

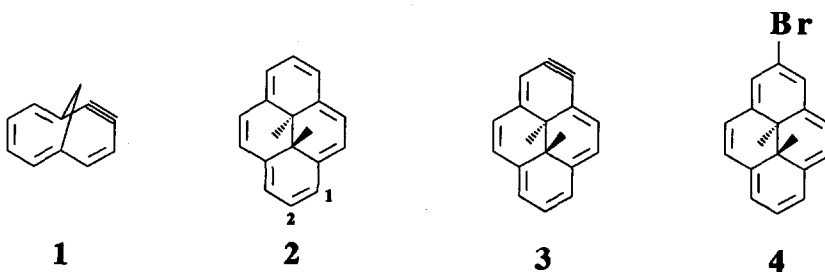
THE SYNTHESIS AND TRAPPING OF THE FIRST [14]ANNULYNE WITH BENZYNE LIKE REACTIVITY. A FAST ROUTE TO SEVERAL ANNELATED BRIDGED ANNULENES.

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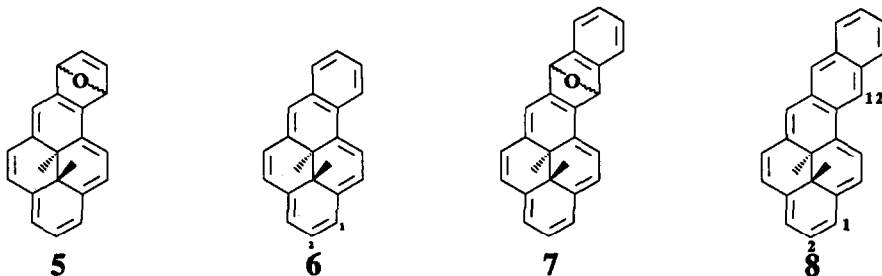
Summary: The macrocyclic "benzyne" **3** was trapped with furan and several annelated furans. The adducts were deoxygenated by $\text{Fe}_2(\text{CO})_9$ in a fast route to yield several new annelated dihydropyrenes. Molecular mechanics calculations indicate that the strain energy of **3** is similar to benzyne.

Whilst benzyne is a well documented and studied reactive intermediate,¹ macrocyclic arynes are rare. Sondheimer and Nakagawa² have described a number of dehydroannulenes with ring sizes from 12-30. However, because the triple bond can be incorporated into the macrocyclic ring without too much strain, none show the reactivity of benzyne. The only larger "annulyne" known with benzyne reactivity is **1**, reported by Boll³ and Vogel.⁴ The exceptional stability and reasonable accessibility of the bridged 14 π annulene, dimethyldihydropyrene **2**, encouraged us to attempt the preparation of the [14]annulyne, **3**. It is of additional interest, in that whilst small ring cycloalkynes have also been extensively studied,⁵ cycloalkenyne are much rarer.⁶ Note that while **3** contains an annulyne perimeter, it also contains a cyclohexenyne ring. The prospect of trapping **3** with furan and several benzannelated isobenzofurans was also appealing, since relatively few arene [a]-annelated derivatives of **2** are known.⁷

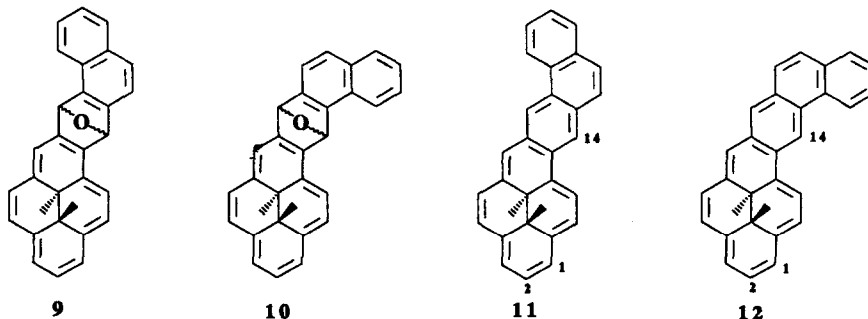


Improved⁸ conversion (80%) of dihydropyrene **2** to the monobromide **4** was achieved using NBS in DMF

at 0°C for 5 minutes. Reaction of 4 with any of *n*-, *t*-, *sec*-butyl or phenyllithium in the presence of furan did not yield any Diels-Alder adduct of 3. However, reaction of bromide 4 with NaNH₂ in the presence of furan did, and a 62% yield of the adducts 5 could be obtained by using five equivalents of amide with a catalytic amount of potassium *t*-butoxide and a large excess of furan in THF at 20°C.⁹ The ¹H nmr spectrum of the adduct indicated that it was a 1:1 mixture of the two isomers of 5 (O on top and O below).¹⁰ Deoxygenation of these was best achieved using one equivalent of Fe₂(CO)₉ in refluxing benzene¹¹ when a 90% yield of the benzannelated annulene 6 was obtained. The previous 4.7% yield 16-step route¹² to 6 has thus been improved to a 19% yield 12-step process via the annulyne 3. Trapping¹³ 3 with isobenzofuran, generated in-situ¹⁴ from 1-methoxyphthalan, gave a 42% yield of the adducts 7, which on deoxygenation as previously gave 70% of the new 2,3-naphthannelated annulene 8, as dark red crystals, mp 182-183°C. Its structure was indicated by its ¹H nmr spectrum¹⁵ in which both the internal methyl protons appeared at δ -0.44, and by an X-ray structure

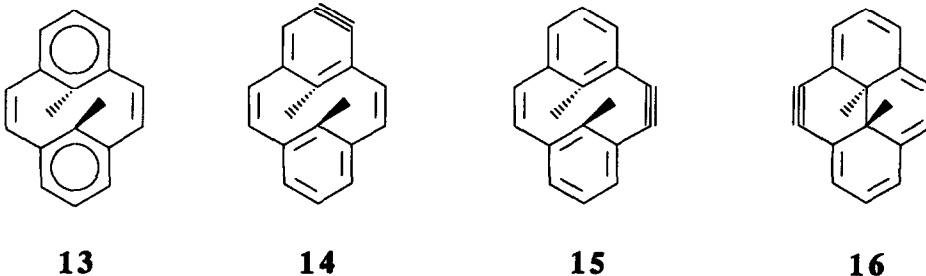


determination.¹⁶ Trapping 3 with naphtho[1,2-*c*]furan¹⁷ gave a 47% yield of a mixture of four adducts 9 (O up,down) and 10 (O up,down) which were directly deoxygenated with Fe₂(CO)₉, as before to yield the two annulenes 11 and 12 in about 45% yield. Although the adducts 9 and 10 were formed in about a 1:1 ratio, the deoxygenation step yielded more of 12 than 11. Deoxygenation also occurs when a large excess of NaNH₂ is used in the original trapping reaction, and under these conditions, the ratio of 11:12 produced is about 1:1. On chromatography over silica gel, 11 travels somewhat more slowly than 12. Crystallization of the later fractions serendipitously produced two types of crystals which could be hand-separated from each other, 12 forming cubes



and 11, needles. While the chemical shift of the internal methyl protons of 12 and 11 were very similar, δ -0.878, -0.882 and -0.896, -0.899 respectively, 12 could be easily distinguished from 11 by its most downfield singlet at δ 9.90 for H-14, which for 11 was at δ 9.03.¹⁸ The structure of 12 was subsequently confirmed by an X-ray determination.¹⁹

No adducts derived from cyclophanedienes could be detected in all of the above reactions. We thought at first that this might be possible, since a valence isomerization exists⁷ between 2 and its cyclophanediene 13. Introduction of the triple bond might change the relative stabilities of 2 and 13. However molecular mechanics calculations²⁰ indicate that the benzyne 14 is more unstable relative to 13 by about 5 kcal/mole, than 3 is relative to 2. Thus on this basis, it seems likely that 3 would valence isomerize to 14 with more difficulty than 2 does to 13, consistent with the absence of any cyclophanediene adducts. MM calculations also indicate that the isomeric cycloalkyne 15 is some 20 kcal/mole more stable than 14, while annulyne 16 has about the same stability as 3. Since isomerization of [e]-fused dihydropyrenes to the cyclophanediene seems much easier⁷ than in the [a]-fused series, trapping of 16 may well lead to derivatives of 15. We are investigating this interesting possibility. MM calculations also indicate that 3 is higher in energy than 2 by about 80 kcal/mole, (ΔH_f), of which about 30 kcal/mole is strain energy. These values are similar for those of benzyne and benzene, 87 and 28 kcal/mole, respectively. These at least seem consistent with the similarity in reactivity between 3 and benzyne.



The chemical shifts of the internal methyl protons of 6, 12 and 8 are -1.62, -0.88 and -0.44 ppm respectively, which is the same order as the most distant (from the annelating ring) protons, H-2, which are at 7.13, 6.86 and 6.66 ppm, respectively, and indicates that the macrocyclic ring current follows the order 6>12>8. This can be correlated with the resonance energies of the annelating rings, and is presented in detail in the accompanying succeeding paper. We thank the Natural Sciences and Engineering Research Council of Canada and the University of Victoria for financial support.²¹

NOTES AND REFERENCES.

1. (a) Hoffman, R. W. *Org. Chem.* 1967, 11, 1-386. (b) Fields, E. K. *Org. Chem.* 1973, 26, 449-508.
2. Balaban, A. T.; Banciu, M.; Ciorba, V. "Annulenes, Benzo-, Hetero-, Homo-Derivatives., CRC Press, Boca Raton, Florida, Vol I-III, 1987.

3. Boll, W. A. *Angew. Chem., Int. Ed. Engl.* 1966, **5**, 733-734.
4. Tanimoto, S.; Schafer, R.; Ippen, J.; Vogel, E. *Angew. Chem., Int. Ed. Engl.* 1976, **15**, 613-614.
5. Krebs, A.; Wilke, J. *Top. Curr. Chem.* 1983, **109**, 189-233.
6. Meier, H.; Hanold, N.; Molz, T.; Bissinger, H. J.; Kolshorn, H.; Zountsas, J. *Tetrahedron* 1986, **42**, 1711-1719.
7. Mitchell, R. H. *Adv. in Theoret. Interesting Molec.* 1989, **1**, 135-199.
8. Mitchell, R. H.; Lai, Y.-H.; Williams, R. V. *J. Org. Chem.* 1979, **44**, 4733-4735.
9. *Typical procedure:* NaNH₂ (63 mg, 1.6 mmol) and *t*-BuOK (5 mg) were added to a solution of bromide **4** (100 mg, 0.32 mmol) and furan (1 mL) in THF (5 mL) under N₂ at 20°C. The mixture was stirred for 6 h, decomposed with MeOH, and the solvent evaporated. The residue was preadsorbed on silica gel, and chromatographed using 1:9 diethyl ether:hexane as eluant. After small amounts of **2** and **4**, product, **5** was eluted, 59 mg (62%). Fractional recrystallization from dichloromethane-heptane, yielded one isomer of **5**, as green crystals, mp 171-173°C, whose internal methyl protons appear at δ -3.34 and -3.51 in its ¹H nmr spectrum.
10. All new compounds were characterized by ¹H and ¹³C nmr, mass, ir and uv spectra, and elemental analyses.
11. Best, W. M.; Collins, P. A.; McCulloch, R. K.; Wege, D. *Aust. J. Chem.* 1982, **35**, 843-848.
12. Mitchell, R. H.; Carruthers, R. J.; Mazuch, L.; Dingle, T. W. *J. Am. Chem. Soc.* 1982, **104**, 2544-2551.
13. *Typical procedure:* NaNH₂ (350 mg, 9 mmol) was added to a soln of 1-methoxyphthalan¹⁴ (1.2 g, 8 mmol) in THF (10 mL) under N₂ at 20°C. After 8 h, bromide **4** (100 mg, 0.32 mmol) and *t*-BuOK (5 mg) was added and workup was carried out as described in note 9 above to yield **7** and some **8**. In this case the isomer of **7** that crystallized, mp 203-204°C, had its internal methyl protons at δ -3.66 and -4.01.
14. (a) Naito, K.; Rickborn, B. *J. Org. Chem.* 1980, **45**, 4061-4062. (b) Crump, S. L.; Netka, J.; Rickborn, B. *J. Org. Chem.* 1985, **50**, 2746-2750.
15. ¹H nmr shifts (360 MHz, CDCl₃, amb.) for H-1 → H-14: (δ) 6.968, 6.659, 6.775, 7.068, 7.177, 7.551, 8.193, 8.008, 7.535, 7.535, 8.054, 8.898, 7.690, 6.814.
16. An attempted X-ray structure determination clearly indicated the carbon skeleton, but would not complete using a least squares refinement to give the hydrogen atoms. The crystal system was orthorhombic, space group Pccn (No. 56), with $a = 24.392 \text{ \AA}$, $b = 23.785 \text{ \AA}$, $c = 6.140 \text{ \AA}$.
17. Moursounidinis, J.; Wege, D. *Aust. J. Chem.* 1988, **41**, 235-249.
18. ¹H nmr spectrum of **11**, (360 MHz, CDCl₃, amb.) shifts for H-1 → H-16: (δ) 7.204, 6.864, 7.027, 7.443, 7.319, 7.877, 9.105, 8.878, 7.718, 7.635, 7.924, 7.776, 7.955, 9.030, 7.954, 7.071; of **12**: 7.215, 6.865, 7.026, 7.313, 7.418, 7.779, 8.306, 7.903, 7.774, 7.926, 7.638, 7.737, 8.984, 9.900, 8.071, 7.101.
19. An attempted X-ray structure determination clearly indicated the carbon skeleton, but would not converge past R=0.13 to give the hydrogen atoms. The crystal system was tetragonal, space group P4₂/n (No. 86), with $a = 17.311 \text{ \AA}$, $b = 17.304 \text{ \AA}$, $c = 13.606 \text{ \AA}$.
20. MMPI type calculations were made using Serena Software's PCMODEL 3 and MMX programs, available from Box 3076, Bloomington, Indiana, USA 47402-3076.
21. Presented at the 72nd Canadian Chemical Conference, Victoria, BC, Canada, June 1989 and the 31st National Organic Symposium of the American Chemical Society, Ithaca, New York, June 1989. Taken from the Ph.D Thesis of P. Zhou, University of Victoria, June 1990.