

*cis*- and *trans*-1,2-divinylcyclohexane<sup>15</sup> were observed, with the former reagent giving a preponderance of the *cis* isomer and the latter favoring the *trans* isomer with a ratio of *ca.* 1:2; no 1,5-cyclodecadiene<sup>15,16</sup> could be detected spectroscopically or by vpc.

Although it has not yet been shown experimentally that the cyclization of allylic dibromides by nickel carbonyl can be used for the synthesis of ring sizes larger than 18, the efficiency of cyclization in the 18-membered case strongly suggests that it can.<sup>17</sup> The formation of essentially the same cyclization product from *cis*-*trans* isomeric dibromides is not surprising in view of earlier findings and similar results in intermolecular coupling reactions,<sup>18</sup> and it can be explained simply by allylic isomerization either because of allylic halogen-nickel exchange<sup>18</sup> or allylic rearrangement within the organonickel complexes *via*  $\sigma$ -allylnickel structures.<sup>19</sup>

The fact that the cyclization of **1**, *n* = 2 and 4, leads mainly to six-membered ring structures indicates that the formation of this ring size relative to the alternative eight- and ten-membered structures is sufficiently favorable to overcome the marked preference for the joining of primary over secondary over tertiary carbons in allylic coupling.<sup>18,20,21</sup>

It is noteworthy that the efficiency of cyclization of the substrates **1**, *n* = 2, 4, 6, 8, and 12, is strongly dependent on the solvent which is used; solvents such as dimethylformamide and N-methylpyrrolidone are much superior to, *e.g.*, tetrahydrofuran or glyme solvents. A discussion of these effects and detailed considerations of the mechanism of the cyclization process will be presented in due course.

It is apparent that the cyclization discussed herein is a very useful synthetic method. In principle it is applicable, for example, to a synthesis of elemol,<sup>22</sup>  $\beta$ -maaliene,<sup>23</sup> or cembrene.<sup>24</sup> A total synthesis of humulene has already been accomplished using this method.<sup>25,26</sup>

(15) Authentic samples of *cis*-1,2-divinylcyclohexane and *cis,trans*-1,5-cyclodecadiene were kindly provided by Dr. P. Heimbach, Max-Planck Institut, Mülheim, Germany; see P. Heimbach, *Angew. Chem. Intern. Ed. Engl.*, **3**, 702 (1964); **5**, 595 (1966).

(16) It was shown by a control experiment that *cis,trans*-1,5-cyclodecadiene was recovered unchanged after being subjected to cyclization conditions.

(17) A study of the cyclization of 1,40-dibromo-2,38-tetracontadiene which could give a 40-membered ring is now under way. The yields given for the cyclization of **1**, *n* = 6, 8, 12, are probably not optimal, since only one set of reaction conditions was tried.

(18) E. J. Corey and M. F. Semmelhack, to be published.

(19) The intervention of allylnickel(I) bromide complexes in these cyclizations is clear from the development of the deep red color characteristic of such complexes during reaction. This color develops rapidly as the addition of dibromide to nickel carbonyl is started, and at the end of the addition it fades and gives way to the characteristic green color of nickel(II) bromide in dimethylformamide solution.

(20) I. D. Webb and G. T. Borchardt, *J. Am. Chem. Soc.*, **73**, 2654 (1951).

(21) E. J. Corey and M. F. Semmelhack, *ibid.*, **89**, 2755 (1967).

(22) V. Sykora, V. Herout, and F. Sorm, *Collection Czech. Chem. Commun.*, **20**, 220 (1955).

(23) V. Herout, *et al.*, Abstracts, IUPAC Congress on Natural Products, Stockholm, Sweden, 1966, p 57.

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(25) E. J. Corey and E. Hamanaka, *ibid.*, **89**, 2758 (1967).

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E. J. Corey, Edward K. W. Wat  
Department of Chemistry, Harvard University  
Cambridge, Massachusetts 02138  
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## Total Synthesis of Humulene

Sir:

We describe herein a total synthesis of humulene, **7** (2,6,6,9-tetramethyl-*trans,trans,trans*-cycloundeca-1,4,8-triene),<sup>1-4</sup> a fundamental monocyclic trisoprenoid structure which is a likely precursor of a number of other naturally occurring sesquiterpenes.<sup>5</sup> The key step in the synthesis is formation of the 11-membered ring by cyclization of a 1,11-dibromo-2,5,9-undecatriene derivative using nickel carbonyl.<sup>6</sup>

One important intermediate in the synthesis is the phosphonium ylide **1** which was obtained starting with dimethyl *trans*-3-methylglutaconate<sup>7</sup> by a sequence involving (1) reduction to the corresponding diol (**2**, U = V = OH) using lithium aluminum hydride-aluminum chloride (3:1)<sup>8</sup> in ether; (2) conversion to the dibromide **2**, U = V = Br,<sup>9</sup> then selective displacement of the allylic bromine with trimethylbenzylammonium dichloroacetate in acetone to give **2**, U = Br, V = OCOCHCl<sub>2</sub>; (3) basic hydrolysis to the bromohydrin **2**, U = Br, V = OH; (4) acid-catalyzed addition to dihydropyran to form **2**, U = Br, V = OTHP (THP = 2-tetrahydropyranyl ether), and (5) reaction with triphenylphosphine in acetonitrile at 80° for 24 hr to form the phosphonium (bromide), U = P<sup>+</sup>(C<sub>6</sub>H<sub>5</sub>)<sub>3</sub>, V = OTHP.

A second key intermediate is the aldehyde **3**, the synthesis of which proceeded from 1-chloro-2-methyl-4-acetoxy-2-butene,<sup>10</sup> **4**, W = Cl, X = OAc, as follows: (1) displacement of chloride from **4**, W = Cl, X = OAc, by trimethylbenzylammonium mesitoate in ethanol at 80° for 24 hr to form **4**, W = mesityloxy, X = OAc; (2) selective alkaline hydrolysis to **4**, W = mesityloxy, X = OH; and (3) reaction with phosphorus tribromide<sup>11</sup> in ether to give **4**, W = mesityloxy, X = Br, which was used to alkylate the magnesium derivative formed from N-(2-methylpropylidene)cyclohexylamine<sup>12,13</sup> to afford an imine which yielded **3** by hydrolysis with aqueous oxalic acid at 25° for 4 hr.

Wittig condensation of the ylide **1** with the aldehyde **3** in dimethyl sulfoxide<sup>14</sup> afforded the triene **5**, Y =

(1) S. Dev, *Tetrahedron*, **9**, 1 (1960).

(2) M. D. Sutherland and O. J. Waters, *Australian J. Chem.*, **14**, 596 (1961).

(3) A. T. McPhail, R. I. Reed, and G. A. Sim, *Chem. Ind. (London)*, 976 (1964).

(4) J. A. Hartsuck and I. C. Paul, *ibid.*, 977 (1964).

(5) For example: (a) caryophyllene: E. J. Corey, R. B. Mitra, and H. Uda, *J. Am. Chem. Soc.*, **86**, 485 (1964), and references therein cited; (b) zarumbone: S. Dev, *Tetrahedron*, **8**, 171 (1960); (c) humulene mono- and dioxide: S. K. Ramaswami and S. C. Bhattacharyya, *ibid.*, **18**, 575 (1962); (d) humulenol: N. P. Damodaren and S. Dev, *Tetrahedron Letters*, 1941 (1963).

(6) See (a) E. J. Corey and E. Hamanaka, *J. Am. Chem. Soc.*, **86**, 1641 (1964); (b) E. J. Corey and M. F. Semmelhack, *Tetrahedron Letters*, 6237 (1966); (c) E. J. Corey and E. K. W. Wat, *J. Am. Chem. Soc.*, **89**, 2757 (1967).

(7) Obtained from a commercially available mixture of *trans* and *cis* isomers (ratio 45:55) by fractional distillation; any *cis* isomer remaining as an impurity in this starting material could easily be removed in the transformation to **2**. U = Br, V = OH.

(8) M. J. Jorgenson, *Tetrahedron Letters*, 559 (1962).

(9) Procedure of I. T. Harrison and B. Lythgoe, *J. Chem. Soc.*, 843 (1958).

(10) W. Oroshnik and R. Mallory, *J. Am. Chem. Soc.*, **72**, 4608 (1950).

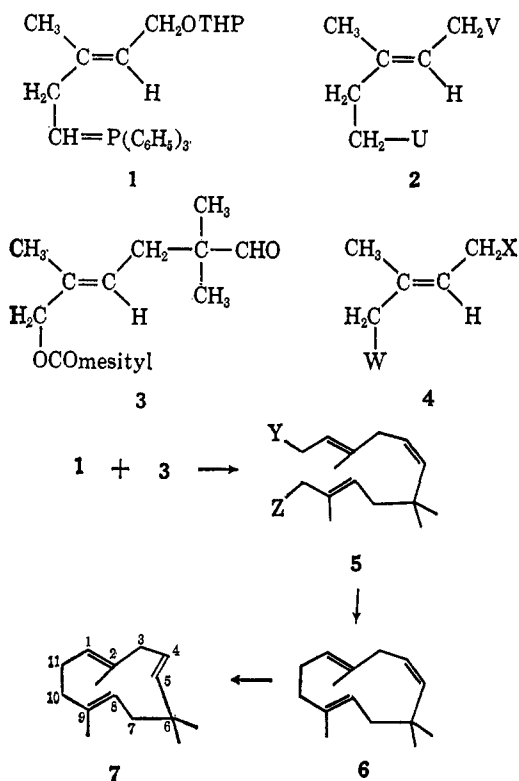
(11) J. M. Osbond, *J. Chem. Soc.*, 5270 (1961).

(12) G. Stork and S. R. Dowd, *J. Am. Chem. Soc.*, **85**, 2179 (1963).

(13) G. Wittig, H. D. Frommelt, and P. Suchanek, *Angew. Chem. Intern. Ed. Engl.*, **2**, 693 (1963).

(14) R. Greenwald, M. Chaykovsky, and E. J. Corey, *J. Org. Chem.*, **28**, 1128 (1963).

THP, Z = mesityloxy, with the central (5,6) double bond *cis*.<sup>15</sup> The mesityl and tetrahydropyranyl pro-



tecting groups were removed by sequential treatment with lithium aluminum hydride in ether (25°, 1 hr) and slightly acidic methanol at 25° to give the diol **5**, Y = Z = OH, which was converted by phosphorus tribromide<sup>11</sup> to the dibromide **5**, Y = Z = Br.

The 4,5-*cis* isomer of humulene (**6**) was formed as the major product when a solution of the dibromide **5**, Y = Z = Br, in N-methylpyrrolidone was added slowly (automatic syringe drive) to 4 mole equiv of nickel carbonyl in the same solvent at 50° under argon together with three other volatile products (0.7, 0.5, and 0.4 parts per part of **6**). Irradiation of the crude cyclization product (>350 m $\mu$ ) and diphenyl disulfide<sup>16</sup> in cyclohexane at 25° for 2.5 hr caused isomerization of **6** to humulene (**7**) which was obtained from the mixture using extraction with 50% aqueous silver nitrate.<sup>18</sup> Separation of pure humulene from the only contaminant **6** was readily accomplished by preparative vapor phase chromatography (fluorosilicone column, 150°). The synthetic product behaved exactly as did natural humulene<sup>19</sup> upon vpc analysis with fluorosilicone, diethylene glycol succinate, and Carbowax 20M columns

(15) The *cis* geometry for the 5,6-double bond in **5** is indicated by the absence of the absorption characteristic of *trans* -CH=CH- at 10.3–10.4  $\mu$ , by the ready photoisomerization using diphenyl disulfide<sup>16</sup> to an isomer which *did* exhibit infrared absorption at 10.3  $\mu$ , and finally from the observation that the model reaction of pivalaldehyde with *n*-octylidene- and  $\beta$ -phenylethylidene-triphenylphosphorane in dimethyl sulfoxide afforded olefinic product of >98% *cis* content.<sup>17</sup> The subsequent synthetic transformations also allow the *cis* assignment.

(16) C. Moussebois and J. Dale, *J. Chem. Soc.*, 260 (1966).

(17) E. J. Corey and G. T. Kwiatkowski, *J. Am. Chem. Soc.*, **88**, 5653 (1966).

(18) R. P. Hildebrand and M. D. Sutherland, *Australian J. Chem.*, **14**, 272 (1961), have described an efficient purification of naturally occurring humulene by this technique. In the present case the extraction removes only humulene and any unisomerized 4,5-*cis*-humulene (**6**) from the mixture.

(19) We are indebted to Drs. F. Sorm, S. Dev, and M. D. Sutherland for samples of natural humulene for comparison.

(which cleanly resolve a large number of sesquiterpenes). Identity was further established by the correspondence of infrared, nuclear magnetic resonance, and mass spectra.<sup>20</sup>

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E. J. Corey, E. Hamanaka

Department of Chemistry, Harvard University  
Cambridge, Massachusetts 02138

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## Structures of Two Compounds Containing Strong Metal-to-Metal Bonds

Sir:

It has been established that the  $\text{Re}_2\text{Cl}_8^{2-}$  and  $\text{Re}_2\text{Br}_8^{2-}$  ions have an eclipsed structure<sup>1</sup> with a quadruple bond between the metal atoms.<sup>2</sup> It has been shown that ligand substitution reactions of various kinds proceed readily with these ions.<sup>3</sup> In particular, a compound of empirical formula  $\text{ReCl}_3\text{P}(\text{C}_6\text{H}_5)_3$  was obtained<sup>3a</sup> by treating  $\text{Re}_2\text{Cl}_8^{2-}$  with  $\text{P}(\text{C}_6\text{H}_5)_3$ . Unfortunately this compound, which was shown<sup>3a</sup> not to be of the  $\text{Re}_3\text{Cl}_9\text{L}_3$  type obtained<sup>4</sup> from  $\text{Re}_3\text{Cl}_9$ , was too insoluble to permit positive structural characterization. It was postulated, however, that it is the dinuclear, 1,2-disubstituted derivative,  $(\text{C}_6\text{H}_5)_3\text{PReCl}_3\text{-ReCl}_3\text{P}(\text{C}_6\text{H}_5)_3$ . In order to obtain direct evidence on this, and particularly to see if such a compound retains the short Re-Re bond and the eclipsed configuration which is a consequence<sup>2</sup> of the  $\delta$  component of the quadruple bond, a soluble, crystallizable analog was sought. The  $\text{P}(\text{C}_2\text{H}_5)_3$  analog proved satisfactory; its structure has been determined by single-crystal X-ray methods and is described here.

$\text{Re}_2\text{Cl}_6[\text{P}(\text{C}_2\text{H}_5)_3]_2$  crystallizes in the space group  $\text{P2}_1/\text{n}$  with unit cell dimensions  $a = 7.644 \pm 0.003$ ,  $b = 10.985 \pm 0.005$ ,  $c = 14.206 \pm 0.006$  Å;  $\beta = 96.5 \pm 0.1^\circ$ ;  $Z = 2$ . Intensities were recorded using a counter diffractometer and Cu  $K\alpha$  radiation (Ni filtered) within a sphere limited by  $\theta = 55^\circ$ . The structure was solved by conventional Patterson and Fourier syntheses and has been refined to an  $R$  value<sup>5</sup> of 0.066 neglecting statistically unreliable reflections.

The molecule, shown in Figure 1, lies on a crystallographic inversion center and possesses the expected eclipsed configuration. Important bond lengths and angles are: Re-Re,  $2.222 \pm 0.003$  Å; Re-Cl<sub>1</sub>,  $2.35 \pm 0.01$  Å; Re-Cl<sub>2</sub> and Re-Cl<sub>3</sub>,  $2.30 \pm 0.01$  Å; Re-P,  $2.46 \pm 0.01$  Å; Re-Re-Cl<sub>1</sub>,  $116.3 \pm 0.2^\circ$ ; Re-Re-Cl<sub>2</sub>,  $104.0 \pm 0.2^\circ$ ; Re-Re-Cl<sub>3</sub>,  $103.0 \pm 0.2^\circ$ ; Re-Re-P,  $97.4 \pm 0.2^\circ$ . While the significant difference in Re-Cl distances may be explained in terms of the *trans* effect, there is no immediately apparent reason for the observed angular distortions.

This is the first substitution product (not involving oxidation or reduction) of an  $\text{Re}_2\text{X}_8^{2-}$  ion which has

(1) (a) F. A. Cotton and C. B. Harris, *Inorg. Chem.*, **4**, 330 (1965); (b) V. G. Kuznetsov and P. A. Koz'min, *Zh. Strukt. Khim.*, **4**, 55 (1963); (c) V. G. Koz'min, V. G. Kuznetsov, and Z. V. Popova, *ibid.*, **6**, 651 (1965); (d) W. R. Robinson, Thesis, MIT, 1966.

(2) F. A. Cotton, *Inorg. Chem.*, **4**, 334 (1965).

(3) (a) F. A. Cotton, N. F. Curtis, and W. R. Robinson, *ibid.*, **4**, 1696 (1965); (b) F. A. Cotton, N. F. Curtis, B. F. G. Johnson, and W. R. Robinson, *ibid.*, **4**, 326 (1965); (c) F. A. Cotton, C. Oldham, and W. R. Robinson, *ibid.*, **5**, 1798 (1966).

(4) F. A. Cotton, S. J. Lippard, and J. T. Magee, *ibid.*, **4**, 508 (1965).

(5) Defined as  $\sum |F_o| - |F_c| / \sum |F_o|$ .