## BENEFICIAL ROLE OF CONFORMATIONAL 1,3-INTERACTIONS IN ACYLOIN CONDENSATION REACTIONS OF ESTERS OF SOME BRANCHED DICARBOXYLIC ACIDS

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According to [1,2], the presence of gem-dialkyl groupings facilitates the conversion of open systems to cyclic systems (the so-called gem effect). However, ring formation can be facilitated not only by a geminal, but also by a single branching of the chain [3,4]. In the ketonization of dicarboxylic acids a replacement of the  $CH_3$  group by a gem-dimethyl grouping does not increase the yield of the cyclic ketone, which was explained by the conformational 1,3-interaction of the side chains with the H atoms of the backbone chain [5-7]. For other reactions the absence of the gem effect was observed only for complex cases with high-molecular-weight compounds [3]. A number of facts, explained by the gem effect, can be interpreted in the light of 1,3-interactions. The accumulation of data for compounds, in which the gem groupings are replaced by single  $CH_3$  groups, like in [5], makes it possible to reevaluate the role of both the gem effect and 1,3-interactions.

In the acyloin condensation of the diesters of azelaic, 5, 5-dimethyl-, and 3, 3, 7, 7-tetramethylazelaic acids [8,9] the yields of the acyloins were 35-40, 66-70, and 84%. This order in the yields was attributed [9] to the gem effect. In the present paper, in order to verify the validity of this conclusion, we prepared the dimethylesters of azelaic (I), 5-methyl-(II), and 3, 7-dimethylazalaic (III) acids and subjected them to acyloin condensation under the same conditions. A comparison of the course of the yields of the acyloins obtained in the present paper and in [8,9] is shown in Fig.1. According to our data, the yields of the acyloins, the same as the yields of cyclanones from dicarboxylic acids [5], increase linearly from the unsubstituted acid to the acid that has two  $CH_3$  groups on different C atoms of the backbone chain. The data from [8,9] that are plotted in Fig.1 for the geminal analogs demonstrate a very similar relation. This permits the thought that the principal reason for the increase in the yields is common for all six cases and is not associated with the gem effect. At the same time, similar results ensue from the concepts regarding 1,3-interactions [5]. It is interesting that in [8] the yield of the acyloin from (II) (60%) is close to our data (56%) and the yield of the acyloin from 5,5-dimethylazelaic acid, but this fact was not given due importance in [8]. Only in [10] was it concluded that even one methyl facilitates cyclization, but the explanation of this fact evokes doubt.

A somewhat greater slope for the line that refers to the geminal compounds can be associated either with the existence of a small gem effect, which plays a subordinate role, or with an inadequate uniformity in setting up the experiment in [8,9]. The effect of small differences in the experimental conditions during acyloin condensation is well known. At the same time, different diesters of the gem-substituted acids, different solvents, and different reaction temperatures were used in [8,9]. For this reason the question relating to the difference in the slopes of the straight lines remains unanswered, although it does not affect the main conclusion regarding the important beneficial role of conformational 1,3-interactions in the acyloin condensation.

In [5] it was mentioned that the agreement of the experimental data with the conclusion that 1, 3-interactions exist between the side chains and the H atoms of the backbone chain is possibly associated with

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Fig.1. Effect of 1,3-interactions of side chains with H atoms of backbone chain of starting dicarboxylic acid diester on yields of acyloins. 1) Effect of single  $CH_3$  groups: dimethyl esters of azelaic (a), 5-methylazelaic (b) (o = our data, and + = data from [8]), and 3,7-di-methylazelaic (c) acids; 2) effect of geminal dimethyl groupings (dimethyl ester of azelaic (a'), diethyl ester of 5,5-dimethylazelaic (b'), and dimethyl ester of 3,3-7,7-tetramethylazelaic (c') acids [8,9]. n is the number of C atoms of the backbone chain that carry branching.

the fact that the ketonization of dicarboxylic acid salts takes place on the surface of the crystal faces, where the most favorable conformations of the molecules are more or less rigidly fixed. In the liquid and vapor phases, where the presence of energetically richer conformations is also possible [11], the picture of the 1,3-interactions can become complicated. During acyloin condensation the reaction takes place on the surface of the molten sodium as if in a two-dimensional liquid phase. For this reason it would be impossible to say in advance whether 1,3-interaction will be manifested in this more complicated case. It proved that the picture is also quite clear here. This encouraging result permits the thought that the gamut of cyclization reactions, in which the discussed effect is manifested, will be expanded even more in the future.

## EXPERIMENTAL METHOD

<u>Acyloin Condensation</u>. All of the experiments were run as described in [8,9,12], but under strictly identical conditions. Using a stirrer with ~5000 rpm, to 5.75 g of finely dispersed Na in 800 ml of abs. xylene was added in 8 h, at 125-130°C, in drops a solution of 0.05 mole of the dimethyl ester of the appropriate acid in 70 ml of abs. xylene. The reaction was run in a N<sub>2</sub> atmosphere, which had been freed of O<sub>2</sub> traces by passage at 150-160° over finely dispersed copper, which had been prepared by the reduction of CuO with H<sub>2</sub> below 175°, and then dried in a column packed with silica gel.

<u>4-Methylpimelonitrile (IV)</u>. Obtained from ethyl cyanoacetate via 3-methylglutaric acid [7], 3-methyl-1,5-pentanediol [13], and 3-methyl-1,5-dibromopentane [14]. Under conditions similar to those given in [15], from 179.7 g of this dibromide we obtained 87.7 g (87.6%) of (IV), bp 137.0° (2 mm);  $n_D^{20}$  1.4471. Found: C 70.25; H 8.93; N 20.34%. C<sub>8</sub>H<sub>12</sub>N<sub>2</sub>. Calculated: C 70.55; H 8.88; N 20.57%.

5-Methylazelaic Acid (V) and Its Dimethyl E ster (II). Using the method given in [15], we obtained 5-methylazelonitrile (VII) from (IV) via 4-methylpimelic acid, its dimethyl ester, 5-methyl-1,7-heptanediol [16], and the dibromide [17]. The hydrolysis of 29.3 g of (VII) with conc. HCl gave 35.3 g (97.7%) of crude (V), mp 64.1-65.1°, the esterification of which with MeOH gave 36.6 g (91.0%) of (II), bp 111.8° (1.3 mm);  $nD^{20}$  1.4399;  $d_4^{20}$  0.9975. Found: C 62.66; H 9.68%.  $C_{12}H_{22}O_4$ . Calculated: C 62.58; H 9.63%. Infrared spectrum: 1744 cm<sup>-1</sup> (carbalkoxyl CO). NMR spectrum ( $\delta$ , ppm): 3.54 s (6H, OCH<sub>3</sub>); 2.35-2.13 distorted t (4H, CH<sub>2</sub> of carbalkoxyls); 1.83-1.33 m [9H, CH(CH<sub>2</sub>CH<sub>2</sub>)<sub>2</sub>]; 0.85 d (3H, CH<sub>3</sub>).

The hydrolysis of 17.5 g of (II) with alcoholic KOH solution gave 15.1 g (98.0%) of pure (V) with mp 66.7-67.6°; and acid number 96.4. Found: C 59.21; H 8.85%.  $C_{10}H_{18}O_4$ . Calculated: C 59.39; H 8.97%. Infrared spectrum: 1705 cm<sup>-1</sup> (carboxyl CO).

The dimethyl ester of 3,7-dimethylazelaic acid (III) was obtained as described in [7].

Acyloins. a. Cyclononanol-2-one from (I). Yield 40-43%, bp 84-85° (2.5 mm). b. 6-Methylcyclononanol-2-one from (II). From 11.5 g of (II) we obtained 4.8 g (56%) of the acyloin, bp 98.2-99.2° (3 mm);  $n_D^{20}$  1.4847;  $d_4^{20}$  1.0281. Found: C 70.57; H 10.57%.  $C_{10}H_{18}O_2$ . Calculated: C 70.55; H 10.66%. Infrared spectrum: 1700 (CO) and 3470 cm<sup>-1</sup> (OH). NMR spectrum ( $\delta$ , ppm): 4.37-4.10 m (1H, CH at OH), 3.65 s (1H, OH); 3.17-1.13 m [13 H, CH(CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>)<sub>2</sub>]; 0.85 d (3H, CH<sub>3</sub>). c. 4, 8-Dimethylcyclononanol-2-one from (III). From 12.2 g of (III) we obtained 6.8 g (74%) of the acyloin, bp 105.0-106.0° (3 mm);  $n_D^{20}$  1.4790;  $d_4^{20}$  1.0024. Found: C 71.45; H 10.75%.  $C_{11}H_{20}O_2$ . Calculated: C 71.69; H 10.94%. Infrared spectrum: 1700 (CO) and 3475 cm<sup>-1</sup> (OH). NMR spectrum ( $\delta$ , ppm): 4.22-3.90 m (1H, CH at OH); 3.57 s (1H, OH); 2.98-1.00 m (CH<sub>2</sub>(CH<sub>2</sub>CHCH<sub>2</sub>)<sub>2</sub>; 0.95 d (3H, CH<sub>3</sub>); 0.87 d (3H, CH<sub>3</sub>).

## CONCLUSIONS

1. The yields of acyloins in acyloin condensation reactions are quite dependent on the presence of 1,3-interactions of the side chains with the H atoms of the backbone chain of the starting dicarboxylic acid esters. Contrary to the literature data, the gem effect has a comparatively small role in this reaction.

2. We synthesized 4-methylpimelonitrile, 5-methylazelaic acid and its dimethyl ester, and 4.8dimethylcyclononanol-2-one.

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