## KISHNER SYNTHESIS OF DI-, TRI-, AND TETRASUBSTITUTED CYCLOPROPANE HYDROCARBONS

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In 1910-1911, Kishner [1,2] discovered the method of synthesis of hydrocarbons of the  $C_nH_{2n+2}$  and  $C_nH_{2n}$  series consisting in the catalytic decomposition of alkylidenehydrazines and pyrazolines upon heating in the presence of potassium hydroxide or potassium hydroxide and platinum. Only in 1912, Wolff [3] decomposed alkylidenehydrazines with sodium ethoxide, and his name, without sufficient justification, became associated in the literature with the name of the Kishner reaction.

Kishner's reaction found the widest application in organic synthesis, and its mechanism was elucidated in a series of papers [4, 5, 6]. We decomposed pyrazoline bases by Kishner's method in order to prepare the corresponding ditetraalkylsubstituted derivatives of cyclopropane. It is noteworthy that Kishner had already noticed the ease of formation of pyrazoline bases from mesityl oxide and its homologs containing the group -C-CH=C-C. We

obtained such homologs from acid chlorides and isobutylene as described by Kondakov [5]. This reaction leads to the formation, together with mesityl oxide homologs, mostly of  $\beta$ -chloroketones. The latter, similarly to unsaturated ketones, react with hydrazine to give 3,5,5-pyrazolines [7, 8, 9] which yield, upon decomposition,1,1,2-trisubstituted cyclopropane derivatives. For the preparation of 1,1,2,3-tetrasubstituted alkyl derivatives of cyclopropane, we used  $\alpha$ ,  $\beta$ -alkyl substituted unsaturated ketones of the type R-C-C=C-C.

0

С

The formation of 3,4,5,5-tetrasubstituted pyrazoline derivatives from such ketones and hydrazine hydrate occurs rather slowly, with weak evolution of heat and low yields. This is due to the fact that hydrazine first reacts with an

 $\alpha,\beta$ -unsaturated ketone to give a hydrazone of the unsaturated type, viz.,  $\alpha,\beta$ -unsaturated ketone to give a hydrazone of the unsaturated type, viz., C-C=C-C which, because of the  $\| i \|$  R' C  $N-NH_2$   $\|$ R

screening influence of the radical R' next to the double bond, is slowly converted into 3,4,5,5-tetraalkylpyrazoline, and reacts much more rapidly with a second molecule of the ketone forming a ketazine and polymerization products. In comparison with, for instance, 3,5,5-trialkylpyrazolines, because of the increased steric hindrances during composition, 3,4,5,5-tetraalkylpyrazolines lead to lower yields of 3,4,5,5-tetraalkylcyclopropanes. As shown by Kishner, alkylidenehydrazines are easily split upon heating in the presence of potassium hydroxide, and it is necessary to add the alkali slowly and dropwise in order to avoid an explosive decomposition. As a rule, pyrazoline derivatives are rather stable compounds, and they decompose with difficulty upon continuous heating. Their decomposition is attained by different methods: by prolonged heating in sealed ampuls [3] or in an autoclave [10], by heating in a flask with a high-boiling solvent [11, 12], or in a catalytic furnace over potassium hydroxide [13], and, finally, by heating in a flask in the absence of catalysts [9]. In the present work, we decomposed pyrazoline derivatives by a method analogous to that used for the decomposition of alkylidenehydrazines.

## EXPERIMENTAL

The bases were decomposed in a long-necked 100 ml copper flask fitted with a tube for the insertion of a thermometer. The flask was connected to a two-necked adapter. In one of the necks of the adapter was fitted a dropping funnel with a long stem ending 2.5 cm above the layer of potassium hydroxide in the flask. The other neck was connected to a fractionating column (fitted with a thermometer), a condenser pointing downwards and cooled with ice, and a trap placed in a Dewar bottle filled with dry ice. The flask was charged with 30-50 g of dry potassium hydroxide (preliminarily dried by heating in a copper crucible at 300-350°), and heated to 270-310°. This temperature was maintained throughout the experiment. The pyrazoline base was slowly added from the dropping funnel. Its decomposition was accompanied by a continuous evolution of nitrogen. The hydrocarbon produced during the reaction, together with a small amount of the starting material, was dried over  $K_2CO_3$ , and distilled in a Favorskii flask to remove the base. The distilled hydrocarbon was washed with an equal volume of 50% acetic acid to remove the last traces of the base. After washing with alkali and water, the product was dried again over anhyrous potassium carbonate and distilled, first as such, and then, 3 to 5 times with the addition of metallic sodium, using fractionating columns with efficiencies of the order of 18-38 theoretical plates. Raman spectra were recorded for all the hydrocarbons obtained in these experiments.

First, in order to adjust the experimental conditions, 3,5,5-trimethylpyrazoline was decomposed to 1.1,2-trimethylcyclopropane, b. p. 52.5° (745 mm); d<sup>20</sup><sub>4</sub> 0.6944, n<sup>20</sup>D 1.3868. Reported b. p. 52.8°; d<sup>20</sup><sub>4</sub> 0.6927; n<sup>20</sup>D 1.3872 [14].

Then, the following pyrazoline bases were prepared and decomposed to the corresponding cyclopropane hydrocarbons:

ethylene and acetyl chloride by Kondakov's method, b. p. 55° (16 mm);  $d^{20}_4$  0.9745;  $n^{20}$ D 1.4414; found MR 38.91; calculated MR 39.40.

of 92 g of the chloroketone, 50 g of hydrazine hydrate, and 50 ml of ethyl alcohol; b. p. 68-70° (15 mm);  $d_4^{20}$  0.9036;  $n_2^{20}$  D 1.4600; found MR 38.60; calculated MR 38.07; yield 50%.

1,1,2,3-Tetramethylcyclopropane (C<sub>7</sub>H<sub>14</sub>) 
$$CH_3 CH CH_3 CH$$
 was prepared by the decomposition of 3,4,5,5-  
CH<sub>3</sub> CH<sub>3</sub> CH cH<sub>3</sub>

tetramethylpyrazoline, b. p. 77-78°; d<sup>20</sup><sub>4</sub> 0.7193; n<sup>20</sup>D 1.4020; found MR 33.114; calculated MR 33.118 (acc. to Vogel [15]). Found: C 85.7; H 14.30%. Calculated: C 85.63; H 14.37%.

Cl O  

$$\downarrow$$
 O  
 $\downarrow$   $\parallel$   $\parallel$   
Chloro-2-methylheptane-4-one (C<sub>8</sub>H<sub>15</sub>OCl) CH<sub>3</sub>-C-CH<sub>2</sub>-CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub> was prepared from butyryl  
 $\downarrow$   $\downarrow$  CH<sub>3</sub>

chloride and isobutylene in the presence of 10% ZnCl<sub>2</sub> by stirring the reaction mixture at 0° for 2 days. Yield, 45.8%; b. p. 59-63° (15 mm);  $d^{20}_4$  0.8660; for  $n^{20}$ D 1.4470.

3-Propy1-5,5-dimethylpyrazoline ( $C_8H_{16}N_2$ )  $CH_3$   $CH_3$   $C-CH_2CH_2CH_3$  was prepared from 101 g of 2-chloro-

2-methylheptane-4-one and 57 g of hydrazine hydrate in alcohol by refluxing the reaction mixture for 6 hr on a water bath. The base boiled at 67-68° (7 mm);  $d^{20}_{4}$  0.8856;  $n^{20}$ D 1.4583; found MR 43.23; calculated MR 43.22; yield 91%.

1,1-Dimethyl-2-propylcyclopropane ( $C_8H_{16}$ ) CH<sub>2</sub>
CH<sub></sub>

position of 79 g of 3-propyl-5,5-dimethylpyrazoline at 260-270°. After usual treatment and five-fold distillation over sodium metal, the product boiled at 105.5° (745 mm); d<sup>20</sup><sub>4</sub> 0.7292; n<sup>20</sup>D 1.4060; found MR 37.79; calculated MR 37.704; yield 42.8%. Found: C 85.94; H 14.20%. Calculated: C 85.63; H 14.37%.

C1 O 3. 5-Chloro-2,5-dimethylcyclohexane-3-one (C<sub>8</sub>H<sub>15</sub>OC1) 3 CH<sub>3</sub>- $\overset{|}{C}$ -CH<sub>2</sub>- $\overset{|}{C}$ -CH<sub>-</sub>CH<sub>3</sub> was synthesized from  $\overset{|}{C}$ H<sub>3</sub> CH<sub>3</sub>

isobutyryl chloride and isobutylene in the presence of 10% ZnCl<sub>2</sub>. Yield, 28%; b. p. 62-70° (12 mm); d<sup>20</sup>, 0,9049; n<sup>20</sup>D 1.4390.

3-Isopropy1-5,5-dimethylpyrazoline ( $C_8H_{16}N_2$ )  $CH_3$   $C-CH_2-C-CH_2-C-CH_3$ . was prepared from 50 g of 5-chloro-  $CH_3$  I I I HN-----N CH

2,5-dimethylcyclohexane-3-one, and an alcoholic solution of 23.1 g of hydrazine hydrate. Yield, 38 g (88%), b. p. 85-86° (12 mm); d<sup>20</sup><sub>4</sub> 0.8801; n<sup>20</sup>D 1.4543; found MR 43.08; calculated MR 43.85 (acc. to Vogel).

1,1-Dimethy1-2-isopropylcyclopropane ( $C_8H_{16}$ )  $CH_3$   $CH_2$   $CH_3$   $CH_3$  was obtained by the catalytic de-

composition of 38 g of 3-isopropyl-5,5-dimethylpyrazoline at 280-300°. After usual treatment and repeated distillation over metallic sodium, 15 g (49.3%) of 1,1-dimethyl-2-isopropylcyclopropane was obtained, b. p. 94-95° (762 mm); d<sup>20</sup>, 0.7137; n<sup>20</sup>D 1.3970; found MR 37.56; calculated MR 37.76. Found: C 85.84; H 14.16%. Calculated: C 85.63; H 14.37%.

Decomposition in the absence of the catalyst led to an identical product (from the point of view of properties and Raman spectra).

4. 2-Chloro-2-methyldecane-4-one ( $C_{11}H_{21}OC1$ ) CH<sub>3</sub>-C-CH<sub>2</sub>-C-(CH<sub>2</sub>)<sub>5</sub>CH<sub>3</sub> was prepared from the acid  $\begin{vmatrix} & \parallel \\ & \parallel \\ & CH_3 & O \end{vmatrix}$ 

chloride of enanthic acid and isobutylene in the presence of ZnCl<sub>2</sub>. Yield, 47.8%; b. p. 99-100° (8 mm); d<sup>20</sup><sub>4</sub> 0.8844; n<sup>20</sup>D 1.4430.

2-methyldecane-4-one to 56 g of hydrazine hydrate in 56 ml of ethyl alcohol, and refluxing the mixture for 6 hr with stirring. After distillation of the reaction product, 61 g (82%) of the pyrazoline derivative was obtained, b. p. 106-107° (7 mm); d<sup>20</sup>, 0.8736; n<sup>20</sup>D 1.4598; found MR 57.14; calculated MR 57.07.

1,1-Dimethyl-2-hexylcyclopropane ( $C_{11}H_{22}$ ) ( $CH_{3}$ )<sub>2</sub>-C- $CH_{-}(CH_{2})_{5}$ - $CH_{3}$  was prepared by the decomposition

of 80.5 g of 3-hexyl-5.5-dimethylpyrazoline at 250-270° in the presence of 40 g of potassium hydroxide. After usual treatment and four-fold distillation over sodium with a fractionating column of 38 theoretical plates, 39.6 g of 1.1-dimethyl-2-hexylcyclopropane was obtained, b. p. 176.5° (736 mm);  $d^{20}_4$  0.7612;  $n^{20}$ D 1.4240; found MR 51.65; calculated MR 51.61. Found: C 85.74; H 14.32%. Calculated: C 85.63; H 14.37%.

5. 2-Chloro-2-methyl-5-ethylnonane-4-one (C<sub>12</sub>H<sub>23</sub>OCl) CH<sub>3</sub>-C-CH<sub>2</sub>-C-CH<sub>2</sub>(CH<sub>2</sub>)<sub>5</sub>CH<sub>3</sub> was prepared from  

$$H_{1}$$
  $H_{2}$   $H_{2}$   
CH<sub>3</sub>  $O$  CH<sub>2</sub>  
 $H_{3}$   $CH_{3}$   $O$  CH<sub>2</sub>  
 $H_{3}$   $CH_{3}$   $CH_{3}$ 

the acid chloride of  $\alpha$  -ethylcapronic acid and isobutylene in the presence of 10% ZnCl<sub>2</sub> (method [5]). Yield 62%; b. p. 120-125° (5 mm);  $d^{20}_{4}$  0.9021;  $n^{20}$ D 1.4465.

pared as follows: 34.4 g of hydrazine hydrate in 50 ml of ethanol was treated with 100 g of 2-chloro-2-methyl-5ethylnonane-4-one in 70 ml of alcohol. The mixture was refluxed for 6 hr at 80°, with stirring. After alcohol and hydrazine hydrate were driven off by distillation, 75.8 g (84.4%) of the pyrazoline base was obtained, b. p. 143-144° (20 mm);  $d^{20}_{4}$  0.8748;  $n^{20}D$  1.4580; found MR 61.12; calculated MR 61.68.

1,1-Dimethyl-2-(1'-ethylpentyl)cyclopropane (
$$C_{12}H_{24}$$
)  

$$CH_3 CH_2 CH_-CH_-CH_2-CH_2-CH_2-CH_3 \text{ was pre-}$$

pared by the thermal decomposition of 84 g of 3-(1'-ethylpentyl)-5,5-dimethylpyrazoline at 290° in the absence of a catalyst. The hydrocarbon thus produced was distilled at 190-200°, washed with 50% acetic acid to remove any undecomposed base, neutralized with a 25% solution of sodium hydroxide, washed with water, dried over calcium chloride, and distilled twice over metallic sodium. Yield of 1,1-dimethyl-2-(1'-ethylpentyl)cyclopropane, 52 g (65%); b. p. 186.5-187.5°;  $d^{20}_{4}$  0.7738;  $n^{20}$ D 1.4309; found MR 56.15; calculated MR 56.35. Found: C 85.59; H 14.45%. Calculated: C 85.63; H 14.37%.

6. 3-Ethyl-1-heptenylcyclopropyl ketone (C<sub>13</sub>H<sub>22</sub>O) 
$$\begin{array}{c} CH_3 - CH_2 - CH_2$$

mixture of 50 g of methyl cyclopropyl ketone, 1 g of KOH, and 10 ml of ethanol was treated dropwise during 2 hr, while stirring and cooling the flask with water, with 64 g of 2-ethylhexaldehyde  $[d^{20}_4 \ 0.8388, n^{20}D \ 1.4320;$  found MR38.92; calculated MR39.20 (acc. to Vogel)]. 2,4-dinitrophenylhydrazone m.p. 122°. Stirring was continued without cooling for a further period of 10 hr. After 2 days, the contents of the flask were poured on 400 ml of water, and the mixture thus obtained extracted thrice with ether. The combined ethereal extracts were dried over CaCl<sub>2</sub>, the °-lvent driven off, and the residue distilled in vacuum. Yield, 40.8 g (41.2%) of the ketone, b. p. 141° (17 mm);  $d^{20}_{-4} \ 0.8870;$   $n^{20}D \ 1.4715;$  found MR 61.28; calculated MR 60.49. Found: C 80.30, 80.47; H 11.60, 11.60%. C<sub>13</sub>H<sub>22</sub>O. Calculated: C 80.35; H 11.41%.

was prepared by adding 34 g of 3-ethyl-1-heptenylcyclopropyl ketone to a solution of 17 g of hydrazine hydrate in 20 ml of ethanol. The temperature of the reaction mixture rose during the addition from 21 to 48°. Then it was heated with stirring on a water bath at 80° for 5.5 hr. Finally, the lower layer of the mixture was separated, and the upper layer was distilled in vacuum. Yield of 3-cyclopropyl-5-(1'-ethylpentyl)-pyrazoline, 26 g (71.4%); b. p. 131° (5 mm);  $d^{20}_{4}$  0.9269;  $n^{20}D$  1.4880; found MR 64.75; calculated MR 63.06.

As the newly synthesized pyrazoline bases decompose even upon standing at room temperature, their elemental analysis was dispensed with.

prepared as follows: 26 g of 3-cyclopropyl-5-(1'-ethylpentyl)-pyrazoline was added to 10 g of KOH heated to 260-270° at such a rate as to keep the temperature of the vapors issuing from the rectifying column below 160-180°. The distillate thus obtained (14 ml) was washed thrice with 50% acetic acid (10 ml portions), neutralized with sodium carbonate, and dried over KOH. The acid extract yielded 3 g of the recovered pyrazoline base. The 1-cyclopropyl-2-(1'-ethylpentyl)-cyclopropane obtained in this experiment was distilled once without adding sodium metal, and twice in vacuum over sodium. As the Raman spectrum of this product revealed the presence of a small amount of contaminating alkenes, the latter were removed by oxidation with 1% potassium permanganate. After steam distillation, extraction with ether, drying over CaCl<sub>2</sub>, and distillation of the solvent, the resulting product was twice distilled in vacuum over sodium metal. Yiele of 1-cyclopropyl-2-(1'-ethylpentyl)-cyclopropane, 7 g (35%):b. p. 111° (24 mm);  $d^{20}_4$  0.8178;  $\pi^{20}$ D 1.4485; found MR 59.08; calculated MR 59.53. Found: C 86.61, 86.86; H 13.11, 13.10%. Calculated; C 86.58; H 13.41%.

## SUMMARY

1. 1,1,2,3-Tetramethylcyclopropane; 1,1-dimethyl-2-propylcyclopropane; 1,1-dimethyl-2-isopropylcyclopropane; 1,1-dimethyl-2-hexylcyclopropane; 1,1-dimethyl-2-(1'-ethylpentyl)cyclopropane; and 1-cyclopropyl-2-(1'-ethylpentyl)cyclopropane were synthesized for the first time.

2. As the structure of the  $\alpha$ ,  $\beta$ -unsaturated ketone becomes more complicated, and  $\alpha$ -substituents are introduced into the molecule, the screening effect over the double bond during the reaction with hydrazine becomes more important, and considerably hinders the formation of the pyrazoline base.

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