 1293. (b) An, Y.-Z.; Rubin, Y.; Schaller, C.; Mc Elevany, S. W. *J. Org. Chem.* **1994**, *59*, 2927.

[5] *Synthesis of **11a***: Ketone **9a** (680 mg, 3.07 mmol), 2,2-dimethylpropanediol (1.60 g, 15.4 mmol), and *p*-TsOH (583 mg, 3.07 mmol) were refluxed for 18 h in 340 mL of benzene using a Dean−Stark trap. The yellow solution was extracted three times with water/methanol (1:1). Evaporation of the benzene phase and recrystallization from methanol (80 mL, 69 °C → −20 °C) afforded (690 mg, 72%) **10a**. Then **10a** (500 mg, 1.62 mmol), potassium carbonate (ca. 4.0 g), 3 drops of water and methanol (140 mL) were stirred for 90 min at 21 °C. Aqueous workup and crystallization from hexane furnished **11a** (260 mg, 97%; mp 79 °C); ^1H NMR ($CDCl_3$) δ 1.01 (s, 6 H), 2.71 (s, 2 H), 3.74 (s, 4 H); EI-MS m/z 164.3 (M^+), 119.3, 56.4. Anal. Calcd for $C_{10}H_{12}O_2$: C, 73.14; H, 7.36. Found: C, 72.90; H, 7.31.- **11b**: the preparation was analogous to that of **11a**, using **9b** (3.00 g, 9.78 mmol), diol (5.09 g, 48.9 mmol), and TsOH (1.86 g, 9.78 mmol) to afford **10b** (3.34 g, 87%; yellow oil). Deprotection of **10b** (3.00 g, 7.64 mmol) gave **11b** (2.02 g, 83%; colorless oil, bp 95 °C/0.1 mmHg): ^1H NMR ($CDCl_3$) δ 0.86 (s, 3 H), 1.09 (s, 24 H), 2.63 (s, 1 H), 3.59 (d, $J = 11.62$ Hz, 2 H), 3.87 (d, $J = 11.62$ Hz, 2 H); FD-MS m/z 320.2 (M^+). Anal. Calcd for $C_{19}H_{32}O_2Si$: C, 71.19; H, 10.06. Found: C, 69.93; H, 9.84.

[6] (a) Berscheid, R.; Vögtle, F. *Synthesis* **1992**, 58. Vögtle assigns the enhanced yield of cyclizations compared to the classic Eglington conditions to a template effect of the acetonitrile.

[7] **Synthesis of 12**: Alkyne **11b** (2.70 g, 8.42 mmol), $Cu(OAc)_2$ (7.64 g, 42.1 mmol), and 110 mL of acetonitrile were stirred for 6 h at 60 °C. Aqueous workup and crystallization from methanol furnished the bis-TIPS-protected **12** (2.07 g, 77%); the diyne (1.00 g, 1.56 mmol), 6.3 mL of Bu_4NF (1 M in THF), and THF (140 mL) were stirred for 4 h. Aqueous workup yielded **12** (350 mg, 68%; colorless powder, decomp > 160 °C): ^1H NMR ($CDCl_3$) δ 0.96 (s, 6 H), 1.06 (s, 6 H), 2.72 (s, 2 H), 3.68 (d, $J = 11.35$ Hz, 4 H), 3.78 (d, $J = 11.35$ Hz, 4 H); FD-MS m/z 326.4 (M^+). Anal. Calcd for $C_{20}H_{22}O_4$: C, 73.59; H, 6.79. Found: C, 73.44; H, 6.84.

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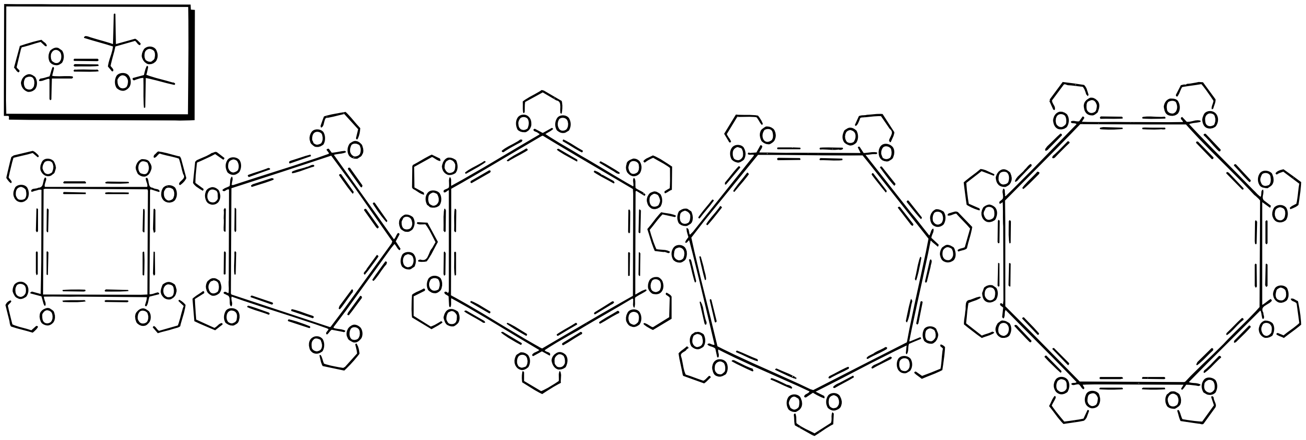
Chart 1



4 **5** **6** **7** **8**

The molecular mass of the cycles was determined by FAB-mass spectroscopy; **4**−**7** gave signals corresponding to their respective molecule ions, while the octamer decomposed in the mass spectrometer. The molecular weights were corroborated by the elution order in the GPC, the largest cycle (either **8** or **7**) eluted first, followed by the smaller ones with increasing amount of eluent. To confirm these results, we grew crystals from **6** suitable for X-ray analysis.[11] While the bond lengths and angles (see Figure 1)[9] are inconspicuous, the exploded cyclohexane is in a perfect chair conformation as is Scotts' and de Meijeres' perspirocyclopropanated hexameric pericyclyne.[10]

All of the cycles are stable under laboratory conditions for days, but decomposition occurrs in a period of weeks. The ^{13}C NMR spectra of **5**−**8** display the expected six signals; the spectra resemble each other and are almost superimposable, while the signals of the butadiyne carbons in the ^{13}C NMR spectrum of **4** show a considerable shift to higher field (0.8−2.4 ppm) in comparison to the analogous resonances of the larger cycles (Table 1).

Table 1. ^{13}C NMR Chemical Shifts of 4−8 and 11^a

cpd	Me	C(Me)2	C≡C	CH$_2$C	C≡C	ketal C
4	22.2	29.9	69.1	73.4	77.2	87.9
5	22.3	29.9	68.3	73.1	74.8	87.2
6	22.3	29.9	68.3	73.1	74.8	87.2
7	22.3	29.9	68.2	73.1	74.7	87.2
8	22.2	29.9	68.2	73.1	74.7	87.1
11a	22.3	29.8	72.5	72.9	78.3	86.3
11b	22.2, 22.7	30.3	72.0, 80.1	72.9	88.2, 100.8	87.1

^{a} CDCl$_3$; Bruker AM 300; 75 MHz; 21 °C.

The reason for this shift is probably due to a slight geometric distortion of the butadiynes in **4** adjusting the bond angles from tetrahedral to 90°, while **5**−**8** can adopt unstrained (*vide supra*) conformations.

Several features about the cyclooligomerizations are worthy of note. (a) We do not observe the formation of a cyclotrimer in this reaction, in variance with the experiments of Scott, who finds (albeit in low yield) trimer (**1**, X = CMe$_2$, n =1), besides tetramer (traces) and pentamer (4.2%) using the shotgun[1] cyclization of 3,3-dimethyl-1,4-pentadiyne. (b) The utilization of ketal **11a** raises the isolated yield of cycles to a respectable 30.6% with **5** and **6** (analogously to Scotts' case) as the most abundant species. The proclivity toward the formation of **6** is even more pronounced in the trimerization reaction of **12** giving rise to a 32.7% yield of the cyclohexamer and a 60% isolated total yield of cycles. What is responsible for the enhanced coupling propensity of **11a** compared to other 3,3-substituted 1,4-pentadiynes[10] is not clear at the moment, but if **11a** is subjected to Hay[3] conditions, formation of larger cycles and higher oligomers with diminished yields of **4**−**8** is observed, suggesting that the method of coupling may be crucial for the success.

In conclusion, we have been able to show that the novel all-oxygen-substituted pericyclynes **4**−**8** are accessible in respectable to good yields using a one-step cyclization approach of the two monomers **11a** and **12**, respectively. Assessment of the material science properties of **4**−**8** and deketalization experiments to the corresponding cyclooxocarbons **2** are underway.

Acknowledgment. We thank Prof. Dr. Klaus Müllen for generous support and the DFG, Volkswagen-Stiftung, and the Fonds der Chemischen Industrie for financial aid. U.H.F.B. is a Liebig (1992−1994) and DFG (1994−1996) scholar. We thank Frank Beer for the GPC separations.

Note Added in Proof. Similar cycles have been prepared and characterized (relatively low yields) by: Boldi, A. M.; Knobler, C. B.; Diederich, F. Unpublished results. Boldi, A. M. Dissertation, UCLA, 1994.

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[8] (a) **Cyclization of 11a**: The diyne (330 mg, 2.01 mmol), Cu(OAc)$_2$ (3.00 g, 16.5 mmol), and acetonitrile (220 mL) were stirred for 3.5 h at 60 °C. Aqueous workup and preparative GPC (two GPC columns directly attached to each other (100 Å, 10 μm, 60 × 2 cm; 500 Å, 10 μm, 60 × 2 cm); eluent chloroform, polystyrene gel as stationary phase; flow rate 7 mL/min, pressure 80 bar; pump system Abimed Analysen Technik, Elutionspumpe M305) yielded the rings **4**−**7**. **4**: ^{1}H NMR (CDCl$_3$) δ 0.98 (s, 24 H), 3.68 (s, 16 H); IR (neat) 2959, 2875, 2165, 1469, 1406, 1163, 1103, 984 cm^{-1}; FAB-MS m/z 648.2 (MH$^+$). Anal. Calcd for $C_{40}H_{40}O_8$: C, 74.05; H, 6.21. Found: C, 74.05; H, 6.23. **5**: ^{1}H NMR (CDCl$_3$) δ 0.99 (s, 30 H), 3.70 (s, 20 H); IR (neat) 2963, 2868, 2158, 1462, 1392, 1165, 1103, 983 cm^{-1}; FAB-MS m/z 811.4 (MH$^+$). Anal. Calcd for $C_{50}H_{50}O_{10}$: C,74.05; H, 6.21. Found: C, 72.89; H, 5.77. **6**: ^{1}H NMR (CDCl$_3$) δ 0.99 (s, 36 H), 3.70 (s, 24 H); IR (neat) 2959, 2875, 2158 1469, 1399, 1165, 1103, 983 cm^{-1}; FAB-MS m/z 974.6 (MH$^+$). Anal. Calcd for $C_{60}H_{60}O_{12}$: C, 74.05; H, 6.21. Found: C, 74.06; H, 6.17. **7**: ^{1}H NMR (CDCl$_3$) δ 0.99 (s, 42 H), 3.71 (s, 28 H); IR (neat) 2960, 2868, 2165, 1469, 1399, 1165, 1103, 983 cm^{-1}; FAB-MS m/z 1135.4 (MH$^+$). Anal. Calcd for $^{C}{}_{70}H_{70}O_{14}$: C, 74.05; H, 6.21. Found: C, 74.80; H, 6.49. (b) **Cyclization of 12**: The diyne **12** (280 mg, 860 μmol), Cu(OAc)$_2$ (2.80 g, 15.4 mmol), and acetonitrile (140 mL) were stirred for 3.5 h at 60 °C. Workup and GPC gave rise to the isolation of **4**, **6,** and **8** (yields *vide supra*). **8**: ^{1}H NMR (CDCl$_3$) δ 1.00 (s, 48 H), 3.71 (s, 32 H); IR (neat) 2967, 2875, 2158, 1468, 1398, 1160, 1103, 983 cm^{-1}. Anal. Calcd for $C_{80}H_{80}O_{16}$: C, 74.05; H, 6.21. Found: C, 74.05; H, 6.23.

[9] Data were collected on a Nonius CAD-4 diffractometer at 194 K. Crystal data of **6**: monoclinic, $P21/c$; a = 16.770(2), b = 9.448(1), and c = 23.187(4) Å, β = 102.57(1)°, Z = 2, D_x = 1.158 g/mL, least-squares refinement based on 4179 obseved reflections with $I > 2\sigma(I)$ led to final values of R = 0.066 and R_w = 0.066. The structure contains 3 mol of toluene per ring, from which one is disordered.

[10] de Meijere, A.; Kozhushkov, S.; Haumann, T.; Boese, R.; Puls, C.; Cooney, M. J.; Scott, L. T. *Chem. Eur. J.* **1995**, *1*, 124 and therein cited references.

[11] The author has deposited atomic coordinates for this structure with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.