The Mechanism of Trimerization of Bicyclo[2.2.2]alkynes

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Abstract: Evidence in support of the stepwise mechanism shown in Scheme IV is presented for the formation of aromatic "trimer" **5** from bicycloalkyne **6**. With mono- and dimethyl bridgehead analogues, evidence is presented that each type of intermediate ((α-halovinyl)lithium **2**, bicycloalkyne **6**, dienic vinyllithium **15**, and trienic vinyllithium **16**) lies along the reaction pathway from **1** to **5**. For example, bicycloalkynes **22** and **30** have been intercepted with diphenylisobenzofuran. Bicycloalkyne **22** was trapped in nearly identical yield from regioisomeric precursors **18** and **19**. Changing the solvent from THF to the less polar 5:1 hexanes/THF in the reaction of **1** with butyllithium substantially increased the yield of "dimer" **4** at the expense of "trimer" **5**, presumably due to the decreased solubility of vinyllithium intermediate **15** en route from **1** to **5**. Vinyl chloride **18** and butyllithium gave mainly "dimer" **24** (X = H) and the C_{3h} trimer **25**, the latter presumably formed by further reaction of "dimer" **24'** (X = Li) with bicycloalkyne **22**. In contrast, **19** and butyllithium gave "dimer" **27** (X = H) and the C_s trimer **26**. The bridgehead dimethyl precursor **29** with butyllithium gave diene **32** (X = H) and hexatriene **33** (X = H) but no aromatic trimer because of steric hindrance to ring closure of **33** (X = Li).

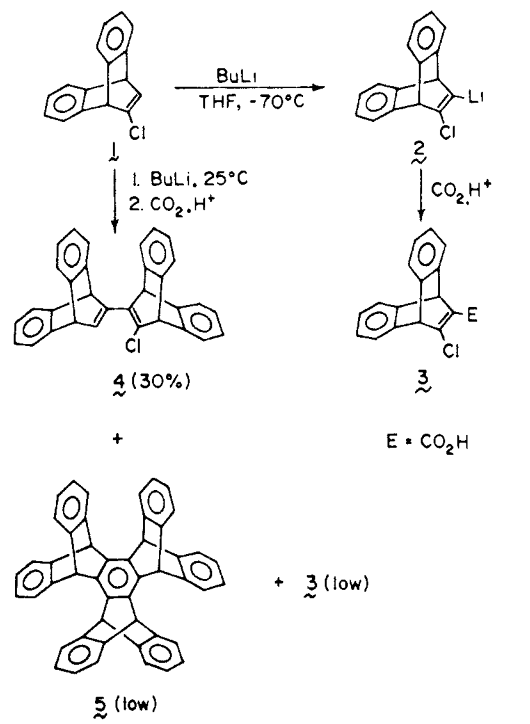
The cyclotrimerization of acetylene to benzene is a reaction that dates from the same era[1] as the Kekulê structure itself.[2] Since then, trimerizations or oligomerizations of alkynes have been accomplished thermally, photochemically, and through a wide variety of metal catalysts,[3] and consequently occur by a variety of mechanisms.

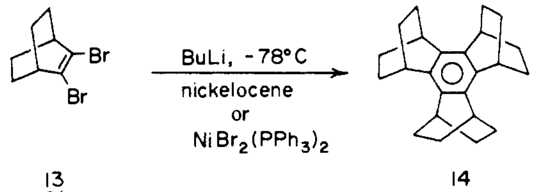
This paper deals with one such trimerization mechanism, the formation of arenes from strained bicycloalkynes generated via (α-halovinyl)lithium intermediates. The first pertinent literature is summarized in Scheme I.[4] Metalation of **1** with butyllithium at −70 °C occurred on the vinyl carbon atom α to the chlorine, as demonstrated by carbonation to give **3** (E = CO_2H). At 25 °C, however, the same sequence gave a much reduced yield of **3**, a 30% yield of the "Fittig type coupling" product **4**, and a low yield of the "structurally fascinating Byzantine" trimer **5**. In a reexamination of this work (using *t*-BuLi at −23 °C) we verified the formation of **2** by quenching to give **3** (E = CO_2H, D, CH_3, Br) and found that adding a solution of **2** to refluxing THF gave **4** (39%) and **5** (20%).[5] If, however, the THF in the latter experiment contained a reactive diene (for example, 2,5-dimethylfuran, 5,5-dimethoxy-1,2,3,4-tetrachlorocyclopentadiene, or 1,3-diphenylisobenzofuran), the product was diverted to a cycloadduct of the presumed intermediate bicycloalkyne **6** (Scheme II).

In a series of somewhat parallel experiments in the more strained bicyclo[2.2.1]heptyl system, Gassman presented evidence for the intermediacy of norbornyne (**12**) (Scheme III).[6] In this instance, however, the presumed intermediate **12** could not be trapped with dienes,[7] although if excess BuLi was used to prepare **10**, butylnorbornenes were formed, presumably through nucleophilic addition to **12**.[6] Interestingly, the bromo analogue of **10** gave the same aromatic trimers when heated in the presence of nickelocene or other metal catalysts but not when only heated.

After the present work was completed, Komatsu reported the preparation of an aromatic trimer (**14**) from **13**[8] and proposed a tentative mechanism for its formation that did not, however, include bicyclo[2.2.2]octyne as an intermediate.

Scheme I





We present here evidence that "trimers" like **5** are produced from lithio intermediate **2** via a stepwise mechanism that involves the intermediacy of bicycloalkynes such as **6**.

Results and Discussion

In view of the trapping of bicycloalkyne **6** with dienes[5] and the isolation of "dimer" **4** in addition to cyclotrimer **5**,[4,5] we adopted as an initial hypothesis for the trimerization mechanism the stepwise sequence shown in Scheme IV.[9] Initially formed bi-

(1) Berthelot, M. *Justus Liebigs Ann. Chem.* **1866**, *139*, 273.
(2) Kekulê, A. *Justus Liebigs Ann. Chem.* **1866**, *137*, 129.
(3) For brief reviews and leading references, see: Hoffmann, R. W. *Dehydrobenzene and Cycloalkynes*; Academic: New York, 1967; pp 350–355. Jäger, V.; Viehe, H. G. In *Methoden der Organischen Chemie (Houben-Weyl)*; Müller, E., Ed.; G. Thieme: Stuttgart, 1977; Vol 5/2a, pp 870–882. Vollhardt, K. P. C. *Acc. Chem. Res.* **1977**, *10*, 1.
(4) Huebner, C. F.; Puckett, R. T.; Brezchfta, M.; Schwartz, S. L. *Tetrahedron Lett.* **1970**, 359.
(5) Hart, H.; Shamouilian, S.; Takehira, Y. *J. Org. Chem.* **1981**, *46*, 4427.
(6) Gassman, P. G.; Gennick, I. *J. Am. Chem. Soc.* **1980**, *102*, 6863. See also: Gassman, P. G.; Valcho, J. J. *J. Am. Chem. Soc.* **1975**, *97*, 4768 and Gassman, P. G.; Atkins, T. J. *Tetrahedron Lett.* **1975**, 3035.
(7) See ref 5, footnote 27.
(8) Komatsu, K.; Akamatsu, H.; Jinbu, Y.; Okamoto, K. *J. Am. Chem. Soc.* **1988**, *110*, 633.

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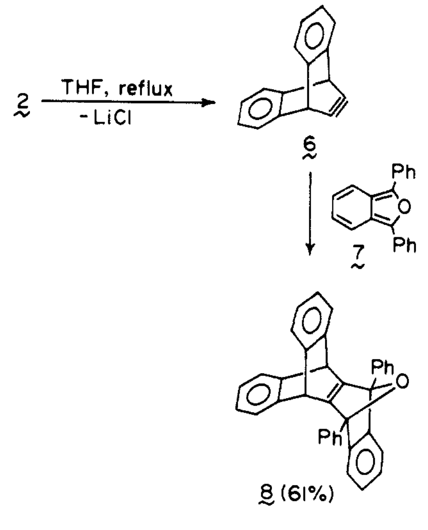
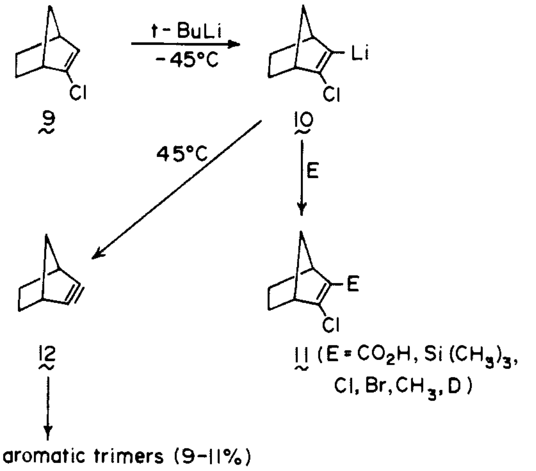
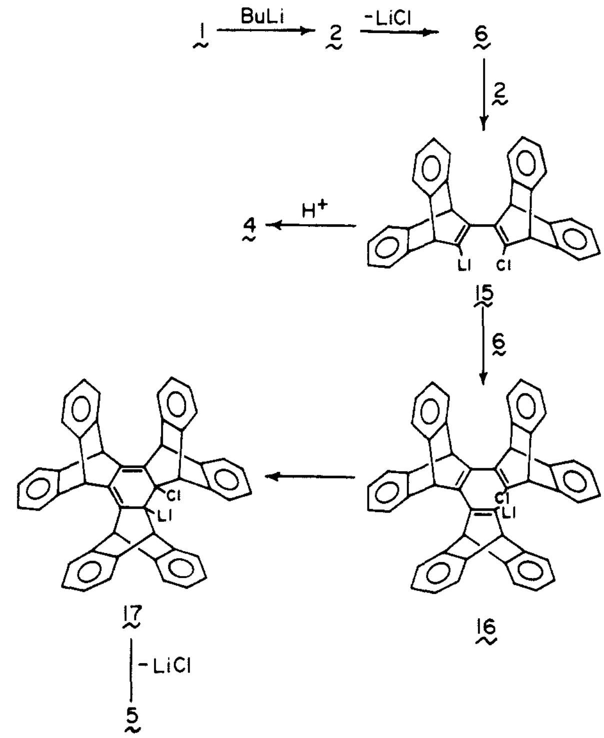
Scheme II



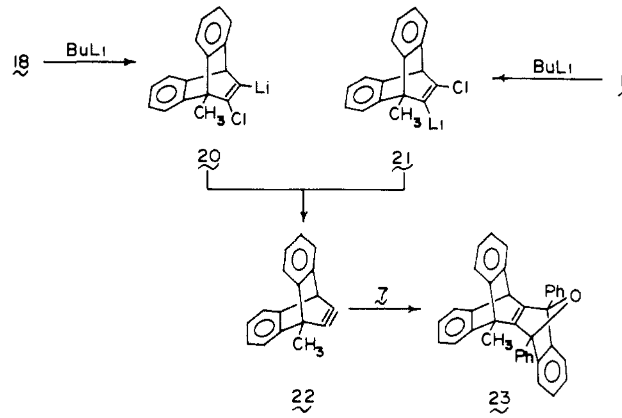
Scheme III



Scheme IV



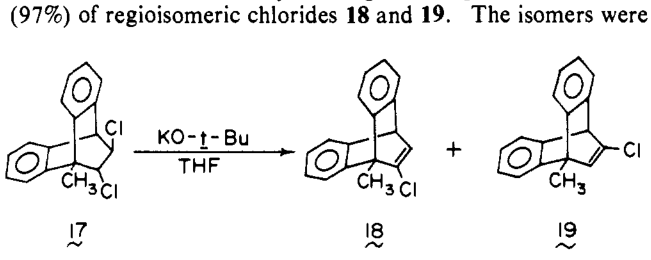
Scheme V



cycloalkyne **6** reacts rapidly with the starting vinyllithium compound **2** to form the "dimeric" organolithium compound **15**. This intermediate may survive and, on aqueous quenching, furnish chloro diene **4**. Alternatively, it may add to a second equivalent of bicycloalkyne **6** to furnish hexatriene **16**. Cyclization of **16** to cyclohexadiene **17** followed by loss of lithium chloride then furnishes the aromatic "trimer" **5**.

In this paper we will present three lines of evidence for the correctness of this scheme. In particular, we will show that two differently substituted precursors generate the same bicycloalkyne intermediate and that "dimeric" and "trimeric" vinyllithiums of the type **15** and **16**, respectively, lie along the pathway to aromatic "trimers" such as **5**.

Additional Evidence for a Bicycloalkyne Intermediate. Reaction of 9-methylanthracene with *trans*-dichloroethylene gave the known adduct **17**,[10] which, on dehydrohalogenation, gave a 1:1 mixture (97%) of regioisomeric chlorides **18** and **19**. The isomers were



separated by fractional crystallization and the structures were distinguished mainly by their ^1H NMR spectra. In one isomer (**18**) the bridgehead and vinyl protons appear as doublets (J = 7 Hz) whereas in the other isomer the long-range coupling between these protons is small (J = 2 Hz).

Treatment of either **18** or **19** and 1,3-diphenylisobenzofuran in THF with BuLi (−78 °C) followed by heating at reflux afforded crystalline adduct **23** in good yield. This experiment shows that a common intermediate, bicycloalkyne **22**, is formed from each precursor (Scheme V). In the next section the trimers derived from **22** will be discussed.

Evidence That "Dimer" Vinyllithiums of the Type 15 Are Intermediates en Route to "Trimer". The earlier studies on the formation of "trimer" **5** from **1** and BuLi used tetrahydrofuran as the solvent. If the mechanism in Scheme IV is correct and **15** is an intermediate en route to **5**,[11] then we reasoned that the formation of **5** might be interrupted by precipitating **15** from the reaction medium by using a less polar solvent than THF. Accordingly, **1** was dissolved in a minimum volume of a 5:1 hexane/THF mixture, treated with BuLi at −78 °C, then warmed, and heated at reflux for 30 min. During the reaction a black

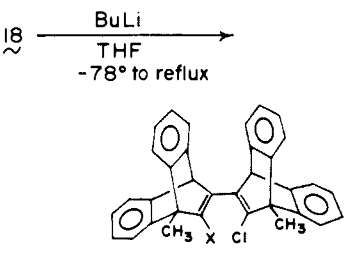
(9) For convenience only, we draw all carbon–lithium bonds as covalent and monomeric.

(10) Cristol, S. J.; Perry, J. S., Jr.; Beckley, R. S. *J. Org. Chem.* **1976**, *41*, 1912.

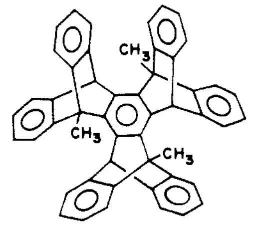
(11) An alternative mechanism could be that **6** is the bifurcation point; it could trimerize thermally to **5** or add **2** to form **15** as an end product.

gummy precipitate formed which decolorized on quenching with methanol. Workup gave a 75–83% yield of **4** and only traces of **5**. This experiment clearly supports the proposal that **15** is an intermediate en route to **5**.

We next carried out trimerization studies on the methyl analogues of **1**, that is **18** and **19**. Treatment of **18** with BuLi in THF at −78 °C, followed by 2 h at room temperature and 30 min at reflux, gave a 3:2 mixture (74% overall yield) of "dimer" **24** (X = H) and "trimer" **25**.

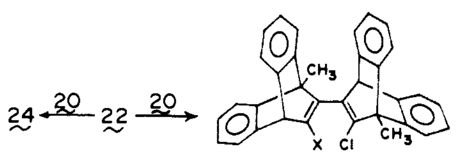


24 (X = H, Li)



25

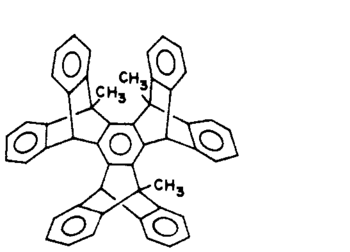
Structure **24** (X = H) is based on spectral data.[12] The bridgehead proton in the chlorine-containing moiety appears as a singlet (δ 4.96) whereas the other bridgehead proton appears as a doublet (δ 4.67, J = 2 Hz) coupled to the vinyl proton at δ 6.14. If Scheme IV is correct, we expect this "dimer" to have either structure **24** or **24′**, since either regioisomer could arise from addition of vinyllithium **20** to cycloalkyne **22**. We can rule out structure **24′** (X = H) for the isolated "dimer" because we would expect it to show a larger coupling constant (J = 5–7 Hz) between the vinyl and bridgehead protons.



24′ (X = H, Li)

The C_{3h} symmetry of "trimer" **25** was evident from its NMR spectra. The methyl protons appeared as a singlet at δ 3.02 (9 H) and the bridgehead protons gave a singlet at δ 6.73 (3 H). The aromatic protons also appeared as two sets of multiplets at δ 6.95 and 7.36 (12 H each). The ^{13}C NMR spectrum of **25** showed single peaks at δ 20.19, 48.70, and 51.82 for the methyl, tertiary bridgehead, and quaternary bridgehead carbons, respectively.

This trimer was contaminated with about 5% of the other possible trimer, **26** (C_s symmetry), as detected by NMR (vide infra).

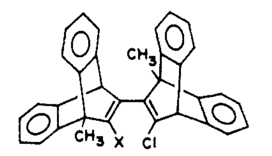


26

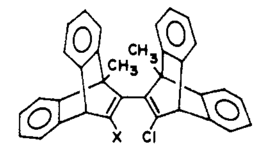
The symmetry of the major trimer **25** requires (if Scheme IV is correct) that it arise from the regioselective addition of **24′** (X = Li) to bicycloalkyne **22**. This addition mode is favored sterically. Indeed, one cannot construct a CPK model of trimer **26** due to steric compression between the opposed bridgehead methyl groups. "Dimer" **24** (X = Li) cannot give the observed "trimer" **25**, but only the trace "trimer" **26**. Consequently it seems reasonable to assume that both **24** (X = Li) and **24′** (X = Li) are formed from the addition of **20** to bicycloalkyne **22** and that **24′** (X = H) is not isolated because its lithio derivative reacts further with additional **22** to give mainly the C_{3h} trimer **25**. The traces of the sterically strained C_s trimer **26** may arise from the addition of either **24** (X = Li) or **24′** (X = Li) to **22**.

To test these ideas further, a 3:1 mixture of **18**/**19** was subjected to the usual trimerization conditions. The products were **24** (X = H, 30%), a second "dimer" (**27**) (X = H, 10%), and a 3:1 mixture of trimers **25**/**26** (total yield 32%).

The new "dimer" must arise from precursor **19** and this conclusion is consistent with the observed 3:1 ratio of **24**/**27**. According to Scheme IV, two structures are possible, **27** or **27′** (X = H). The latter structure can be ruled out from the ^{1}H NMR



27 (X = H, Li)



27′ (X = H, Li)

spectrum, which showed a singlet at δ 4.99 (bridgehead proton adjacent to Cl) and doublets with a small coupling constant (J = 2 Hz) at δ 5.66 (other bridgehead proton) and at δ 6.68 (vinyl proton). Had the structure been **27′** (X = H), the vinyl proton and adjacent bridgehead proton would have appeared as doublets with a much larger J. The formation of **27** instead of **27′** is probably due to steric factors (in the preferred s-trans conformers, **27** is clearly favored, due to severe CH_3–Cl interactions in **27′**).

Trimer **26** could not be separated from trimer **25**, but its ^{1}H NMR spectrum was easily deduced from the mixture. It showed three methyl singlets (δ 2.78, 2.79, 3.02) and three bridgehead singlets (δ 6.02, 6.08, 6.71) as required by the C_s symmetry. Since the trimers were formed in the same ratio (3:1) as that of the precursors **18** and **19**, and since nearly pure C_{3h} trimer was formed from **18** alone, we conclude that the C_s trimer arises predominantly from **19**. This would not be the case if the trimer were formed directly from some sort of thermal trimerization of bicycloalkyne **22**, since we have shown through the trapping experiment (vide supra) that both precursors gave the same bicycloalkyne. Therefore the trimers must arise from further reactions of the dimeric vinyllithium intermediates, as depicted in Scheme IV. Note that reaction of **27** or **27′** (X = Li) with **22** can *only* give the C_s trimer.

Since one bridgehead methyl substituent was insufficient to prevent trimerization, we next studied a precursor with two bridgehead methyl groups.

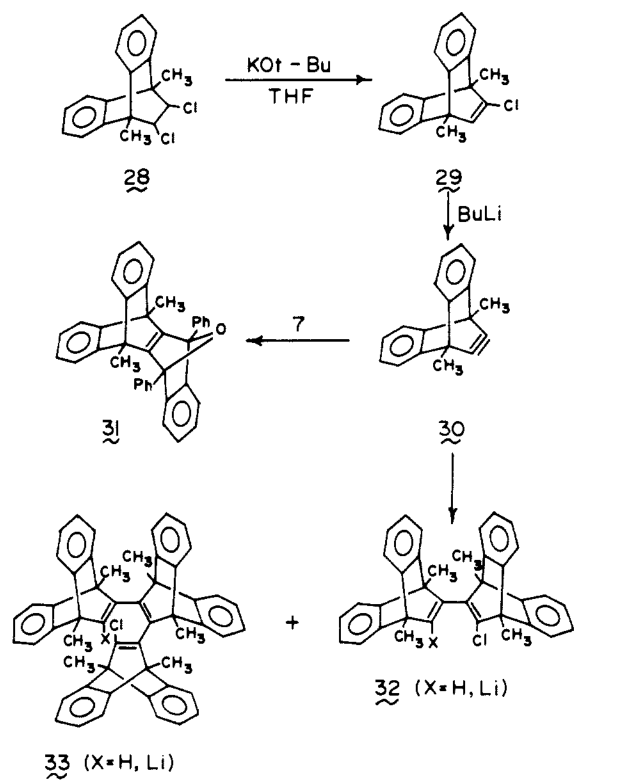
Evidence for the Hexatrienyllithium Type Intermediate 16. Treatment of the known **28**[10] with KO-*t*-Bu in THF gave the desired **29**, the bridgehead dimethyl analogue of **1** (Scheme VI). The structure of **29** was clear from its ^{1}H NMR spectrum (methyl singlets at δ 2.08 and 2.13 and a vinyl proton singlet at δ 6.55).

Treatment of **29** with BuLi in the presence of 1,3-diphenylisobenzofuran (**7**) gave the adduct **31** [methyl proton singlets at δ 1.82; ^{13}C NMR peaks at δ 15.53 (methyls), 51.49 (bridgehead carbons with attached methyls), and 66.65 (oxygen-bridged carbons)], showing that the intermediate bicycloalkyne **30** is formed.

In the absence of a trap for **30**, the products were the "dimer" **32** (X = H, 26%) and the hexatriene **33** (X = H, 11%). The mass spectrum of **32** (X = H) showed an M^+ peak, and its ^{1}H NMR spectrum showed four separate methyl proton singlets (δ 1.38, 1.44, 2.05, 2.09) and one vinyl proton singlet (δ 6.07), as required. The mass spectrum of **33** (X = H) did not show an M^+ peak, but had a base peak corresponding to 9,10-dimethylanthracene. The ^{1}H NMR spectrum of **33** showed six methyl singlets (δ 1.28, 1.33,

(12) Although drawn as s-cis for convenience, these "dimeric" dienes most likely prefer the s-trans conformation. The s-cis conformation is accessible, however, as shown by the formation of cycloadducts with various dienophiles (unpublished results).

Scheme VI

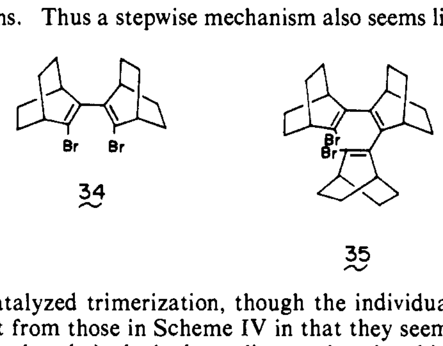


1.51, 1.58, 1.79, 1.82) and one vinyl singlet (δ 5.96) as required, and the ^{13}C NMR spectrum was also consistent with the assigned structure.

The isolation of **33** (X = H) strongly supports the final steps in the mechanism shown in Scheme IV. Clearly the bridgehead methyl substituents in **33** (X = Li) prevent its cyclization to an aromatic "trimer".

In summary, the evidence presented here, though admittedly circumstantial, strongly supports the stepwise mechanism in Scheme IV; that is, supporting evidence now exists for each of the major types of intermediates: **2**, **6**, **15**, and **16**. A similar mechanism has also been proposed for the trimerization to triphenylenes of benzynes produced from *o*-lithiohaloarenes.[13]

Finally, it should be mentioned that in the recently reported nickel-catalyzed trimerization of **13** to **14**, Komatsu[8] has isolated "dimeric" and "trimeric" intermediates **34** and **35**, respectively, and shown that **35** can be converted to **14** under the reaction conditions. Thus a stepwise mechanism also seems likely in this



metal-catalyzed trimerization, though the individual steps are different from those in Scheme IV in that they seem to involve metal-catalyzed vinyl–vinyl couplings rather than bicycloalkyne intermediates.[14]

(13) See ref 3 (Hoffmann), pp 109–111. The final step in this mechanism (loss of LiX) may be somewhat different from that shown in Scheme IV. It may involve a nucleophilic addition of the aryllithium moiety to the halogen-bearing ring instead of a hexadiene–cyclohexatriene cyclization, since in the triphenylene synthesis this latter mechanism would involve disruption of the aromaticity in all three benzenoid rings.

(14) No trapping experiments designed to detect a bicycloalkyne intermediate were reported in the preliminary communication.

Experimental Section

General Procedures. NMR spectra were recorded on a Brucker WM 250-MHz spectrometer using $CDCl_3$ as the solvent and $(CH_3)_4Si$ as the internal reference. IR spectra were determined on a Perkin-Elmer 167 spectrometer. Mass spectra were measured at 70 eV with a Finnigan 4000 spectrometer with the INCOS data system (operated by Ernest Oliver or Richard Olson). High-resolution mass spectra were obtained with a JEOL HX110 HF spectrometer at the Michigan State University Mass Spectrometry Facility. Melting points were determined with an electrothermal melting point apparatus (Fisher Scientific) or with a Thomas-Hoover melting point apparatus and are uncorrected. All chromatography was carried out over silica gel (230–400 mesh). Microanalyses were performed by Spang Microanalytical Laboratory, Eagle Harbor, MI.

11- and 12-Chloro-9-methyl-9,10-etheno-9,10-dihydroanthracenes (18 and 19). To a solution of 5.8 g (20 mmol) of 11,12-dichloro-9-methyl-9,10-ethano-9,10-dihydroanthracene (17)[10] in 125 mL of THF was added 3.0 g (excess) of potassium *tert*-butoxide. The mixture was heated at reflux for 12 h. The solvent was removed (rotavap) and the brown, oily residue was taken up in ether, washed with water, and saturated sodium chloride solution, and dried ($MgSO_4$). Evaporation of the solvent and chromatography of the residue using hexanes as the eluent gave 4.8 g (94%) of a 1:1 mixture (NMR) of **18** and **19**. The two isomers were separated by fractional recrystallization from hexanes as follows. A concentrated solution of the mixture was allowed to stand in a refrigerator for 3–5 days, during which time crystallization occurred. The cold solution was diluted with hexanes, and the collected crystals were enriched in **18**, which was further purified by recrystallization from hexanes. The second isomer **19** was purified by removing the hexanes from the mother liquor (rotavap) and recrystallizing the residue from methanol. For **18**: mp 132–133 °C; ^1H NMR ($CDCl_3$) δ 2.15 (s, 3 H), 5.01 (d, 1 H), 6.93 (d, 1 H), 6.97 (m, 4 H), 7.28 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 15.30, 50.90, 58.57, 120.40, 122.85, 124.69, 125.30, 136.90, 145.30, 145.91, 147.34; mass spectrum, *m/e* (relative intensity) 252 (13), 218 (17), 217 (100), 215 (25), 202 (34), 120 (26), 108 (17). Anal. Calcd for $C_{17}H_{13}Cl$: C, 80.82; H, 5.14. Found: C, 80.77; H, 5.16. For **19**: mp 108–109 °C; ^1H NMR ($CDCl_3$) δ 2.20 (s, 3 H), 4.94 (s, 1 H), 6.41 (s, 1 H), 7.00 (m, 4 H), 7.28 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 13.75, 51.25, 53.45, 120.85, 123.16, 124.58, 125.21, 134.54, 146.45, 147.50, 147.91; mass spectrum, *m/e* (relative intensity) 252 (23), 218 (18), 217 (100), 216 (20), 215 (29), 202 (51), 192 (16). Anal. Calcd for $C_{17}H_{13}Cl$: C, 80.82; H, 5.14. Found: C, 80.86; H, 5.12.

Trapping Bicycloalkyne 22. To a solution of **18** (0.5 g, 2 mmol) and 1,3-diphenylisobenzofuran (1.0 g, 4 mmol) in 25 mL of anhydrous THF under argon at −78 °C was added dropwise 0.9 mL (1.1 equiv) of 2.5 M *n*-BuLi in hexanes. The mixture was warmed to room temperature, stirred (2 h), heated at gentle reflux for 30 min, and then quenched with methanol (1 mL). The solvent was removed (rotavap) and the residue was taken up in ether (100 mL). The ether solution was washed successively with water and saturated sodium chloride solution and dried ($MgSO_4$). Evaporation of the solvent and chromatography of the residue on a preparative TLC plate (silica gel, 1 mm) using 1:2 hexanes/methylene chloride gave 0.57 g (59%) of **23**, which was recrystallized from ether/hexanes: mp 259–260 °C; ^1H NMR ($CDCl_3$) δ 1.65 (s, 3 H), 5.24 (s, 1 H), 6.26 (d, 1 H), 6.72 (m, 3 H), 6.96 (m, 7 H), 7.09 (d, 2 H), 7.15 (m, 2 H), 7.27 (d, 1 H), 7.42 (m, 2 H), 7.58 (m, 3 H), 7.73 (d, 1 H); ^{13}C NMR ($CDCl_3$) δ 18.71, 50.60, 51.78, 65.52, 120.40, 122.65, 124.89, 126.66, 127.47, 127.72, 128.03, 128.37, 129.10, 129.48, 130.25, 131.94, 132.54, 133.41, 140.34, 141.28, 142.68, 143.61, 146.12; mass spectrum, *m/e* (relative intensity) 487 (35), 486 (98), 472 (10), 471 (17), 409 (35), 294 (28), 265 (88), 194 (30), 192 (100), 191 (59). Anal. Calcd for $C_{37}H_{26}O$: C, 91.32; H, 5.38. Found: C, 91.26; H, 5.33.

An identical reaction, but with **19** in place of **18**, gave **23** in 57% yield.

Improved Yield of 4 from 1. To a suspension of 9.55 g (40 mmol) of 11-chloro-9,10-dihydro-9,10-ethenoanthracene (**1**) in 100 mL of anhydrous hexanes and 20 mL of anhydrous THF under argon at −78 °C was added dropwise 18 mL (45 mmol) of 2.5 M *n*-butyllithium in hexanes. The mixture was brought to room temperature, stirred vigorously for 2 h, heated at reflux for 30 min, and then allowed to cool to room temperature. Water (50 mL) was slowly added, followed by 200 mL of methylene chloride. The aqueous layer was discarded. The organic layer was washed with saturated sodium chloride solution and dried ($MgSO_4$). Removal of the solvent and chromatography of the residue using a 1:5 mixture of methylene chloride/hexanes as eluent gave 6.95 g (78%) of 3-chloro-1,4,1′,4′-tetrahydro-1,4:1′,4′-di-*o*-benzeno-2,2′-binaphthyl (**4**) as a white solid, mp 268 °C (lit.[4] mp 268 °C).

Trimerization of 18. To a solution of 0.5 g (2 mmol) of **18** in 25 mL of anhydrous THF under argon at −78 °C was added dropwise 1.0 mL (1.1 equiv) of 2.2 M *n*-butyllithium in hexanes. The mixture was warmed to room temperature, stirred for 2 h, heated at reflux for 30 min, and then quenched with methanol (1 mL). The solvent was removed (rotavap) and the residue dissolved in methylene chloride, washed with water and saturated brine, and dried ($MgSO_4$). Evaporation of the solvent and chromatography of the dark brown residue using 4:1 hexanes/methylene chloride as eluent gave 0.14 g (46%) of **24** (X = H) and 0.12 g (28%) of **25**. For **24** (X = H): mp 209–210 °C; ^1H NMR ($CDCl_3$) δ 1.62 (s, 3 H), 2.11 (s, 3 H), 4.67 (d, 1 H), 4.94 (s, 1 H), 6.14 (d, 1 H), 6.98 (m, 8 H), 7.23 (m, 8 H); ^{13}C NMR ($CDCl_3$) δ 14.30, 15.39, 49.82, 52.71, 53.68, 55.76, 119.96, 120.49, 122.78, 123.40, 124.28, 124.72, 125.07, 140.36, 141.10, 145.51, 145.59, 146.92, 148.36, 150.04; mass spectrum, *m/e* (relative intensity) 470 (1), 468 (4), 433 (3), 256 (3), 217 (11), 215 (12), 192 (100), 191 (28), 178 (30). Anal. Calcd for $C_{34}H_{25}Cl$: C, 87.10; H, 5.33. Found: C, 86.96; H, 5.30. For **25**: mp >500 °C; ^1H NMR ($CDCl_3$) δ 3.02 (s, 9 H), 6.73 (s, 3 H), 6.95 (m, 12 H), 7.36 (m, 12 H); ^{13}C NMR ($CDCl_3$) δ 20.19, 48.70, 121.72, 123.48, 125.74, 146.21, 148.30; mass spectrum, *m/e* (relative intensity) 649 (30), 648 (95), 633 (43), 456 (21), 441 (29), 426 (28), 262 (16), 191 (76), 85 (100). Anal. Calcd for $C_{51}H_{36}$: C, 94.45; H, 5.55. Found: C, 94.33; H, 5.51.

Trimerization of a 3:1 Mixture of 18/19. The procedure is similar to that described for the trimerization of **18**. To 5.1 g (20 mmol) of a 3:1 mixture of **18/19** in 100 mL of THF (argon, −78 °C) was added 8.8 mL (1.1 equiv) of 2.5 M *n*-BuLi in hexanes. The mixture was stirred (1 h), brought to room temperature, heated at reflux (2 h), and worked up as before. Chromatography gave 3.4 g of a mixture of **24–27**. A 0.5-g sample of this mixture was subjected to preparative TLC (silica gel, 1.0 mm) using 4:1 hexanes/methylene chloride as eluent to afford 0.21 g (30%) of **24** (X = H), 0.07 g (10%) of **27** (X = H), and 0.22 g (32%) of a 3:1 mixture of **25/26**. For **27**: mp 259–261 °C; ^1H NMR ($CDCl_3$) δ 2.14 (s, 3 H), 2.16 (s, 3 H), 4.99 (s, 1 H), 5.66 (d, 1 H), 6.68 (d, 1 H), 6.91 (m, 8 H), 7.20 (m, 8 H); ^{13}C NMR ($CDCl_3$) δ 15.45, 15.66, 50.47, 53.53, 56.26, 58.94, 120.28, 120.69, 123.43, 123.54, 124.57, 124.66, 125.16, 125.49, 141.63, 142.36, 144.72, 146.28, 147.33, 147.78, 147.87, 148.10, 148.72; mass spectrum, *m/e* (relative intensity) same as for **24**. Anal. Calcd for $C_{34}H_{25}Cl$: C, 87.10; H, 5.33. Found: C, 87.04; H, 5.38. For **26**: ^1H NMR (deduced from the spectrum of the mixture with **25**) δ 2.78 (s, 3 H), 2.79 (s, 3 H), 3.02 (s, 3 H), 6.02 (s, 1 H). 6.08 (s, 1 H), 6.71 (s, 1 H), and peaks in the aromatic region.

11-Chloro-9,10-dimethyl-9,10-etheno-9,10-dihydroanthracene (29). To a solution of 6.1 g (20 mmol) of 11,12-dichloro-9,10-dimethyl-9,10-ethano-9,10-dihydroanthracene (**28**)[10] in 125 mL of THF was added 3.0 g (excess) of potassium *tert*-butoxide. The mixture was heated at reflux for 16 h. The solvent was removed (rotavap), and the residue was taken up in ether, washed with water and saturated sodium chloride solution, and dried ($MgSO_4$). Evaporation of the solvent and chromatography of the oily residue using hexanes as eluent gave 4.9 g (91%) of **29** as a white solid: mp 106–107 °C; ^1H NMR ($CDCl_3$) δ 2.08 (s, 3 H), 2.12 (s, 3 H), 6.55 (s, 1 H), 6.99 (m, 4 H), 7.24 (m, 4 H). Anal. Calcd for $C_{18}H_{15}Cl$: C, 81.04; H, 5.66. Found: C, 81.05; H, 5.53.

Trapping of Bicycloalkyne 30. To a solution of 0.54 g (2 mmol) of **29** and 0.60 g (2.2 mmol) of 1,3-diphenylisobenzofuran in 25 mL of anhydrous THF at −78 °C under argon was added dropwise 1.0 mL (1.1 equiv) of 2.2 M *n*-butyllithium in hexanes. The mixture was stirred for 2 h, brought to room temperature, and heated at reflux for another 2 h. The cooled reaction mixture was quenched with a small amount of methanol and the solvent was removed. The residue was taken up in methylene chloride, washed with water and saturated sodium chloride solution, and dried ($MgSO_4$). Evaporation of the solvent and chromatography of the residue using 2:1 hexanes/methylene chloride as eluent gave 190 mg (19%) of **31** as a white solid: mp 306–308 °C; ^1H NMR ($CDCl_3$) δ 1.82 (s, 6 H), 6.64 (m, 4 H), 6.75 (q, 2 H), 7.11 (m, 4 H), 7.31 (q, 2 H), 7.43 (m, 6 H), 7.73 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 15.53, 51.49, 66.65, 120.83, 123.12, 124.79, 125.22, 125.41, 129.10, 130.00, 130.93, 135.27, 148.10, 149.59, 150.83; mass spectrum, *m/e* (relative intensity) 501 (2), 500 (6), 396 (5), 395 (15), 365 (8), 194 (10), 270 (100), 105 (35). Anal. Calcd for $C_{38}H_{28}O$: C, 91.16; H, 5.63. Found: C, 91.11; H, 5.61.

Attempted Trimerization of 29. Formation of Diene 32 and Triene 33. To a solution of 1.35 g (5 mmol) of **29** in 50 mL of anhydrous THF at −78 °C under argon was added dropwise 2.2 mL (1.1 equiv) of 2.5 M *n*-butyllithium in hexanes. The mixture was stirred for 1 h, brought to room temperature, heated at reflux for 2 h, and then cooled, and methanol (1 mL) was added. The solvent was removed (rotavap) and the dark brown residue was taken up in methylene chloride. The methylene chloride solution was washed with water and saturated sodium chloride solution and dried ($MgSO_4$). Evaporation of the solvent and chromatography of the residue using 3:1 hexanes/methylene chloride gave **32** and **33** as the major products.

For **32** (X = H): 320 mg (26%), mp 263–264 °C; ^1H NMR ($CDCl_3$) δ 1.38 (s, 3 H), 1.44 (s, 3 H), 2.05 (s, 3 H), 2.09 (s, 3 H), 6.07 (s, 1 H), 7.07 (m, 16 H); ^{13}C NMR ($CDCl_3$) δ 13.90, 14.74, 15.33, 15.83, 49.49, 52.55, 52.64, 119.84, 120.11, 120.60, 124.29, 124.83, 125.20, 142.49, 145.11, 149.48, 150.02, 151.04; mass spectrum, *m/e* (relative intensity) 498 (0.3), 497 (0.3), 496 (0.9), 373 (1.2), 207 (19), 206 (100), 191 (14). Anal. Calcd for $C_{36}H_{29}Cl$: C, 87.02, H, 5.83. Found: C, 86.95; H, 5.86.

For **33** (X = H): 130 mg (11%), mp 378–380 °C; ^1H NMR ($CDCl_3$) δ 1.28 (s, 3 H), 1.33 (s, 3 H), 1.51 (s, 3 H), 1.58 (s, 3 H), 1.79 (s, 3 H), 1.82 (s, 3 H), 5.96 (s, 1 H). 6.91 (m, 24 H); ^{13}C NMR ($CDCl_3$) δ 45.38, 47.85, 48.59, 49.81, 50.59, 52.11, 123.17, 123.96, 124.21, 124.67, 125.36, 126.37, 126.66, 127.20, 128.92, 130.75, 140.16, 142.04, 143.37, 144.01, 144.54; no mass spectrum could be obtained. Anal. Calcd for $C_{54}H_{43}Cl\cdot H_2O$: C, 86.37; H, 5.80. Found: C, 86.28; H, 5.77.

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Allosteric Cooperativity and Transport: Studies in a Circulating System

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Abstract: A model system is used to probe the effects of binding cooperativity on transport. The system involves a crown ether which transports $Hg(SCN)_2$ through a solvent circulating between two solid phases. It is shown that the positive cooperativity exhibited by the carrier reduces transport effectiveness. This appears to be due to the slower release rate of the cooperative ligand. The model system is contrasted with hemoglobin-mediated O_2 transport.

Biochemical systems continue to provide a rich source of inspiration for bioorganic modeling, with good reason. Phenomena such as catalysis, regulation, transport, and recognition are so exotic that they were once believed to be unique properties of molecules the size of proteins and nucleic acids. Moreover, their names bear little structural information. The model builders have had surprising success in imagining which structural features are required for such behavior. These have been engineered into molecules that are synthetically accessible, and such structures can now perform many of these functions. Regulation—in the form of allostery—is one of the phenomena that has been much

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