Macrocyclic Hydrocarbons by Oxidative Coupling of 5,5-Dimethylnona-1,8-diyne

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A series of macrocyclic polyacetylenes have been obtained by oxidative coupling of 5,5-dimethylnona-1,8-diyne. The individual members were not isolated as such, but the mixture hydrogenated to the corresponding cycloalkanes and the saturated cyclic "dimer", "trimer", and "tetramer" isolated. Higher cyclic "oligomers" were present but not obtained pure.

The yields of cyclic compounds were lower than in the case of nona-1,8-diyne itself (negative *gem*-dimethyl effect).

In the "rectangular" diamond-lattice conformations considered most favourable for large-ring cycloalkanes[1], only the corner positions can accommodate two substituents. We have already briefly reported[2-4] several synthetic routes to certain *gem*-dimethyl-substituted cycloalkanes and studied the effect of such substituents on the physical properties. In this paper we describe in more detail the somewhat limited approach *via* cyclic acetylenes.
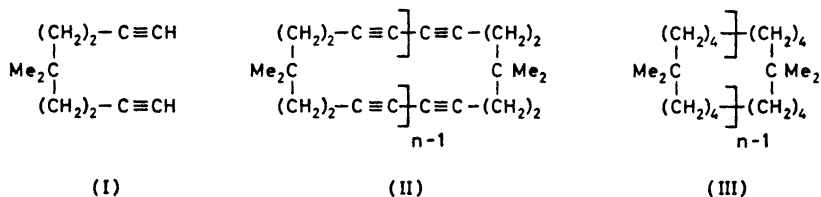
In view of Sondheimer's success in preparing large-ring polyacetylenes[5] by the use of the Eglinton-Galbraith variety[6] (cupric acetate in pyridine) of the oxidative coupling of terminal diacetylenes, it was natural to try the coupling of 4,4-dimethylhepta-1,6-diyne, which should in principle lead to a 14-membered ring, as well as higher oligomers. However, all attempts to prepare this dimethylheptadiyne failed, obviously because of the neopentyl-like steric hindrance exerted by the *gem*-dimethyl group. Thus, 1,3-dibromo-2,2-dimethylpropane could be recovered to 75 % after 6 h stirring with sodium acetylide in liquid ammonia. In dimethylsulphoxide, a small quantity of terminal acetylene was formed after 30 h, but methyl migration had also occurred. Attempts to couple the dibromide with ethynylmagnesium bromide in the presence of cobaltous chloride in tetrahydrofuran were also unsuccessful, and 85 % of the dibromide was recovered after 12 h.

The next simple diacetylene that seemed attractive for our purpose was 5,5-dimethylnona-1,8-diyne (I), since it might lead to an 18-membered ring, as well as higher oligomers. Its synthesis was similarly unsuccessful when 1,3-dibromo-2,2-dimethylpropane was tried in a coupling with propargyl-

magnesium bromide in the presence of cuprous chloride, and only traces of terminal acetylene were formed. The dibromide was recovered when diethyl ether was the solvent, while polymeric products were obtained when tetrahydrofuran was the solvent. On the other hand, the diyne could be prepared in good yield (67 %) from 1,5-dibromo-3,3-dimethylpentane and sodium acetylide in liquid ammonia.

Cyclization of 5,5-dimethylnona-1,8-diyne was carried out by oxidative coupling with cupric acetate in pyridine under the same conditions that were used by Sondheimer and collaborators in the case of nona-1,8-diyne itself.[5] The only modification was an extension of the reaction time from 3 to 7 h.

Scheme

$$(CH_2)_2-C\equiv CH$$
$$Me_2C$$
$$(CH_2)_2-C\equiv CH$$

(I)

$$(CH_2)_2-C\equiv C\!\!-\!\!\left[\,C\equiv C-(CH_2)_2\right.$$
$$Me_2C \qquad\qquad C\,Me_2$$
$$(CH_2)_2-C\equiv C\!\!-\!\!\left]\,C\equiv C-(CH_2)_2\right._{n-1}$$

(II)

$$(CH_2)_4\!\!-\!\!\left[\,(CH_2)_4\right.$$
$$Me_2C \qquad C\,Me_2$$
$$(CH_2)_4\!\!-\!\!\left]\,(CH_2)_4\right._{n-1}$$

(III)

The air- and light-sensitive benzene-soluble product was shown to be a mixture of cyclic acetylenes (II) of various sizes, since the infrared spectrum contained no bands due to terminal acetylene, only the 1,3-diyne absorption at $2150-2250$ cm^{-1}, and since at least three sharp close-lying lines for methyl were observed at δ $0.85-0.92$ in the NMR spectrum. Chromatographic separation of the mixture failed both on alumina, using hexane and benzene, and on Sephadex, using ethyl acetate and chloroform. The mixture of unstable cyclic polyacetylenes was therefore completely hydrogenated, and the saturated hydrocarbons (III) separated by vacuum distillation to give 1,1,10,10-tetramethylcyclo-octadecane ($n=2$), which crystallized immediately; 1,1,10,10,19,

Table 1. Yields (%) in oxidative coupling of nona-1,8-diynes.

	Benzene soluble products. Total	Cyclic dimer	Cyclic trimer	Cyclic tetramer	Higher cyclic oligomers
From unsubstituted diyne	*ca.* 100	10.3	13.1	10.9	7.9
From 5,5-dimethyl derivative	52	4.5	3.2	0.9	3.8

19-hexamethylcycloheptacosane ($n = 3$), which remained liquid; and 1,1,10,10,19,19,28,28-octamethylcyclohexatriacontane ($n = 4$), which was again a solid. The distillation residue was liquid, and was shown by mass spectrometry to contain the next homologue, 1,1,10,10,19,19,28,28,37,37-decamethylcyclopentatetracontane ($n = 5$). Higher homologues were probably also present. The NMR spectra make no distinction between these saturated rings; they all show a sharp methyl line at δ 1.2.

Both the total yield of benzene-soluble products and the yields of isolated cyclic compounds are seen (Table 1) to be significantly lower than the yields obtained by Sondheimer from nona-1,8-diyne.[5] This can hardly be attributed to the different method of product isolation on which is based the determination of the yields of rings of various sizes. It seemed more likely that the experimental conditions during cyclization might have influenced the yields. Since these were not what is generally called "high-dilution conditions", it was tried in one experiment to add the diyne to the pyridine-cupric acetate solution dropwise over one hour instead of adding all at the same time. However, the yield of cyclic dimer did not increase, but dropped slightly (from 4.5 % to 3.6 %). It therefore seems clear that we have here a case where the presence of the *gem*-dimethyl branching impedes the tendency for cyclization instead of promoting it, as has been earlier observed for many other ring systems.[7]

Of course, there is no *a priori* reason why *gem*-dimethyl substitution should necessarily lead to a higher probability for those chain conformations that have the bent shape best fitted for cyclization. In the present case it is easy to see (Fig. 1) how 5,5-dimethyl substitution in nona-1,8-diyne (or in this
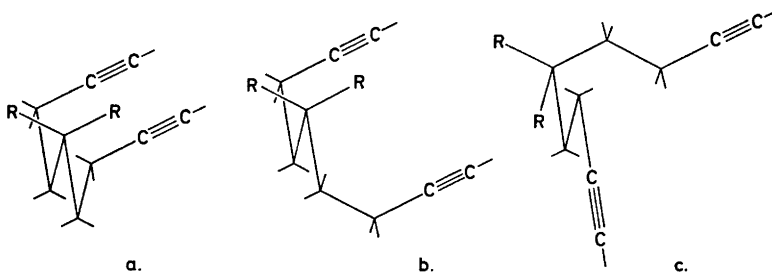

Fig. 1. The conformations of nona-1,8-diyne of shortest end-to-end distance. With $R = H$, *a* is most likely, and *b* and *c* permitted. With $R = CH_3$, *c* becomes more likely than even the fully extended chain, while *a* and *b* are excluded.

unit when it forms part of a ring) introduces steric hindrance exactly in those two conformers which in the unsubstituted case bring the ends closest together. These conformers have two "chain-bends"; at carbon atoms 3 and 7, or at carbon atoms 3 and 6. It is also clear that the *gem*-dimethyl group favours a single "chain-bend" at carbon atom 5 whereby the ends become more separated.

Among the isolated cycloalkanes, the 18-ring compound (dimer) was of particular interest. The conformational situation for cyclo-octadecane has already been discussed,[1,2,4] and it has been shown that two diametrically placed *gem*-dimethyl groups can be accommodated on all four possible diamond-lattice conformations. One would not therefore expect that this compound should be conformationally homogeneous outside the crystal lattice. The infrared spectrum (Fig. 2) is in agreement with this, showing sharp bands
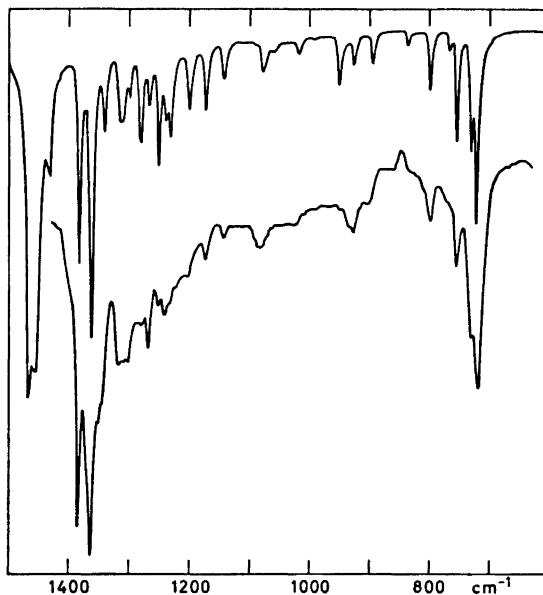

Fig. 2. Infrared spectra of 1,1,10,10-tetramethylcyclo-octadecane (III, $n = 2$). Upper curve: solid in KBr. Lower curve: solution in CS_2.

in the solid and broad areas in solution. Nevertheless, the spectrum, partic-ularly in the CH_2-rocking region ($700 - 800$ cm^{-1}), suggests that the preponderant conformation in solution may be the same as the unique crystal conformation. The already published calorimetric data [2] show that the whole melting process takes place at the macroscopic melting point, so that the expanded crystal phase, stable above a transition point for cyclo-octadecane and containing a conformer mixture,[2] is rendered unstable by the methyl substitution.

That the 27-ring cycloalkane (trimer) is liquid was not surprising, since no rings containing an odd number of ring atoms can fit the diamond lattice.

The 36-ring compound (tetramer) would be able to form a large "square" conformation with *gem*-dimethyl groups stabilizing all four corners so as to give a relatively large hole in the interior measuring about 7 Å × 7 Å. This might be expected to lead to occlusion of solvent molecules. However, no clear tendency of this sort was observed. The measured entropy of melting

$(\Delta S_m = 23$ e.u. at $T_m = 79°)$ seems small for such a large molecule. Since the infrared spectrum of this solid is just as nonspecific as that of the liquid trimer, the explanation cannot be that the liquid tetramer is conformationally homogeneous, but rather that its crystal lattice is non-discriminating and contains a conformer mixture. A transition point was not observed calorimetrically above $-90°$.

EXPERIMENTAL

5,5-Dimethylnona-1,8-diyne. Monosodium acetylide was prepared [8] by passing acetylene into a solution of sodium amide, prepared from sodium (9.2 g = 0.4 mol) in liquid ammonia (300 ml). 1,5-Dibromo-3,3-dimethylpentane [9] (25.8 g = 0.1 mol) was added during 20 min and the reaction mixture stirred for 12 h. The ammonia was allowed to evaporate, water and ether added, the ether extract washed with water and dried over magnesium sulphate. Vacuum distillation gave the 5,5-dimethylnona-1,8-diyne (10 g = 67 %), b.p. $39°/0.01$ mm. (Found: C 89.44; H 10.53. Calc. for $C_{11}H_{16}$: C 89.12; H 10.88.)

1,1,10,10-Tetramethylcyclooctadecane and higher homologues. To finely ground neutral cupric acetate monohydrate (150 g) was added redistilled pyridine (1000 ml). The mixture was stirred and cooled to room temperature. 5,5-Dimethylnona-1,8-diyne (10 g) was added, and the mixture stirred for 7 h at 60 − 70°C, then overnight at room temperature. The solution was filtered, the solid washed with benzene, and combined filtrates were evaporated to dryness. The residue was taken up in water/ether, and the water phase extracted with ether. The combined ether solutions were washed with dilute hydrochloric acid, then with water and dried over magnesium sulphate. After filtration and evaporation of the ether, the residue was dissolved in benzene, filtered through a short alumina column, and the column washed with benzene. The benzene was evaporated, and the residue (5.2 g) dissolved in cyclohexane (70 ml). Palladium on charcoal (0.6 g) was added and the solution fully hydrogenated at 66 p.s.i. The catalyst was filtered off, the solvent evaporated, the residue dissolved in pentane and filtered through alumina. Vacuum distillation of the evaporated solution gave the following cyclic hydrocarbons:

1,1,10,10-Tetramethylcyclooctadecane, b.p. $150°/0.1$ mm, m.p. 87°. Mol.w. 308 (mass spectrometry). (Found: C 85.49; H 14.11. Calc. for $C_{22}H_{44}$: C 85.63; H 14.37.)

1,1,10,10,19,19-Hexamethylcycloheptacosane, b.p. $210°/0.1$ mm. Mol.w. 462 (mass spectrometry). (Found: C 85.54; H 14.37. Calc. for $C_{33}H_{66}$: C 85.63; H 14.37.)

1,1,10,10,19,19,28,28-Octamethyl-cyclohexatriacontane, b.p. $280°/0.1$ mm, m.p. 79° after recrystallization from methanol. Mol.w. 616 (mass spectrometry). (Found: C 85.10; H 14.18. Calc. for $C_{44}H_{88}$: C 85.63; H 14.37.)

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