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The Synthesis of Bis(*gem*-dimethyl)cycloalkanones and Tetrakis(*gem*-dimethyl)cycloalkanediones

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By Dieckmann, Ziegler, and Blomquist cyclization of doubly *gem*-dimethyl-substituted diesters, dinitriles, and diketenes, respectively, medium-ring monoketones and large-ring diketones are obtained. The yield of monoketone in the diester cyclization depends strongly on the relative position of the *gem*-dimethyl groups and can be correlated wit the favoured conformation of the diester chain.

For the synthesis of macrocyclic hydrocarbons having *gem*-dimethyl substituents in such relative positions as to fit "corner" positions of diamond-lattice conformations,[1] we have already described a limited synthetic route *via* diacetylenic hydrocarbons.[2] Another route *via* macrocyclic diketones as intermediates proved to be more general and useful and will be reported in this paper.

Three well-established and stoichiometrically equivalent methods are available for the preparation of unsubstituted cyclic ketones, and they have all the advantage for the present purpose that when a synthesis is designed for a medium-ring monoketone, also the large-ring diketone is obtained by doubling. These methods are known as the Dieckmann cyclization of diesters,[3] the Ziegler cyclization of dinitriles,[4] and the Blomquist cyclization of diketenes.[5]

SYNTHETIC PATHS

Several approaches were tried for the synthesis of the necessary *gem*-dimethyl substituted diesters, dinitriles, or bis-acid chlorides. Thus, the reaction between 1,3-dibromo-2,2-dimethylpropane and potassium cyanide failed completely. This was not unexpected, since the neopentyl-like steric hindrance had already been found to prevent the reaction between the same dibromide and sodium acetylide.[2] Also, double addition of sodium malonate to phorone was unsuccessful.

From β,β-dimethylglutaric acid it was possible to build up two series of bis(*gem*-dimethyl) substituted dicarboxylic acid derivatives, some of which

have been described earlier. [6-8] The syntheses followed two different, although similar routes, both starting from the mono-methyl ester. One series of compounds was obtained by the Kolbe anodic coupling [6] in the first step to give a suberic acid derivative, which then by bilateral chain extension according to standard methods gave a sebacic acid and a dodecanedioic acid derivative. These compounds all have two methylene groups between the dimethyl branchings. A second series of compounds was obtained through a first step involving a Blomquist ketene dimerization [7] after conversion of the free carboxylic acid group to the acid chloride.[9] Subsequent hydrolysis, decarboxylation, and Wolff-Kishner reduction gave an azelaic acid derivative, which then by bilateral chain extension gave an undecanedioic acid and a tridecanedioic acid derivative. These compounds all have three methylene groups between the dimethyl branchings.

The cyclization method used depended on the type of end-group obtained by chain extension and presented no problem in the dinitrile cyclization or the ester cyclization when the obtained cyclic diketone was an 18-membered or larger ring. However, the diesters of tetramethylsuberic and tetramethylazelaic acid gave no 14- and 16-membered rings, the former only 7-ring compounds (mono-ketone and small amounts of 2-carboxy-3,3,6,6-tetramethylcycloheptene). Starting material was largely recovered, so that it is clear that the main reason is a low reactivity due to the proximity of the dimethyl branching, which hinders either the attack on the α-CH_2 group by the base or, more likely, attack by the formed bulky anion on the carbonyl carbon of another ester group.

The dinitrile ought to be less bulky, but an attempt to prepare the 14-membered ring by Ziegler cyclization also failed, and did not even give the 7-membered ring. It was expected that the Blomquist cyclization should have the best chance to succeed, as both the ketene group and its dimerization product, the β-lactone, would be still less bulky and the reaction more rapid and less reversible. This proved to be the case, and both the 14- and 16-membered cyclic diketones were obtained in moderate yield. Surprisingly, the corresponding monoketones were not formed.

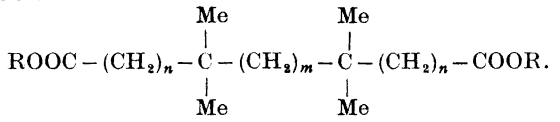
The reaction conditions had to be somewhat modified from those reported for the cyclization of compounds carrying no methyl substituents. Thus, the Dieckmann cyclization as performed here differed from the procedure described by Leonard and Schimelpfenig [3] in that longer reaction times were needed, and that stronger acid and a longer reaction time were necessary to effect the subsequent decarboxylation. The dinitrile cyclization was carried out according to Ziegler,[4] but the decarboxylation time had to be increased from 5 to 24 h. The ketene cyclization gave no ring compound when the procedure of Blomquist and Spencer [5] was followed. Because of the thermal instability of ketene dimers the temperature had to be kept low. Furthermore, the hydrolysis was carried out in dioxan instead of ethanol to prevent competing ethanololytic opening of the β-lactone, which retarded the decarboxylation of the keto-acid.

DISCUSSION OF YIELDS

The obtained yields of cyclic mono- and diketones are compared in Tables 1, 2, and 3 for the three cyclization methods. These yields are also compared with yields obtained from corresponding dicarboxylic acid derivatives carrying no methyl substituents. Whereever observations exist, the quantity of unreacted starting material and the yield of polymer are also given.

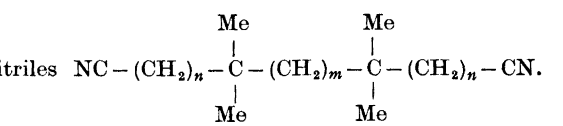
As one would have expected, the tendency to form polymers is highest for the unsubstituted compounds. Thus, only traces of polymers were found in the Dieckmann cyclization when *gem*-dimethyl substituents were present, while in a parallel run the unsubstituted sebacic diester gave 18 % of polymer. From Leonard and Schimelpfenig's publication [3] one can deduce that polymers were

Table 1. Dieckmann cyclization of diesters



m	n	Ring atoms in mono- and diketone	Recovered diacid (%)	Yields [a] Monoketone (%)	Diketone (%)	Polymer (%)
2	1	7, 14	34	30 (47)	0 (0)	0
3	1	8, 16		0 (15)	0 (11)	
2	2	9, 18	10 (0)	30 (0)	7 (25)	0 (18)
3	2	10, 20		0.4 (0)	27 (12)	
2	3	11, 22	9	13 (0.5)	15 (23)	0.9
3	3	12, 24		8 (0.5)	10 (16)	

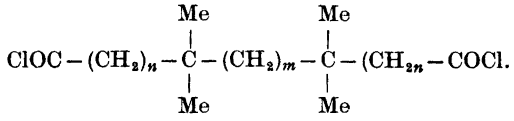
[a] Yield of corresponding unsubstituted compound in parenthesis as reported by Leonard and Schimelpfenig,[3] except for cyclononanone-cyclooctadecanedione.

Table 2. Ziegler cyclization of dinitriles 

m	n	Ring atoms in mono- and diketone	Recovered diacid (%)	Yields [a] Monoketone (%)	Diketone (%)	Polymer (%)
2	1	7, 14	0	traces (96)	0 (0)	traces
2	2	9, 18		2.4 (2.8)	18 (62)	traces
3	2	10, 20	0	0 (0.4)	24 (70)	0

[a] Yield of corresponding unsubstituted compound in parenthesis.[4]

Table 3. Blomquist cyclization of ketenes from



m	n	Ring atoms in mono- and diketone	Yields [a] Monoketone (%)	Diketone (%)
2	1	7, 14	0 (33)	8 (10)
3	1	8, 16	0 (0)	10 (31)

[a] Yield of corresponding unsubstituted compound in parenthesis.[5,13]

usually obtained from unsubstituted diesters. The lower reactivity of the substituted compounds is of course reflected in the larger quantity of recovered starting material.

More difficult to understand is the much lower yield of 7- and 9-ring monoketone in the dinitrile cyclization than in the diester cyclization, since these two reactions and the formed intermediates should be quite similar. The complete absence of 7- and 8-ring monoketone in the Blomquist cyclization of substituted diketenes is also surprising, since the 7-ring is formed in a yield of 33 % when no substituents are present, and *gem*-dimethyl substitution generally favours formation of small rings.[10] It may perhaps be due to the large valency angles imposed by the fused β-lactone group of the intermediate, combined with the restrictions that the *gem*-dimethyl groups put on its conformation.

Even more intriguing is the observation that the yield of monoketone in the Dieckmann cyclization depends on whether the dimethyl branching points are separated by two or three methylene groups (Table 1). On the basis of the well-established [10] cyclization-promoting "*gem*-dimethyl effect" one might have expected that the yield of cyclic monoketones, as compared with the corresponding unsubstituted compounds, should increase quite generally, and that the ratio of cyclic mono- to cyclic diketone should also increase. The data of Table 1 show that this is only the case when the ring is 9-membered or higher, and even then there is much variation. The effect is most pronounced when the two *gem*-dimethyl substituted atoms are separated by two CH_2-groups and less pronounced when they are separated by three CH_2-groups. For the 7- and 8-ring monoketones an apparent negative *gem*-dimethyl effect is observed, but as already noted this must be due to the low reactivity of the starting diester. It looks as if the pattern from the higher members extends down the series, since only the cycloheptane derivative with two CH_2-groups between the branching points, and not the cyclo-octane derivative with three, has been isolated.

An explanation of the observed difference in cyclization-promoting effect of two *gem*-dimethyl groups in 1,4- and in 1,5-position can be arrived at by

considering the conformational possibilities of the diester chain. Cyclization to rings which are 9-membered or smaller is assumed to require a sequence of only *gauche*-bonds, while for cyclization to the larger medium rings separate *anti*-bonds can also be accepted, but not an uninterrupted sequence of two or more *anti*-bonds. The chain CC-bonds immediately adjoining the *gem*-dimethyl-substituted carbon atoms have two times higher probability of being *gauche* than *anti* since no enthalpy difference is expected. In the 1,4 case there is one CH_2-CH_2 bond in the middle, and both the low-energy *anti*-form and the higher energy *gauche*-form (Fig. 1) can lead to cyclization, the former being limited to 10-membered and higher rings.

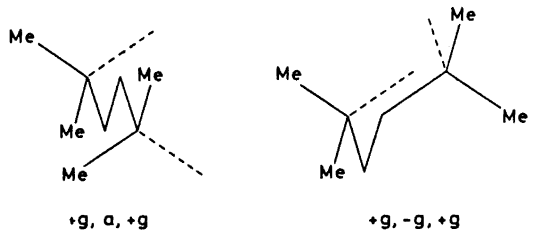


Fig. 1. The conformations of a 1,4-*gem*-dimethyl substituted chain most suitable for cyclization (g = *gauche*, a = *anti*, both with respect to the chain).

In the 1,5 case, on the other hand, there are two bonds of CH_2-CH_2 type in the middle of the chain, and the lowest energy form, *anti,anti* (Fig. 2), will not here permit cyclization except possibly to the 12-membered ring. The next to lowest energy form, *anti, gauche*, will permit cyclization only to 10-membered and higher rings. The probability of having two *gauche*-bonds, and more specifically of the chirality sequence required for cyclization (Fig. 2), is very much lower.

The physical properties of the cyclic mono- and diketones and a discussion of their comformations have already been given in preliminary publications,[11,12] and will be fully reported later.

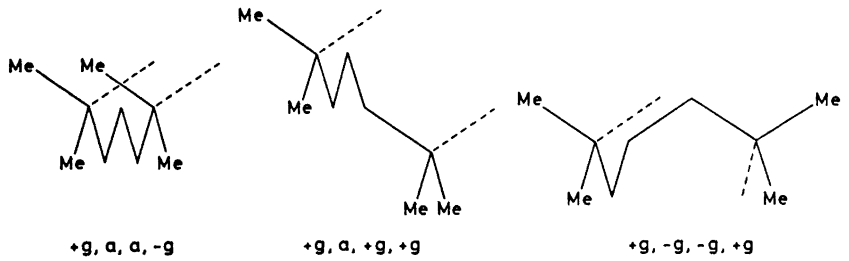


Fig. 2. The conformations of a 1,5-*gem*-dimethyl substituted chain most suitable for cyclization (g = *gauche*, a = *anti*, both with respect to the chain).

EXPERIMENTAL

3,3,6,6-Tetramethylsuberic acid dichloride. Dimethyl 3,3,6,6-tetramethylsuberate was prepared from the monomethyl ester of 3.3-dimethylglutaric acid by electrolysis, and hydrolysed to the free acid with alcoholic potassium hydroxide.[6] A mixture of 3,3,6,6-tetramethylsuberic acid (54 g) and thionyl chloride (195 g) was heated at 60° for 2 h, then stirred and heated on the water bath until evolution of hydrogen chloride and sulfur dioxide had ceased. The excess of thionyl chloride was evaporated in vacuum. On distillation 3,3,6,6-tetramethylsuberic acid dichloride was obtained (33 g = 53 %), b.p. 100°/0.2 mm. (Found: C 54.22; H 7.98; Cl 25.19. Calc. for $C_{12}H_{20}O_2Cl_2$: C 53.94; H 7.55; Cl 26.54.)

3,3,6,6,10,10,13,13-Octamethylcyclotetradecane-1,8-dione. A solution of 3,3,6,6,-tetramethylsuberic acid dichloride (10 g) in dry ether (25 ml) was added to a solution of dry triethylamine (38 ml) in dry ether (250 ml) at 0° under nitrogen. The mixture was stirred at 0° for 10 h, then at room temperature for three days. The precipitated triethylamine hydrochloride and insoluble ketene polymers were removed by filtration, the filtrate washed twice with 5 % hydrochloric acid, then with water, and dried over magnesium sulphate. By evaporation of the ether, the crude "dimerized" ketenes (4.5 g) were obtained. These were added to a solution of potassium hydroxide (3 g) in water (13 ml) and dioxan (75 ml), and the mixture refluxed for two days. Dioxan and some water was distilled off, the rest diluted with water, extracted four times with ether, and the ether solution dried over magnesium sulphate. After evaporation of the ether, the residue was dissolved in pentane and filtered through alumina to give the crude dione (0.29 g). Crystallization from pentane gave the pure 3,3,6,6,10,10,13,13-octamethylcyclotetradecane-1,8-dione, m.p. 219°. Mol. wt. 336 (mass spectrometry). (Found: C 78.91; H 11.53. Calc. for $C_{22}H_{40}O_2$: C 78.51; H 11.98.) The ether-insoluble ketenes (6.5 g) after the same treatment with alkali gave a further small quantity (0.15 g) of the dione. A further quantity (0.05 g) was obtained by decarboxylation of the rest in acetic acid/water/sulphuric acid (6:1:1) together with ether-soluble "dimerized" ketenes which had not been completely decarboxylated in alkali. The total yield was 0.50 g (= 8 %). No other homologs than the octamethylcyclotetradecanedione could be isolated.

3,3,7,7-Tetramethylazelaic acid dichloride. The monomethyl ester of 3,3-dimethylglutaric acid [6] was converted to 4-carbomethoxy-3,3-dimethylbutyryl chloride, which by ketene dimerization, subsequent decarboxylation and Wolff-Kishner reduction gave the 3,3,7,7-tetramethylazelaic acid.[7] Chlorination of this acid (24 g) with thionyl chloride (50 g) was carried out as described above for tetramethylsuberic acid dichloride. On distillation 3,3,7,7,-tetramethylazelaic acid dichloride was obtained (17 g = 61 %), b.p. 116°/0.1 mm. (Found: C 55.48; H 7.52; Cl 25.07. Calc. for $C_{13}H_{22}O_2Cl_2$: C 55.51; H 7.88; Cl 25.22.)

3,3,7,7,11,11,15,15-Octamethylcyclohexadecane-1,9-dione. A solution of 3,3,7,7-tetramethylazelaic acid dichloride (6.2 g) in dry ether (20 ml) was allowed to react with triethylamine (25 ml) dissolved in ether (200 ml) in the manner described for the synthesis of octamethylcyclotetradecanedione. The crude "dimerized" ketenes (4.3 g) were hydrolysed with potassium hydroxide (4 g) in water (8 ml) and dioxan (100 ml), also as described before, to give 3,3,7,7,11,11,15,15-octamethylcyclohexadecane-1,9-dione (0.15 g), m.p. 150°. Mol. wt. 364 (mass spectrometry). (Found: C 79.34; H 11.39. Calc. for $C_{24}H_{44}O_2$: C 79.06; H 12.16.) By decarboxylation in acetic acid/water/sulphuric acid (1:1:3) of the unreacted part, more octamethylcyclohexadecanedione (0.4 g) could be obtained (total yield 0.55 g = 10 %). No other cyclic ketone could be isolated. Polymeric products insoluble in ether amounted to 40 %.

4,4,7,7-Tetramethylsebacic acid and derivatives. The dimethyl ester of 3,3,6,6-tetramethylsuberic acid was prepared by electrolysis of the monomethyl ester of 3,3-dimethylglutaric acid.[6] This diester was reduced to the diol by lithium aluminium hydride and converted into the dibromide by anhydrous hydrogen bromide.[6] *Via* the dinitrile and corresponding diacid the diethyl ester of 4,4,7,7-tetramethylsebacic acid was obtained.[8]

4,4,7,7,-Tetramethylcyclononanone and 4,4,7,7,13,13,16,16-octamethylcyclooctadecane-1,10-dione. A, by Dieckmann cyclization.[3] To a mixture of dry xylene (250 ml) and *t*-butyl alcohol (45 g) potassium (9.4 g) was added under nitrogen. Excess of *t*-butyl alcohol and about 25 ml of xylene were distilled from the flask. A solution of diethyl 4,4,7,7-tetramethylsebacate (13 g) in xylene (100 ml) was added dropwise to the stirred and

refluxing solution during 6 h and alcohol/xylene allowed to distil out at the same rate. Thereafter stirring and refluxing were continued for 12 h. The solution was made acidic with acetic acid, washed with water, filtered, and the filtrate concentrated to about 200 ml. Decarboxylation was effected by refluxing with 3 N HCl (100 ml) for 40 h. The xylene solution was washed with 10 % sodium bicarbonate, then with water. From the dried ether solution a crystalline product (8 g) was obtained which by distillation *in vacuo* gave the pure 4,4,7,7-tetramethylcyclononanone (2.5 g = 30 %), b.p. 122°/14 mm. It melted at 46° after crystallization from chloroform. Mol. wt. 196 (mass spectrometry). (Found: C 79.67; H 12.08. Calc. for $C_{13}H_{24}O$: C 79.53; H 12.32.) A higher boiling fraction contained the 4,4,7,7,13,13,16,16-octamethylcyclooctadecane-1,10-dione (0.6 g = 7 %), b.p. 240°/0.5 mm. It melted at 219° after crystallization from methanol. Mol. wt. 392 (mass spectrometry). (Found: C 79.56; H 12.03. Calc. for $C_{26}H_{48}O_2$: C 79.53; H 12.32.)

B, by Ziegler cyclization.[4] Sodium (15 g) was melted and pulverized by rigorous stirring in dry, heated xylene under nitrogen. The mixture was cooled while stirring, xylene decanted off, and the sodium washed with dry ether. More dry ether (1300 ml) was added, and with slow stirring in a nitrogen atmosphere a solution of styrene (34 g) and redistilled methylaniline (87 g) in dry ether (200 ml) was added dropwise. When all the sodium had dissolved, the solution was refluxed for half an hour, whereafter the 4,4,7,7-tetramethylsebacic dinitrile [8] (22.1 g) dissolved in dry ether (100 ml) was added dropwise over three days. The refluxing was continued for this period and for 11 days thereafter. Water was then added until the solution became clear. The precipitate was filtered off, and the water phase extracted with ether. After drying over magnesium sulphate, the ether was evaporated, and ethylbenzene and methylaniline were distilled off at reduced pressure on a water bath. The residue was refluxed for 20 h with 50 % sulphuric acid (200 ml). The reaction mixture was extracted with ether, the ether solution washed with water and then with sodium hydrogen carbonate, and dried over magnesium sulphate. Vacuum distillation gave 4,4,7,7-tetramethylcyclononanone (0.47 g = 2.4 %) and 4,4,7,7,13,13,16,16-octamethylcyclooctadecane-1,10-dione (3.6 g = 18.4 %). No other homologs could be isolated and only traces of polymers were found.

3,3,7,7-Tetramethylnonane-1,9-diol. A solution of 3,3,7,7-tetramethylazelaic acid (18 g) in dry ether (250 ml) was added to a vigorously stirred solution of lithium-aluminium hydride (15 g) in dry ether (1500 ml) under nitrogen and refluxed overnight. After hydrolysis with 10 % sulphuric acid (500 ml) and extraction with ether, the ether solutions were washed with sodium hydrogen carbonate solution and dried over magnesium sulphate. Distillation gave the 3,3,7,7-tetramethylnonane-1,9-diol (11 g = 69 %), b.p. 149°/0.2 mm. (Found: C 72.31; H 13.24. Calc. for $C_{13}H_{28}O_2$: C 72.16; H 13.05.)

1,9-Dibromo-3,3,7,7-tetramethylnonane. 3,3,7,7-tetramethylnonane-1,9-diol (46 g) was heated to 120° and hydrogen bromide passed into the liquid until the absorption was complete (6 h). The product was extracted with light petroleum (400 ml). The extract was washed with water, then with sodium hydrogen carbonate solution, and dried over calcium chloride. Evaporation afforded the 1,9-dibromo-3,3,7,7-tetramethylnonane (65 g = 89 %), m.p. 27° after crystallization from pentane. (Found: C 45.53; H 7.56; Br 46.89. Calc. for $C_{13}H_{26}Br_2$: C 45.63; H 7.66; Br 46.71.)

4,4,8,8-Tetramethylundecane-11,1-dinitrile. A mixture of 1,9-dibromo-3,3,7,7-tetramethylnonane (63 g), ethanol (450 ml), potassium cyanide (40 g) and water (90 ml) was refluxed for two days. Most of the alcohol was removed by distillation, the residue diluted with water and extracted with ether. The ether solution was dried over magnesium sulphate and evaporated. Distillation gave the 4,4,8,8-tetramethylundecane-1,11-dinitrile (29 g = 68 %), b.p. 158°/0.1 mm, m.p. 26°, mol. wt. 234 (mass spectrometry). (Found: C 76.98; H 11.36; N 11.79. Calc. for $C_{15}H_{26}N_2$: C 76.86; H 11.18; N 11.95.)

4,4,8,8-tetramethylundecane-1,11-dioic acid. A solution of 4,4,8,8-tetramethylundecane-1,11-dinitrile (24 g) and potassium hydroxide (32.5 g) in ethanol (175 ml) and water (40 ml) was refluxed for 24 h. The alcohol was distilled off, the water solution acidified with hydrochloric acid (50 %), extracted with ether and dried over magnesium sulphate. Evaporation of the ether gave the dioic acid (25 g = 90 %) which was used for the next stage without further purification. After recrystallization from petrol ether it melted at 80°. (Found: C 66.05; H 10.16. Calc. for $C_{15}H_{28}O_4$: C 66.14; H 10.36.)

Diethyl ester of 4,4,8,8-tetramethylundecane-1,11-dioic acid. The dioic acid (25 g) was esterified in a mixture of ethanol (80 ml), toluene (40 ml), and sulphuric acid (3 drops), and formed water removed by azoetropic distillation. Vacuum distillation gave the

diethyl ester (24 g = 80 %), b.p. 205°/13 mm. Mol. wt. 328 (mass spectrometry). (Found: C 69.76; H 10.91. Calc. for $C_{19}H_{36}O_4$: C 69.47; H 11.05.)

4,4,8,8-Tetramethylcyclodecanone and 4,4,8,8,14,14,18,18-octamethylcycloeicosane-1,11-dione. A, by Dieckmann cyclization. The procedure was as described above for octamethylcyclooctadecanedione. The diethyl ester of 4,4,8,8-tetramethylundecane-1,11-dioic acid (23 g) in dry xylene was added dropwise to a solution of potassium *t*-butoxide (from 11 g of potassium) in dry xylene during 18 h, alcohol/xylene allowed to distil out at the same rate, and refluxing continued for three days. Refluxing with hydrochloric acid (3 N) for two days was not sufficient to decarboxylate the cyclization product, which was subsequently refluxed with a mixture of sulphuric acid, water, and acetic acid (1:1:3) for 12 h. The solution was extracted with methylene chloride, the extract washed with sodium hydrogen carbonate, then with water and dried over sodium sulphate. Vacuum distillation gave both monomeric, dimeric, and trimeric cyclic ketones:

4,4,8,8-Tetramethylcyclodecanone (0.05 g = 0.35 %), m.p. 105°. Mol. wt. 210 (mass spectrometry).

4,4,8,8,14,14,18,18-Octamethylcycloeicosane-1,11-dione (4.0 g = 27 %), m.p. 145°. Mol. wt. 420 (mass spectrometry). The substance absorbs water and does not give a satisfactory analysis. (Found: C 79.30; H 12.00. Calc. for $C_{28}H_{52}O_2$: C 79.93; H 12.46.)

4,4,8,8,14,14,18,18,24,24,28,28-Dodecamethylcyclotriacontane-1,11,21-trione (0.5 g = 3.5 %), liquid, b.p. *ca.* 300°/0.05 mm. Mol. wt. 630 (mass spectrometry).

B, by Ziegler cyclization. The procedure was as described above for octamethylcyclooctadecanedione, but starting from 4,4,8,8-tetramethylundecane-1,11-dinitrile. No cyclic monomer was found. The yield of the dimer, 4,4,8,8,14,14,18,18-octamethylcycloeicosane-1,11-dione was 24 %. No higher homologs or polymer could be isolated.

5,5,8,8-Tetramethyldodecane-1,12-dioic acid. To a cooled solution of sodium (13.4 g) in abs. ethanol (350 ml) was added diethyl malonate under nitrogen. After half an hour of stirring, a solution of 1,8-dibromo-3,3,6,6-tetramethyloctane (93 g) in abs. ethanol (50 ml) was added, and the solution refluxed on the water bath for 24 h. The precipitate was filtered off, and the filtrate boiled with a solution of potassium hydroxide (75 g) in water (250 ml) for 2 h. The ethanol was distilled off, neutral substances extracted from the alkaline residue with ether, and the aqueous layer acidified with hydrochloric acid (6 N). The next day the precipitate was filtered off, washed with water and dried. Decarboxylation was effected by heating to 200° until evolution of carbon dioxide ceased. The crude 5,5,8,8-tetramethyldodecane-1,12-dioic acid (43 g = 53 %) melted at 133° after crystallization from carbon tetrachloride. The structure was proved by the fragmentation pattern in the mass spectrum. (Found: 66.39; H 10.04. Calc. for $C_{16}H_{30}O_4$: C 67.09; H 10.56.)

Diethyl ester of 5,5,8,8-tetramethyldodecane-1,12-dioic acid. The crude acid (43 g) was esterified in a mixture of ethanol (150 ml), toluene (75 ml), and sulphuric acid (0.3 ml), and formed water removed by azeotropic distillation. Vacuum distillation gave the diethyl ester (46 g = 84 %), b.p. 144°/0.2 mm. (Found: C 70.26; H 10.70. Calc. for $C_{20}H_{38}O_4$: C 70.13; H 11.18.)

5,5,8,8-Tetramethylundecanone and 5,5,8,8,16,16,19,19-octamethylcyclodocosane-1,12-dione. By Dieckmann cyclization and decarboxylation as described earlier, the diethyl ester of tetramethyldodecanedioic acid (25 g) afforded after distillation *in vacuo* 5,5,8,8-tetramethylundecanone (2.2 g = 13 %), b.p. 99°/0.2 mm, mol. wt. 224 (mass spectrometry) and 5,5,8,8,16,16,19,19-octamethylcyclodocosane-1,12-dione (2.6 g = 15 %), b.p. 220°/0.2 mm, m.p. 169 after crystallization from pentane, mol. wt. 448 (mass spectrometry). (Found: C 80.58; H 12.48. Calc. for $C_{30}H_{56}O_2$: C 80.29; H 12.58.) Some of the starting diester was recovered as the dioic acid (1.5 g = 9 %).

5,5,9,9-Tetramethyltridecane-1,13-dioic acid. The reaction of 1,9-dibromo-3,3,7,7-tetramethylnonane (25 g) with diethyl sodiomalonate was carried out as described above for tetramethyldodecanedioic acid and gave 5,5,9,9-tetramethyltridecane-1,13-dioic acid (18 g = 92 %), m.p. 185°. The identity was shown by the fragmentation in mass spectrometry.

Diethyl ester of 5,5,9,9-tetramethyltridecane-1,13-dioic acid. Esterification in ethanol/toluene/sulphuric acid by azeotropic distillation was tried but did not give the diester even after repeated distillations, but was successful following the procedure described by Newman.[14] The partially esterified acid (corresponding to 13 g of acid) was dissolved in cold 100 % sulphuric acid (125 ml) prepared by mixing equal quantities of 96 % sulphuric acid and 65 % fuming sulphuric acid. After 5 min, the solution was poured

into ice-cooled abs. ethanol (1000 ml) with vigorous stirring. Most of the alcohol was removed under reduced pressure, water (100 ml) added and the rest of the alcohol distilled off. The residue was extracted with ether, the ether solution washed with sodium carbonate solution to remove free acid, then with water, and dried over magnesium sulphate. Vacuum distillation gave the diethyl ester of 5,5,9,9-tetramethyltridecane-1,13-dioic acid (5 g = 32 %), b.p. 209/°9 mm. The identity was shown by fragmentation in mass spectrometry.

5,5,9,9-Tetramethylcyclododecanone and 5,5,9,9,17,17,21,21-octamethylcyclotetracosane-1,13-dione. The Dieckmann cyclization was performed as described earlier, but refluxing was extended to six days. From the diethyl ester of tetramethyltridecanedioic acid (5 g) was obtained 5,5,9,9-tetramethylcyclododecanone (0.26 g = 8 %), b.p. 108°/0.2 mm, m.p. 84°, mol. wt. 238 (mass spectrometry) and 5,5,9,9,17,17,21,21-octamethylcyclotetracosane-1,13-dione (0.31 g = 10 %), b.p. 220°/0.2 mm, 107°, mol. wt. 476 (mass spectrometry.)

3,3,6,6-Tetramethylcycloheptanone. The Dieckmann cyclization was carried out as described earlier. A solution of the dimethyl ester of 3,3,6,6-tetramethylsuberic acid [6] (15 g) in xylene was added dropwise to a solution of potassium *t*-butoxide (from 9.4 g potassium and 44 g *t*-butyl alcohol) during 12 h. Refluxing and removal by distillation of xylene/alcohol lasted 27 h. Decarboxylation was performed by refluxing in a mixture of sulphuric acid, water, and acetic acid (1:1:3) for 20 h. After extraction with ether, washing of the ether solution with 2 N sodium hydroxide solution, and drying over magnesium sulphate, vacuum distillation gave 3,3,6,6-tetramethylcycloheptanone (1.7 g = 17 %), b.p. 94°/12 mm, m.p. −7°, mol. wt. 168 (mass spectrometry). (Found: C 78.15; H 12.03. Calc. for $C_{11}H_{20}O$: C 78.51; H 11.98.)

A higher-boiling product proved to be *2-carboxy-3,3,6,6-tetramethylcycloheptene* (0.4 g = 4 %), b.p. 160°/12 mm, m.p. 130°, mol. wt. 196 (mass spectrometry). (Found: C 73.26; H 10.48. Calc. for $C_{12}H_{20}O_2$: C 73.43; H 10.27.) Unreacted ester was recovered as tetramethylsuberic acid (1.8 g = 18 %).

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