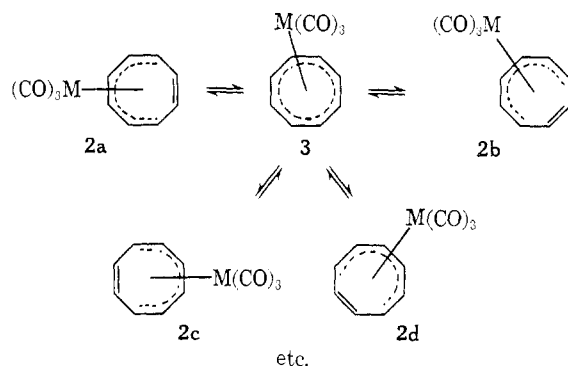


what then can be the explanation of the observed uniform line broadening?

We propose that the rearrangement process is that shown in Scheme I. This involves a symmetrical

Scheme I



“piano-stool” intermediate, **3**, with the metal atom lying over the center of a flat (or nearly flat) octagonally (or nearly) symmetric C_8H_8 ring. In terms of bonding this is a credible intermediate, since the metal atom could still serve as an acceptor of six π electrons, a pair of electrons in a low-lying totally symmetric π MO being left as essentially nonbonding. In terms of accessibility from the ground state configuration, **3** is also satisfactory, since, in the ground state,^{7,8} the metal atom already lies rather close to the central point that will arise as the ring becomes flat and only the two carbon atoms which form the “uncoordinated” double bond need move very much as the other six are already essentially coplanar.

Obviously, one is immediately led to ask why this pathway applies for compounds **2** but not for **1**. The answer, we believe, lies in the steric effect of the four methyl groups upon a planar ring. The planar ring must be appreciably destabilized by repulsive forces upon the introduction of four methyl groups in place of four hydrogen atoms. It is possible to estimate the extent of this destabilization semiquantitatively by referring to the studies of bond shift in cyclooctatetraene⁹ and 1,3,5,7-tetramethylcyclooctatetraene.¹⁰ The bond shift processes are believed to require passage through planar transition states. For C_8H_8 the free energy of activation is <13.7 kcal mol⁻¹ whereas for 1,3,5,7-(CH₃)₄C₈H₄ it is 21.5 ± 2.0 kcal mol⁻¹. Such a difference, *ca.* 8 kcal mol⁻¹, could easily explain why a $C_8H_8M(CO)_3$ compound would undergo rearrangement by a process involving a planar ring in the transition state while the tetramethyl analog would execute a different process in which the planar ring is not required.

Finally, we note that scrambling of the CO groups occurs with a lower activation energy and is therefore necessarily independent of the rearrangement just discussed. It has very similar characteristics to those observed for the comparable process in $C_7H_8Mo(CO)_3$.¹¹ Up to -37° there are sharp signals at 228.2 and 213.4 ppm in an intensity ratio of 1:2. These collapse and give a single broad resonance at 16° ; the coalescence

(9) F. A. L. Anet, *J. Amer. Chem. Soc.*, **84**, 672 (1962); F. A. L. Anet, A. J. R. Bourn, and Y. S. Lin, *ibid.*, **86**, 3576 (1964).

(10) P. Ganis, A. Musco, and P. A. Temussi, *J. Phys. Chem.*, **73**, 3201 (1969).

(11) C. G. Kreiter and M. Lang, *J. Organometal. Chem.*, **55**, C27 (1973).

temperature is $0 \pm 10^\circ$. These studies are being extended to similar molecules.¹²

(12) This work was supported in part by the National Science Foundation under Grant No. 33142X.

(13) On leave from the University of Zaragoza, Spain, under the auspices of the Program of Cultural Cooperation between the United States of America and Spain.

F. A. Cotton,* D. L. Hunter, P. Lahuerta¹³

Department of Chemistry, Texas A&M University
College Station, Texas 77843

Received March 8, 1974

A Synthesis of Cembrene. A 14-Membered Ring Diterpene

Sir:

We wish to describe a total synthesis of cembrene (**1**), 1-isopropyl-4,8,12-trimethylcyclootetradeca-2,4,7,11-tetraene, a monocyclic diterpene hydrocarbon structure of increasing importance in nature.^{1,2} Cembrene was the first example of a rapidly expanding group of diterpenes which contain a 14-membered ring,³ including neocembrene which is a scent-trail pheromone for termites in Australia (*Nasutitermes xitiosus*).⁴ Furthermore, the bicyclic derivatives, such as verticillol from a conifer,⁵ eunicellin from Atlantic coral,⁶ and those diterpenes of the taxane type⁷ may also be re-

(1) (a) W. G. Dauben, W. E. Thiessen, and P. R. Resnick, *J. Org. Chem.*, **30**, 1693 (1965); *J. Amer. Chem. Soc.*, **84**, 2015 (1962); (b) H. Kobayashi and S. Akiyoshi, *Bull. Chem. Soc. Jap.*, **36**, 823 (1963).

(2) Cembrene from (a) pine trees, N. T. Mirov "The Genus Pinus," The Ronald Press, New York, N. Y., 1967; R. Teranishi and W. G. Dauben, unpublished results; S. Akiyoshi, *Imp. Ind. Res. Inst. Rept.*, *Jap.*, **17**, 1 (1931); P. M. Oloff, Jr., and N. T. Mirov, *Amer. Pharm. Ass. J. Sci. Ed.*, **45**, 77 (1956); N. T. Mirov, *U. S. Dep. Agr., Tech. Bull.*, No. 1239 (1961); V. A. Pentegova and N. K. Kashtanova, *Khim. Prir. Soedin.*, **1**, 223 (1965). (b) Fir tree, H. Erdtman, B. Kimland, T. Norin, and P. J. L. Daniels, *Acta Chem. Scand.*, **22**, 938 (1968). (c) Larch tree, E. N. Shmidt, A. I. Lisina, and V. A. Pentegova, *Sin. Prod. Kanifidi Skipidara, Tr. Vses. Nauch.-Tekhn. Soveshch.*, 326 (1964). (d) Order cupressals, Y. Fujise, I. Maruta, S. Ito, and T. Nozoe, *Chem. Pharm. Bull.*, **12**, 991 (1964).

(3) (a) From tobacco and tobacco smoke: D. L. Roberts and R. L. Rowland, *J. Org. Chem.*, **27**, 3989 (1962); A. Rodgman and L. C. Cook, *Tobacco Sci.*, **7**, 151 (1963); R. L. Rowland and D. L. Roberts, *J. Org. Chem.*, **28**, 1165 (1963); R. L. Rowland, A. Rodgman, J. N. Schmacher, D. L. Roberts, L. C. Cook, and W. F. Walker, Jr., *ibid.*, **29**, 16 (1964). (b) Pine trees: N. K. Kashtanova, A. I. Lisina, and V. A. Pentegova, *Khim. Prir. Soedin.*, **4**, 52 (1968); **5**, 10 (1969); A. I. Lisina, A. I. Rezvukhin, and V. A. Pentegova, *ibid.*, **1**, 250 (1965); V. A. Raldugin, N. K. Kashtanova, and V. A. Pentegova, *ibid.*, **7**, 604 (1971); B. Kimland and T. Norin, *Acta Chem. Scand.*, **22**, 943 (1968); V. A. Raldugin and V. A. Pentegova, *Khim. Prir. Soedin.*, **1**, 669 (1971). (c) Frankincense resin: S. Corsano and R. Nicoletti, *Tetrahedron*, **23**, 1977 (1967); M. L. Forcelles, R. N. Coletti, and C. Santarelli, *Tetrahedron Lett.*, 3783 (1973). (d) Corals: A. J. Weinheimer, R. E. Middlebrook, J. Bledsoe, Jr., W. E. Marsico, and T. K. B. Karns, *Chem. Commun.*, 384 (1968); M. Bilayet Hossain, A. F. Nicholas, and D. van der Helm, *Chem. Commun.*, 385 (1968); A. J. Weinheimer, R. A. Gross, Jr., T. K. B. Karns, and L. S. Ciereszko, 1973 American Chemical Society Pacific Conference on Chemistry and Spectroscopy, paper No. 67; F. J. Schmitz, D. J. Vanderak, and L. S. Ciereszko, *J. Chem. Soc., Chem. Commun.*, 407 (1974). (e) Miscellaneous sources: H. Immer, J. Polonsky, R. Toubiana, and Ho Dac An, *Tetrahedron*, **21**, 2117 (1965).

(4) (a) From termites: A. J. Birch, W. V. Brown, J. E. T. Corrie, and B. P. Moore, *J. Chem. Soc., Perkin Trans. I*, 2653 (1972). (b) Commiphora Mukul (Guggulu oil): V. D. Patil, U. R. Nayak, and S. Dev, *Tetrahedron*, **29**, 341 (1973). (c) Pine trees: E. N. Shmidt, N. K. Kashtanova, and V. A. Pentegova, *Khim. Prir. Soedin.*, **6**, 694 (1970).

(5) H. Erdtman, T. Norin, M. Sumimoto, and A. Morrison, *Tetrahedron Lett.*, 3879 (1964).

(6) O. Kennard, D. G. Watson, L. Riva di Sanseverino, B. Tursch, R. Bosmons, and C. Djerassi, *Tetrahedron Lett.*, 2879 (1968).

(7) (a) M. C. Wani, H. L. Taylor, M. E. Wall, P. Coggon, and A. T. McPhail, *J. Amer. Chem. Soc.*, **93**, 2325 (1971); (b) D. P. Della Casa de Marcano, T. G. Halsall, E. Castellano, and O. J. R. Hodder, *Chem.*

lated to cembrene on biogenetic grounds. Synthetically, cembrene offered a number of challenges including the preparation of a 14-membered ring with the correct stereochemistry for four double bonds.

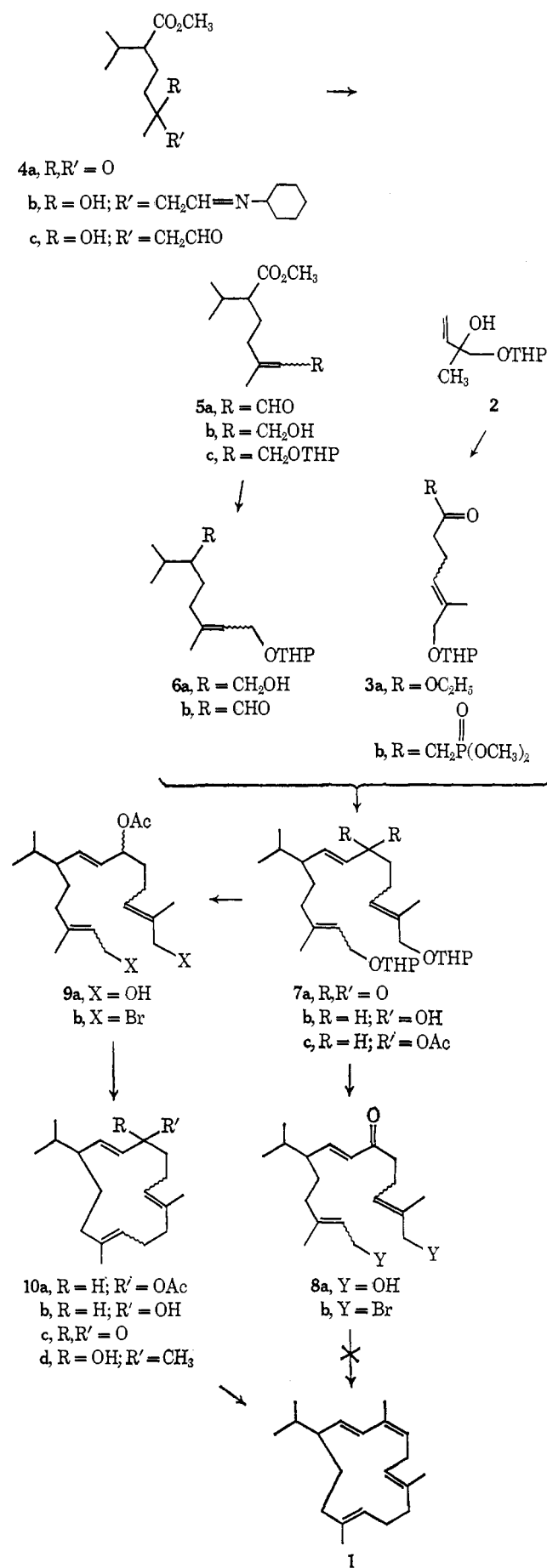
The approach of this synthesis (Scheme I) was based upon earlier studies, both in this laboratory and by others,^{2a,3b} which showed that isocembrol on mild acid treatment stereospecifically yielded cembrene and upon the preparation of medium-sized ring 1,5-dienes by nickel tetracarbonyl induced coupling of terminal allylic bromides.⁸ Thus, an allylic oxygenated derivative could serve as a synthon of the conjugated diene in **1** while the medium-sized ring was closed, the diene being introduced at a later time. With this approach, the synthesis was reduced to the preparation of the intermediates **3b** and **6b** which upon condensation would yield **7a**, stereoselectively. The transformation of **7a** to **9b** followed by nickel tetracarbonyl induced ring closure would lead to the 14-membered ring compound **10a**, a material readily transformed to cembrene (**1**).

The ketophosphonate **3b** was obtained from acetol tetrahydropyranyl ether⁹ in three steps with an overall yield of 50%. By reaction with vinyl lithium there was obtained the allyl alcohol **2**¹⁰ which upon treating with ethyl orthoacetate (trace of propionic acid)¹¹ gave the Claisen rearrangement product **3a**. This ester was transformed into **3b** by reaction with lithium dimethyl methylphosphonate at -70° .

The terminal hydroxylaldehyde derivative **6b** was prepared in seven steps from keto ester **4a**^{1a} with an overall yield of 35%. By reaction with lithium acetaldehydecyclohexylimine¹² followed by controlled hydrolysis (benzene-1% oxalic acid¹³), there was obtained hydroxyaldehyde **4c**. Standard procedures failed to effect the dehydration of **4c** in good yield but the α,β -unsaturated aldehyde **5a** was obtained in 55% yield by heating in DMSO at 160° .¹⁴ The allyl alcohol **5b**, prepared by sodium borohydride reduction, was protected as a tetrahydropyranyl ether, the ester converted to alcohol **6a** by LAH reduction and to aldehyde **6b** by $\text{CrO}_3\text{-Py}_2$ oxidation.¹⁵

The aldehyde **6b** and the ketophosphonate **3b** were coupled¹⁶ to yield the enone **7a** in which the new disubstituted double bond was formed with greater than 95% trans selectivity.¹⁷ The enone **7a** was reduced with LAH to allyl alcohol **7b** which was converted to the

Scheme I



Comm., 1382 (1970); (c) M. C. Woods, K. Nakanishi, and N. S. Bhacca, *Tetrahedron*, **22**, 243 (1966); (d) J. W. Harrison, R. M. Scowston, and B. Lythgoe, *J. Chem. Soc. C*, 1933 (1966), and references cited therein.

(8) E. J. Corey and E. K. W. Wat, *J. Amer. Chem. Soc.*, **89**, 2757 (1967); E. J. Corey and E. Hamanaka, *ibid.*, **89**, 2758 (1967); E. J. Corey and H. A. Kirst, *ibid.*, **94**, 667 (1972).

(9) F. Sondheimer, N. Stjerstrom, and D. Rosenthal, *J. Org. Chem.*, **24**, 1280 (1959).

(10) All new compounds gave analytical and spectral data consistent with assigned structure.

(11) W. S. Johnson, L. Wortheman, W. R. Bartlett, T. J. Brockson, T-t Li, D. J. Faulkner, and M. R. Petersen, *J. Amer. Chem. Soc.*, **92**, 741 (1970).

(12) G. Wittig and H. Reiff, *Angew. Chem., Int. Ed. Engl.*, **7**, 7 (1968); G. Wittig and H. D. Frommelt, *Chem. Ber.*, **97**, 3548 (1964).

(13) W. Nagata and Y. Hayase, *J. Chem. Soc. C*, 460 (1969).

(14) V. J. Traynelis, W. L. Hergenrother, H. T. Hanson, and J. A. Valicenti, *J. Org. Chem.*, **29**, 123 (1964).

(15) R. Radcliffe and R. Rodehorst, *J. Org. Chem.*, **35**, 4000 (1970).

(16) W. S. Wadsworth and W. D. Emmons, *J. Amer. Chem. Soc.*, **83**, 1733 (1961).

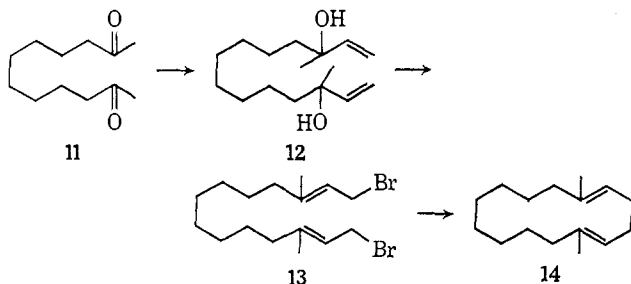
(17) The ir spectrum of **7a** showed strong absorption at 970 cm^{-1} and the nmr spectrum exhibited an AB pattern for the olefinic protons with $J_{AB} = 15\text{ Hz}$, with H_B also coupled with adjacent methine proton.

acetate **7c** with acetic anhydride in pyridine. The tetrahydropyranyl ethers were selectively removed by heating in 95% ethanol containing a trace of *p*-toluenesulfonic acid;¹⁸ the overall yield from **7a** was 90%. The resulting diol **9a** upon treatment with phosphorus tribromide yielded **9b** which upon reaction with nickel tetracarbonyl in *N*-methylpyrrolidone under standard conditions⁸ gave a 25% yield of monomeric products shown to be a mixture of isomeric trienes **10a**.

The mixture of acetates **10a** was treated with LAH followed by Jones oxidation to give in 50% yield enones **10c**. This material upon reaction with methyl lithium gave a mixture of alcohols **10d** which were chromatographically identical with and spectrally similar to natural isocembrol (isolated from *Pinus albicaulis*). The mixed alcohols were treated with a trace of *p*-toluenesulfonic acid in benzene to give a mixture of hydrocarbons which, although a single spot on tlc, proved to be a mixture of two major and several minor components upon vpc analysis. Of the two major components, the more rapidly moving one (35% of mixture) had an identical retention time as cembrene on coinjection. This material was separated from the other components of the mixture by preparative tlc on silver nitrate impregnated plates to give crystalline cembrene which was spectrally identical with authentic material and which upon recrystallization has mp 57–59°, undepressed upon admixture with an authentic sample.

During the course of this investigation, a variety of related synthetic steps was studied, and the following two observations are worthy of mention. When direct coupling of keto dibromide **8b**, prepared from **7a** by hydrolysis to diol **8a**¹⁸ and by conversion to dibromide **8b** using mesyl bromide and lithium bromide,¹⁹ was attempted, there was obtained a complex mixture of products, in which the enone functionality had disappeared. Apparently, the initially formed π -allyl nickel bromide added to the conjugate system followed by further reaction; similar conjugative additions are known.²⁰ Masking the carbonyl group as a methoxyimine derivative did not change the reaction course.

The poor yield on the nickel tetracarbonyl coupling reaction was disappointing and reasons for the low yield were evaluated. It has been reported earlier²¹ that the substitution of methyl groups on both allylic double bonds decreased the yield of 12-membered ring



(18) W. G. Dauben and H. L. Bradlow, *J. Amer. Chem. Soc.*, **74**, 559 (1952).

(19) W. J. Baumann, R. G. Gee, T. H. Madson, and H. K. Mangold, *Chem. Phys. Lipids*, **87** (1972).

(20) M. Dubini, F. Montino, and G. Chiusoli, *Chim. Ind. (Milan)*, **47**, 839 (1965); L. S. Hegedus, E. L. Waterman, and J. Catlin, *J. Amer. Chem. Soc.*, **94**, 7157 (1972).

(21) M. F. Semmelhack in "Organic Reactions," Vol. 19, W. G. Dauben, Ed., Wiley, New York, N. Y., 1972, p 166.

1,5-diene from **59** to 4%. With the 14-membered ring dibromide **13**, prepared from sebacic acid *via* diketone **11** and diallyl alcohol **12**, it was found that the ring formed in 70% yield, an identical result as reported for the unsubstituted case.⁸ This result would indicate in this ring size the other double bond played an important role.

Acknowledgment. This work was kindly supported by National Science Foundation Grant No. GP-8700 and by the Hoffmann-LaRoche Foundation.

(22) National Institutes of Health Postdoctoral Fellow.

(23) Postdoctoral Fellow, Stiftung für Stipendien auf dem Gebiete der Chemie.

W. G. Dauben,* G. H. Beasley,²² M. D. Broadhurst²²
B. Muller, D. J. Peppard, P. Pesnelle, C. Suter²³

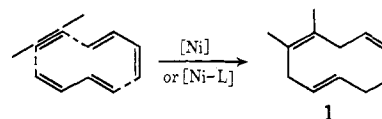
Department of Chemistry, University of California
Berkeley, California 94770

Received March 18, 1974

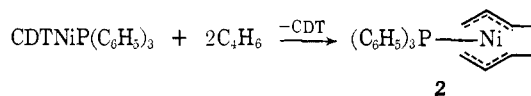
A Model for the Nickel-Catalyzed Cooligomerization of Butadiene with Substituted Alkynes

Sir:

The reaction of butadiene with olefins or alkynes to give ten-membered rings, *e.g.*, 4,5-dimethyl-*cis,cis*-*trans*-1,4,7-cyclodecatriene (**1**) derived from butyne, is



catalyzed by both ligand-free and ligand-modified zerovalent nickel catalysts.¹ This reaction is believed to occur in a stepwise manner and to involve the initial formation of an α,ω -bisallyl- C_8 nickel system which reacts further with the alkyne. The recent isolation of α,ω -octadienediynickel triphenylphosphine (**2**)² has



provided an opportunity to test this hypothesis.

2 may be prepared by treating the triphenylphosphine adduct of cyclododecatrienenickel (CDTNi) with liquid butadiene at -10° .³ The ¹H nmr spectrum⁴ indicates that it contains a symmetrical bis- π -allyl- C_8 chain in contrast to the π -allyl- σ -allyl arrangement observed in systems involving tricyclohexylphosphine.⁵

Dropwise addition of the diethyl ester of acetylenedicarboxylic acid to an ethereal suspension of **2** cooled to -30° results in the formation of a dark red solution

(1) (a) P. Heimbach and G. Wilke, *Justus Liebigs Ann. Chem.*, **727**, 183 (1969); (b) W. Brenner, P. Heimbach, and G. Wilke, *ibid.*, **727**, 194 (1969); (c) P. Heimbach, P. W. Jolly, and G. Wilke, *Advan. Organometal. Chem.*, **8**, 29 (1970); (d) W. Brenner, P. Heimbach, K. J. Ploner, and F. Thömel, *Justus Liebigs Ann. Chem.*, 1882 (1973); (e) P. Heimbach, *Angew. Chem.*, **85**, 1035 (1973).

(2) B. Büssemeier, Doctoral Thesis, University of Bochum, 1973.

(3) All operations were carried out in an argon atmosphere.

(4) Nmr: τ 4.99 (m) meso-H, 6.92 (d, $J_{\text{meso}} = 6.5$ Hz) syn-H, 7.84 (m) CH_2 , 8.48 (dd, $J_{\text{meso}} = 12$ Hz, $J_{\text{v}} = 13$ Hz) anti-H; solvent, toluene-d, temperature -10° .

(5) B. Barnett, B. Büssemeier, P. Heimbach, P. J. Jolly, C. Krüger, I. Tkatchenko, and G. Wilke, *Tetrahedron Lett.*, 1457 (1972).