Bis(*gem*-dimethyl)-substituted Cyclic Diynes

S. L. BJÖRNSTAD and G. BORGEN

Kjemisk Institutt, Universitetet i Oslo, Oslo 3, Norway

Bis-*gem*-dimethyl-substituted 16- and 18-membered cycloalkynes have been synthesized. The importance of the relative positions of the *gem*-dimethyl groups for cyclization yields and conformations is discussed.

Conformational problems have earlier been investigated by use of *gem*-dimethyl substitution of large rings.¹ For further studies 16- and 18-membered cyclic hydrocarbons with *gem*-dimethyl groups in two positions were wanted. The easiest route to such compounds has been found to go over the corresponding cyclic diynes. These cyclic diynes have now been prepared. Also of interest were the conformational consequences of the combination of *gem*-dimethyl groups and triple bonds in cyclizations and in cyclic compounds.

For the cyclization the method of Wotiz *et al.* and Dale *et al.*^{2,3} was used, the reaction between α,ω -dibromoalkanes and the disodium salt of α,ω -diynes in liquid ammonia. The dibromides used in the cyclizations were first synthesized in eight (and nine) steps from

β,β -dimethylglutaric acid, the *gem*-dimethyl-substituted nonadiyne in five steps from the same source.

The cyclization reactions were slow in liquid ammonia at -30°C , and at least five days were needed. The concentration in the cyclization step was *ca.* 0.1 M; however, the poor solubility in liquid ammonia makes it likely that the actual concentrations of dissolved reactants were lower.

The results of the cyclizations to two 16- and one 18-membered rings are shown in Table 1. The isolation of the cyclic diynes from the reaction mixture was difficult and the methods that had to be used and the loss of material differed for the three cyclic diynes. The yields are therefore given both as weight of isolated cyclic product and as cyclic product present in the reaction mixture determined by gas chromatography, the last values most probably being closest to the real cyclization yields.

5,5,13,13-Tetramethylcyclohexadeca-1,8-diyne. The most probable conformation of 5,5-dimethylnona-1,8-diyne before cyclization has

Table 1. Yields in cyclizations of bis-*gem*-dimethyl-substituted dibromides with terminal diynes.

Cyclic product	Reactants		Reaction time, d	Yield of cyclic product, %	
	Dibromide	Diyne		Isolated	In reaction mixture
5,5,13,13-Tetramethylcyclohexadeca-1,8-diyne	1,7-dibromo-4,4-dimethylheptane	5,5-dimethylnona-1,8-diyne	5½	15	34
10,10,13,13-Tetramethylcyclohexadeca-1,5-diyne	1,10-dibromo-4,4,7,7-tetramethyldecane	hexa-1,5-diyne	5	13	40
12,12,15,15-Tetramethylcyclooctadeca-1,7-diyne	»	octa-1,7-diyne	6	17	33

Fig. 1. Conformations in cyclization of 5,5-dimethylnona-1,8-diyne and 1,7-dibromo-4,4-dimethylheptane.

been described earlier^{4,5} and is seen in Fig. 1 together with the conformation of 1,7-dibromo-4,4-dimethylheptane most favourable for cyclization.⁵ There is some distance between the reaction centres and the yield was 15 %.

Cyclization with the same *gem*-dimethyl substituted diyne, but without dimethyl groups on the dibromide chain was tried earlier,⁵ but resulted in no cyclic diyne. This is in accordance with the even longer distance between the reaction centres in this case, because there is no *gem*-dimethyl group that causes a bend on the carbon chain.

The best conformation of the unsubstituted cyclic hexadecadiyne described earlier by Dale *et al.*⁶ with parallel acetylenic bonds is not likely for the 5,5,13,13-tetramethylcyclohexadeca-1,8-diyne, because of the space-demanding *gem*-dimethyl groups. It is also difficult to find other low-energy conformations for the compound, and this explains why it is a liquid and does not crystallize even after cooling to -100°C .

10,10,13,13-Tetramethylcyclohexadeca-1,5-diyne. The most probable conformation of the 4,4,7,7-tetramethyl substituted carbon chain in cyclizations has been discussed earlier.⁷ Of the two conformations of hexa-1,5-diyne (*anti* and *gauche*) only the *gauche* form has to be considered in cyclizations. In Fig. 2 is shown how well these conformations of the reactants fit together for an almost strainfree compact conformation of the 10,10,13,13-tetramethylcyclohexadeca-1,5-diyne.

As shown in Table 1 the cyclization yield of this reaction (determined by gas chromatography) was the highest found in these cyclizations.

The fact that the compound is crystalline, m.p. 50°C , is also in good agreement with the possibility of having a low energy conformation. The enthalpy and entropy of melting were $\Delta H = 4.5$ kcal/mol and $\Delta S = 14.0$ e.u. The infrared spectra were taken of the crystals in potassium bromide and dissolved in carbon disulfide, Fig. 3. Although the spectra are not identical in the two phases, the absorption bands of the crystalline state are strong also in the spectrum of the solution, indicating that the crystal conformer is a main component also in solution.

12,12,15,15-Tetramethylcyclooctadeca-1,7-diyne. For octa-1,7-diyne the +*gauche*, *anti*, +*gauche* form seems best fitted for cyclization, because here the bonds are bent so as to bring the end groups on the same side of the molecular chain. With the most probable conformation of 1,10-dibromo-4,4,7,7-tetramethyldecane, mentioned above and shown in Fig. 2, the reacting end groups will be in reasonably close contact for the final cyclization. A suggestion for a somewhat open conformation of the cyclic compound with retention of the conformations of the reactants is shown in Fig. 4. However, the

Fig. 2. Conformations in cyclization of 1,10-dibromo-4,4,7,7-tetramethyldecane with hexa-1,5-diyne.

Fig. 3. IR-spectra of 10,10,13,13-tetramethylcyclohexadeca-1,5-diyne in the crystalline state in KBr below 0 °C (a), and in carbon disulfide solution (b).

Fig. 4. Conformation of 12,12,15,15-tetramethylcyclooctadeca-1,7-diyne.

cyclic diyne is a liquid and does not crystallize by cooling to -100°C , which indicates that one preferred conformation does not exist for this compound.

EXPERIMENTAL

5,5,13,13-Tetramethylcyclohexadeca-1,8-diyne. 1,7-Dibromo-4,4-dimethylheptane was first synthesized in 8 steps⁹ and 5,5-dimethylnona-1,8-diyne in 4 steps from β,β -dimethylglutaric acid.⁴

Sodium (4.6 g = 0.2 mol) was dissolved in liquid ammonia (1 l) at -30°C in the presence of iron(III) nitrate as catalyst.⁹ The solution was stirred for 1 h and 5,5-dimethylnona-1,8-diyne (14.8 g = 0.1 mol) added dropwise. After another hour of stirring 1,7-dibromo-4,4-dimethylheptane (28.6 g = 0.1 mol) was added slowly and the ammonia solution refluxed at -30°C for 5½ d by use of an acetone/solid carbon dioxide condenser. Ether (250 ml) was added and the ammonia permitted to evaporate. Undissolved residue was dissolved in water, the water layer was extracted 3 times with ether, all ether extracts were dried with magnesium sulfate. After filtration the ether was distilled off and the unreacted 5,5-dimethylnona-1,8-diyne also removed by distillation. The residue was chromatographed on a column with basic alumina. Elution with benzene-pentane 1:10, gave 5,5,13,13-tetramethylcyclohexadeca-1,8-diyne (4.08 g = 15 %). Mol.w. 272. (Mass spectrometry). B.p. $148-154^{\circ}\text{C}/0.04\text{ mmHg}$.

The product was unstable and elemental analysis could only be made of the fully hydrogenated product.¹⁰

4,4,7,7-Tetramethyldecane-1,10-diol. 4,4,7,7-Tetramethylsebacic acid¹¹ was synthesized in 7 steps from β,β -dimethylglutaric acid.

Lithium aluminium hydride (11.4 g = 0.3 mol)

was suspended in dry ether (2 l). 4,4,7,7-Tetramethylsebacic acid (51 g = 0.2 mol) dissolved in dry ether (800 ml) was added dropwise to the vigorously stirred solution. After 39 h of stirring at room temperature and 2 h of refluxing excess of hydride was destroyed by addition of water. Hydrolysis was carried out with 10 % sulfuric acid (600 ml). After separation of the ether layer the aqueous layer was extracted 3 times with ether. The combined ethereal extracts were washed with sodium hydrogen carbonate solution, dried with magnesium sulfate and filtered. The ether was removed, and the residue distilled, fraction 134–138 °C/0.05 mmHg was 4,4,7,7-tetramethyldecane-1,10-diol. (Found: C 72.94; H 12.80. Calc. for $C_{14}H_{30}O_2$: C 72.98, H 13.13). After repeated treatment with lithium aluminium hydride, of the residue from vacuum distillation, the total yield was 66 % (30.6 g).

1,10-Dibromo-4,4,7,7-tetramethyldecane-4,4,7,7-Tetramethyldecane-1,10-diol (29.7 g = 0.12 mol) was treated at 120 °C with hydrogen bromide until absorption was complete. The product was extracted with light petroleum, the extract washed with water, with some drops of concentrated sulfuric acid and finally with sodium hydrogen carbonate solution. After drying with calcium chloride, filtration and removal of solvent the dibromide was isolated by vacuum distillation. Fraction, b.p. 150–152 °C/0.2 mmHg was 1,10-dibromo-4,4,7,7-tetramethyldecane (36.1 g = 85 %). (Found: C 47.59; H 7.73; Br 44.71. Calc. for $C_{14}H_{28}Br_2$: C 47.23; H 7.93; Br 44.89).

10,10,13,13-Tetramethylcyclohexadeca-1,5-diyne. Sodium (2.3 g = 0.1 mol) was dissolved in liquid ammonia (1 l) as described above. After 1 h of stirring freshly distilled hexa-1,5-diyne (Farchan Research Laboratories) (3.9 g = 0.05 mol) was added dropwise. Stirring was continued, and after another hour 1,10-dibromo-4,4,7,7-tetramethyldecane (17.8 g = 0.05 mol) was added slowly. The solution was stirred and the ammonia refluxed for 5 d. The product was isolated as described above for 5,5,13,13-tetramethylcyclohexadeca-1,8-diyne. Recrystallization from ethanol gave 10,10,13,13-tetramethylcyclohexadeca-1,5-diyne (1.75 g = 13 %). Mol.w. 272 (mass spectrometry). (Found: C 87.94; H 11.88. Calc. for $C_{26}H_{32}$: C 88.16; H 11.84).

12,12,15,15-Tetramethylcyclooctadeca-1,7-diyne. As described above, sodium (1.98 g = 0.09 mol) was dissolved in liquid ammonia (0.7 l) and stirred for 1 h. Octa-1,7-diyne¹² (4.55 g = 0.045 mol) was added dropwise. After another hour of stirring 1,10-dibromo-4,4,7,7-tetramethyldecane (15.3 g = 0.045 mol) was added slowly and the solution refluxed at –30 °C for 6 d. Ether was added (300 ml) and the ammonia permitted to evaporate. Then water was added, (250 ml) and the water layer extracted 3 times with ether. All ether extracts were washed successively with 2 N hydrochloric acid, 10 % sodium hydrogen carbonate and water, dried

with magnesium sulfate, filtered and the ether distilled off. Unreacted octa-1,7-diyne was removed by distillation and the rest vacuum-distilled at low pressure. Fraction b.p. 154–156 °C/0.35 mmHg was 12,12,15,15-tetramethylcyclooctadeca-1,7-diyne (2.14 g = 17 %). Mol.w. 300 (mass spectrometry). (Found: C 87.98; H 11.87. Calc. for $C_{22}H_{26}$: C 87.92; H 12.08).

Repeated distillations were necessary because the boiling points of the dibromide and the cyclic diyne were close. Column chromatography was impossible because the retention time of the two compounds with pentane was the same. For the elemental analyses isolation by gas chromatography was necessary.

The infrared spectra were recorded in a Perkin-Elmer Grating Infrared Spectrophotometer 457. For the calorimetric measurements a Perkin-Elmer Differential Scanning Calorimeter IB was used.

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