

## THE SYNTHESIS OF METHYLENE-SUBSTITUTED MACROCYCLIC POLYACETYLENES\*

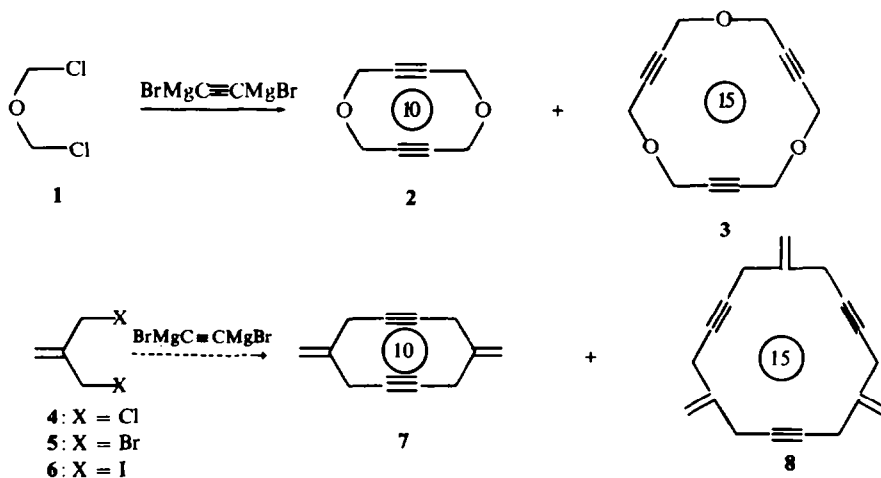
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**Abstract**—Chlorination of 2-methylallyl chloride (9) and subsequent treatment with sodium iodide leads to 3-iodo-2-iodomethyl-1-propene (6), which is converted to 4-methylene-1,6-heptadiyne (10) on reaction with ethynylmagnesium bromide in the presence of cuprous chloride. The bis-Grignard derivative of 10 on treatment with the diiodide 6 in the presence of cuprous chloride gives 4,9,14,19-tetramethylene-1,6,11,16-cycloicosatetrayne (16), a 20-membered ring cyclic tetraacetylene. Oxidative coupling of the diacetylene 10 with oxygen, cuprous chloride and ammonium chloride leads to 6,13-dimethylene-1,3,8,10-cyclotetradecatetrayne, a 14-membered ring cyclic tetraacetylene.

IT HAS been shown that the reaction between dichlorodimethyl ether (1) and acetylenedimagnesium bromide gives rise to the 10-membered heterocyclic diacetylene 2 and the 15-membered triacetylene 3.<sup>1</sup> It was of interest to investigate whether this type of reaction could be applied to the synthesis of *carbocyclic* compounds corresponding to 2 and 3. For this purpose, it seemed appropriate to substitute a 3-halogeno-2-halogenomethyl-1-propene (type 4, 5, 6) for the ether 1, since the presence of the double bond in these allylic halides causes the two halogen atoms to be activated, as in the ether 1.



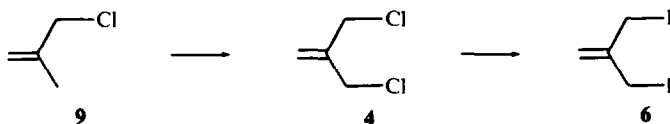
\* Unsaturated Macrocyclic Compounds. LXXXII. For part LXXXI, see F. Sondheimer, K. Stöckel, R. Mason, T. A. Clarke and M. Guss, *J. Am. Chem. Soc.* **93**, in press.

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We now describe the synthesis of 3-iodo-2-iodomethyl-1-propene (**6**), its reaction with acetylenedimagnesium bromide, as well as some related reactions. Although the methylene-substituted 10- and 15-membered ring polyacetylenes **7** and **8** were not obtained, the related 20- and 14-membered ring compounds **16** and **21** were synthesized.

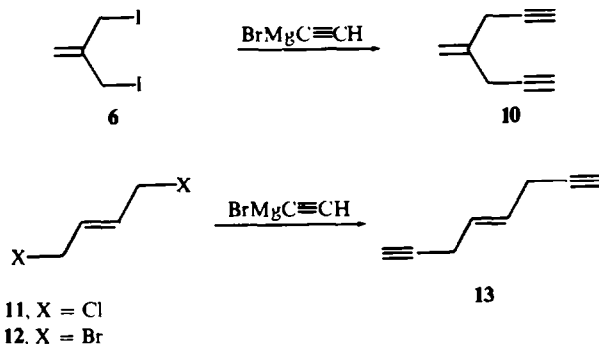
Chlorination of 2-methylallyl chloride (**9**) has been shown to give about equal amounts of 3-chloro-2-chloromethyl-1-propene (**4**) and the isomeric 1,3-dichloro-2-methyl-1-propene (as well as the chlorine addition product, 1,2,3-trichloro-2-methylpropane), from which **4** could be separated by fractional distillation.<sup>2</sup> We have found the isolation of pure **4** (as evidenced by GLC analysis) from this reaction to be



tedious. The most convenient procedure involved direct treatment of the total chlorinated product with sodium iodide in acetone. 3-Iodo-2-iodomethyl-1-propene (**6**), derived from **4** by replacement of both Cl atoms with iodine, could then be isolated by direct crystallization in *ca* 15% over-all yield.

The reaction of the diiodide **6** with acetylenedimagnesium bromide was studied under various conditions, but no cyclic products of type **7** or **8** could be isolated. Equally disappointing results were obtained when the reaction was carried out in the presence of cuprous chloride, which has been shown to be an effective catalyst for the condensation between allylic halides and acetylenic Grignard reagents.<sup>3</sup>

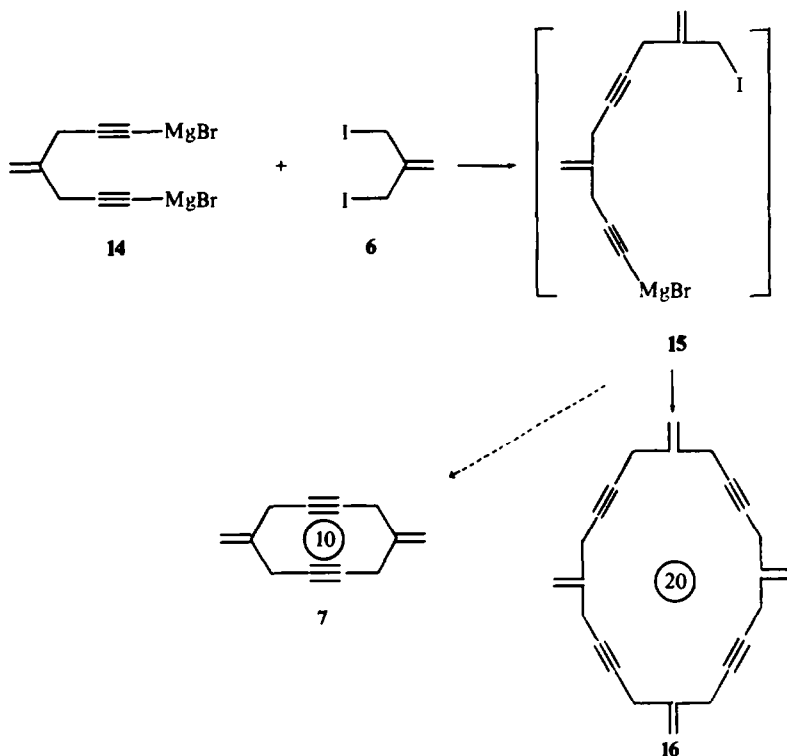
The reaction of **6** with an excess of ethynylmagnesium bromide<sup>4</sup> in the presence of cuprous chloride was then investigated. This led to 4-methylene-1,6-heptadiyne



**(10)** in 58% yield, the reaction being analogous to the conversion of *trans*-1,4-dichloro-2-butene (**11**) or *trans*-1,4-dibromo-2-butene (**12**) to *trans*-4-octene-1,7-diyne (**13**) in *ca* 25% yield by means of ethynylmagnesium bromide.<sup>5</sup>

The bis-Grignard derivative **14** of the diyne **10** was then treated with the diiodide **6** in the presence of cuprous chloride, since this reaction appeared to offer an alterna-

tive route to the 10-membered ring compound **7**\*. In practice, the only cyclic substance isolated (in *ca* 5% yield) proved to be 4,9,14,19-tetramethylene-1,6,11,16-cyclo-eicosatetrayne (**16**), a 20-membered ring cyclic tetraacetylene. Presumably the intermediate **15** undergoes intermolecular condensation with a second molecule to give



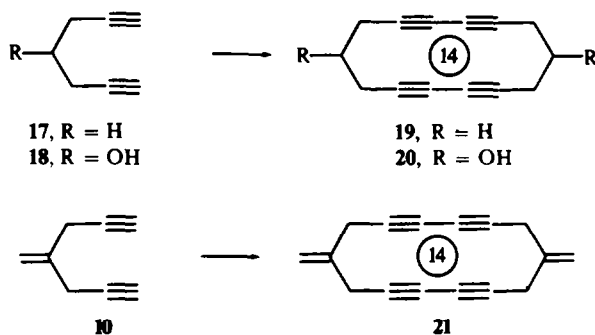
the cyclic "dimer" **16** in preference to intramolecular condensation to give the cyclic "monomer" **7**.

The structure of **16** was established by the spectral data, given in the Experimental Section. Of special importance was the mass spectrum, which indicated the molecular formula  $C_{24}H_{24}$  ( $m/e$  312). The molecular ion peak was quite weak, due to extensive fragmentation, and **16** was therefore subjected to catalytic hydrogenation in ethyl acetate over a platinum catalyst. This resulted in 1,6,11,16-tetramethylcyclo-eicosane, the mass spectrum of which now showed a strong (100%) molecular ion peak corresponding to  $C_{24}H_{48}$  ( $m/e$  336).

It has been shown that 1,6-heptadiyne (**17**) and 1,6-heptadiyn-4-ol (**18**) on oxidative coupling with oxygen in the presence of cuprous chloride and ammonium chloride in aqueous ethyl alcohol give rise to the corresponding 14-membered ring cyclic

\* It has been shown that the bis-sodium derivatives of  $\alpha\omega$ -diacetylenes on reaction with  $\alpha\omega$ -dibromoalkanes in liquid ammonia give rise to cyclic polyacetylenes, the smallest ring obtained being the 11-membered one [J. Dale, A. J. Hubert and G. S. D. King, *J. Chem. Soc.* 73 (1963); see also J. H. Wotiz, R. F. Adams and C. G. Parsons, *J. Am. Chem. Soc.* **83**, 373 (1961)].

"dimers" (**19** and **20**, respectively),<sup>6</sup> 4-Methylene-1,6-heptadiyne (**10**) was therefore subjected to this type of coupling, in order to obtain the cyclic "dimer", 6,13-dimethylene-1,3,8,10-cyclotetradecatetrayne (**21**). This substance was indeed obtained when



the reaction was carried out in the presence of benzene (which has been shown to be advantageous, for solubility reasons),<sup>7</sup> although the yield was poor and compound **21** proved to be very unstable.

The structure of the 14-membered ring tetraacetylene **21** was established by the spectral data (Experimental). It is of interest that the highest wavelength maximum in the ultraviolet spectrum of **21** occurs at 262 nm, which is *ca* 9 nm higher than the usual position (*ca* 253 nm) for a dialkyl-1,3-diacetylene.<sup>6</sup> A similar shift has been observed in the ultraviolet spectra of the related substances **19** and **20**,<sup>6</sup> and is presumably due to the proximity of the two 1,3-diacetylene groupings.

The two methylene-substituted macrocyclic polyacetylenes **16** and **21** are potential precursors of other interesting large-ring compounds. For instance, prototropic rearrangements of these 1,4-enynes might lead to methyl-substituted dehydroannulenes,<sup>8</sup> while cleavage of the double bonds might give macrocyclic acetylenic polyketones. We intend to study these transformations, although preliminary experiments have not been encouraging.

## EXPERIMENTAL

*Spectral data.* UV spectra: on a Unicam SP-800 spectrophotometer. IR spectra: on a Unicam SP-200 spectrophotometer. NMR spectra: on a Varian HA-100 (100 MHz) or a Perkin-Elmer R-10 (60 MHz) instrument (TMS used as internal standard). Mass spectra: on an AEI MS-12 spectrometer (70 eV, direct inlet system).

**3-Iodo-2-iodomethyl-1-propene** (**6**). 2-Methylallyl chloride **9** (100 g, 1.10 mol; B.D.H. Chemicals) was chlorinated, as described by Gragson *et al.*<sup>4</sup> The progress of the reaction was followed by GLC examination of aliquots removed every 10 min. The reaction was terminated after 75 min, when only little **9** remained. The product was washed 3 times with H<sub>2</sub>O, and dried over MgSO<sub>4</sub>. It was then stirred for 16 hr with NaI (330 g, 2.20 mol) in acetone [800 ml, commercial grade, not dried: inferior results were obtained after drying] at room temp, filtered, and the ppt was washed well with dry ether. The combined filtrates were evaporated, finally at *ca* 50° (bath temp) (0.5 mm), and the dark red residue was extracted well with ether. Evaporation and crystallization from petroleum ether (b.p. 60–80°), using freshly activated C, gave **6** (48.0 g, 14%) as colourless crystals, m.p. 32–33°, homogeneous by GLC. (Found: C, 15.97; H, 1.88. C<sub>4</sub>H<sub>6</sub>I<sub>2</sub> requires: C, 15.60; H, 1.96%);  $\nu_{\max}$  (CCl<sub>4</sub>) 1630 (m) and 920 (s) cm<sup>-1</sup> (>C=CH<sub>2</sub>); NMR spectrum (CCl<sub>4</sub>, 100 MHz),  $\tau$  4.72 (s, 2H, olefinic) and 5.94 (s, 4H, allylic); mass spectrum, *m/e* 308 (M<sup>+</sup>). **6** may also be isolated by distillation at *ca* 60–80° (bath temp) (0.5 mm), and subsequent crystallization.

**Caution:** **6** is strongly lachrymatory and vesicant, and rubber gloves should be worn in this experiment.

**4-Methylene-1,6-heptadiyne (10).** A soln of  $\text{HC}\equiv\text{CMgBr}$  in THF (200 ml) was prepared from Mg (4.6 g, 0.19 g-atom), EtBr (23.4 g, 0.215 mol) and acetylene, as described by Jones *et al.*<sup>4</sup> CuCl (0.5 g) was added, followed by a soln of **6** (20 g, 0.065 mol) in THF (10 ml). The mixture was stirred under reflux for 1 hr, at room temp for 16 hr, and then again under reflux for 1 hr.  $\text{H}_2\text{O}$  (20 ml) was added to the cooled mixture, followed by 10% HCl aq (70 ml). The product was extracted with ether, and the organic layer was washed with 10% HCl aq and  $\text{H}_2\text{O}$ . Drying ( $\text{MgSO}_4$ ), evaporation, and distillation through a 15 cm Vigreux column gave **10** (3.9 g, 58%) as a colourless liquid, b.p. 40–42° (20 mm), homogeneous by GLC. (Found: C, 92.28; H, 7.68.  $\text{C}_8\text{H}_8$  requires: C, 92.26; H, 7.74%);  $\nu_{\text{max}}$  (neat) 3350 (s) ( $\equiv\text{C}-\text{H}$ ), 2140 (w) ( $\text{C}\equiv\text{C}$ ), 1660 (m) and 915 (s)  $\text{cm}^{-1}$  ( $\text{>C}=\text{CH}_2$ ); NMR spectrum ( $\text{CCl}_4$ , 100 MHz),  $\tau$  4.85 (narrow m, 2H, olefinic), 7.03 (narrow m, 4H, allylic) and 8.01 (t,  $J = 2$  Hz, 2 H, acetylenic); mass spectrum,  $m/e$  104 ( $\text{M}^+$ ).

**4,9,14,19-Tetramethylene-1,6,11,16-cycloicosatetrayne (16).** A soln of **10** (2.5 g, 24 mmol) in dry THF (100 ml) was added during 15 min to a stirred soln of EtMgBr in THF (70 ml), prepared from Mg (1.4 g, 58 mg-atom) and EtBr (6.28 g, 58 mmol). The mixture was stirred for 1 hr, and cuprous chloride (800 mg), followed by a soln of **6** (7.4 g, 24 mmol) in THF (15 ml), was then added. The mixture was stirred at 60° for 1 hr, and then at room temp for 16 hr.  $\text{H}_2\text{O}$  and EtOAc were added, and the organic layer was washed successively with 10% HCl aq, satd NaCl aq, and  $\text{H}_2\text{O}$ . The soln was dried ( $\text{MgSO}_4$ ), evaporated, and the residue was chromatographed on  $\text{Al}_2\text{O}_3$  (200 g; Spence, type H). Elution with light petroleum (b.p. 40–60°) —benzene (1:1) and crystallization from light petroleum (b.p. 60–80°) gave **16** (188 mg, 5%) as colourless crystals, which decomposed on attempted m.p. determination; homogeneous by TLC. (Found: C, 91.99; H, 8.09.  $\text{C}_{24}\text{H}_{24}$  requires: C, 92.26; H, 7.74%);  $\nu_{\text{max}}$  ( $\text{CHCl}_3$ ) 2250 (w) ( $\text{C}\equiv\text{C}$ ), 1660 (m) and 920 (s)  $\text{cm}^{-1}$  ( $\text{>C}=\text{CH}_2$ ); NMR spectrum ( $\text{CCl}_4$ , 60 MHz),  $\tau$  5.03 (s, 8H, olefinic) and 7.01 (s, 16H, allylic); mass spectrum,  $m/e$  312 ( $\text{M}^+$ ).

**1,6,11,16-Tetramethylcycloicosane.** A soln of **16** (20 mg) in EtOAc (5 ml) was stirred in  $\text{H}_2$  over Pt (*ca* 40 mg) until absorption ceased (*ca* 30 min). The mass spectrum of the product, obtained by removal of the catalyst and the solvent, showed  $m/e$  336 (100%,  $\text{M}^+$ ).

**6,13-Dimethylene-1,3,8,10-cyclotetradecatetrayne (21).**  $\text{NH}_4\text{Cl}$  (7 g), CuCl (4 g), benzene (200 ml),  $\text{H}_2\text{O}$  (17 ml) and conc HCl aq (0.04 ml) were introduced into a 3-neck flask fitted with a mechanical stirrer, gas inlet tube and reflux condenser (cooled with Dry Ice-acetone). The mixture was heated to 50°, a soln of **10** (2 g) in EtOH (4 ml) was added, and  $\text{O}_2$  was then bubbled in vigorously with rapid stirring at 50° for 3 hr. During this time, the volume was maintained by periodic addition of benzene. The mixture was cooled, filtered, and the residue was washed with benzene. The aqueous layer was washed with benzene, and the combined organic extracts were dried ( $\text{MgSO}_4$ ) and evaporated. Chromatography on  $\text{Al}_2\text{O}_3$  (130 g; Spence, type H), elution with light petroleum (b.p. 40–60°)-benzene (1:1) and trituration with ether gave **21** (6 mg, 0.3%) as colourless crystals, which decomposed on attempted melting point determination; homogeneous by TLC;  $\lambda_{\text{max}}$  (MeOH) 230 (*e* 650), 242 (640), and 262 nm (480);  $\nu_{\text{max}}$  ( $\text{CHCl}_3$ ) 2250 (w), 2150 (w) ( $\text{C}\equiv\text{C}$ ), 1640 (m) and 920 (s)  $\text{cm}^{-1}$  ( $\text{>C}=\text{CH}_2$ ); NMR spectrum  $\text{CDCl}_3$ , 60 MHz),  $\tau$  5.02 (narrow m, 4H, olefinic) and 6.95 (narrow m, 8H, allylic); mass spectrum,  $m/e$  204 (100%,  $\text{M}^+$ ). Substance **21** was very unstable, and rapidly formed an insoluble polymer on standing. Solutions were also unstable; *e.g.*, an ether solution deposited a yellow polymer after standing under  $\text{N}_2$  at  $-15^\circ$  in the dark for several hr.

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