SYNTHESIS OF 2-METHYL- AND 2-ETHYLCYCLOTETRADECANONES

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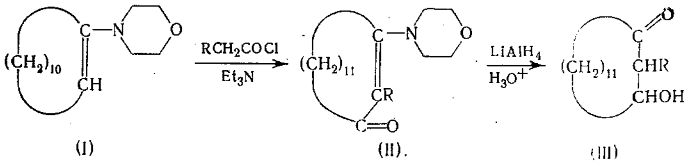
The higher C_{14}-C_{18} cyclic ketones are interesting as perfumes that have a musk odor. The readily available cyclododecanone is currently being used to synthesize the C_{13} and C_{16} cyclic ketones [1-3]. In the present paper we developed a simple method for obtaining the 2-methyl- and 2-ethylcyclotetradecanones, which as perfumes are equal to cyclopentadecanone (exaltone).

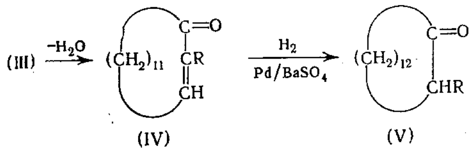
The reaction of 1-morpholinocyclododecene (I) [4] with either propionyl chloride or butyryl chloride in the presence of triethylamine gives the 1-morpholino-2-alkyl-1-cyclotetradecen-3-one (II) in 70-75% yield. After separating the triethylamine hydrochloride, the crude ketone (II) is smoothly reduced by complex aluminum hydrides ($LiAlH_4$, $NaAlH_4$, $NaAlH_2(OCH_2CH_2OCH_3)_2$) and forms the 2-alkyl-3-hydroxycyclotetradecanone (III) on subsequent hydrolysis.



R = CH_3 (a), C_2H_5 (b)

Depending on the hydrolysis conditions, together with ketol (III) (R = CH_3), a certain amount of its dehydration product, 2-methyl-2-cyclotetradecen-1-one, is formed.

Ketol (III) easily cleaves water when refluxed in toluene in the presence of catalytic amounts of p-toluenesulfonic acid to give a mixture of the cis- and trans-2-alkyl-2-cyclotetradecen-1-one (IV) in high yield. The hydrogenation of the unsaturated ketones (IV) over Pd catalyst gives the 2-methyl- and 2-ethylcyclotetradecanones (Va, b) in quantitative yield.



The reaction of ketones (IV) and (V) with 2,4-dinitrophenylhydrazine gives the 2,4-dinitrophenylhydrazones, while ketol (III) (R = CH_3) apparently gives the corresponding pyrazoline derivative.

EXPERIMENTAL

2-Methyl-3-hydroxycyclotetradecanone (IIIa). To stirred solution of 36.5 g of 1-morpholinocyclododecene (I) [4] in 30 ml of abs. $CHCl_3$ and 20 ml of abs. triethylamine was added at 0°, in 1 h, a solution of 15 g of propionyl chloride in 15 ml of $CHCl_3$. The mixture was stirred for 2 h and then left to stand at ~20° for 12 h. The triethylamine hydrochloride was filtered, washed with $CHCl_3$ (2 × 30 ml), and the solvent was removed in vacuo. The residue was dissolved in 150 ml of abs. ether and to the stirred solution at 30° was gradually 4 g of $LiAlH_4$. The mixture was refluxed for 3 h, cooled, followed by the cautious

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addition at 20° of 10 ml of methanol and 150 ml of 15% HCl solution, and the mixture was stirred for 5 h. The ether solution was separated, washed in succession with water and $NaHCO_3$ solution, and dried over Na_2SO_4. Fractional distillation in vacuo gave 7.5 g of 2-methyl-2-cyclotetradecen-1-one (IVa), bp 118-123° (1 mm), and 16.3 g of (IIIa), bp 145-150° (1 mm), and mp 60-61° (hexane). Found: C 74.78; H 11.48%. $C_{15}H_{28}O_2$. Calculated: C 75.00; H 11.65%.

Reaction with 2,4-dinitrophenylhydrazine in alcohol, in the presence of H_2SO_4, gave the pyrazoline derivative, mp 165-166° (CH_3COOH). Found: C 63.08; H 7.11; N 13.87%. $C_{21}H_{30}N_4O_4$. Calculated: C 62.68; H 7.46; N 13.93%.

2-Methyl-2-cyclotetradecen-1-one (IVa). A solution of 9 g of (IIIa) and 0.2 g of p-toluenesulfonic acid in 70 ml of toluene was refluxed for 2 h, with removal of the reaction water by distillation. Then the cooled mixture was washed with water and dried over Na_2SO_4. Vacuum distillation gave 7.2 g (88%) of (IVa), bp 118-120° (1 mm); n_D^{20} 1.4977; d_4^{20} 0.8073. Found: C 80.81; H 11.75%. $C_{15}H_{26}O$. Calculated: C 81.07; H 11.70%.

The dehydration of a mixture of (IIIa) and (IVa) proceeds in a similar manner. Based on the GLC data, 2-methyl-2-cyclotetradecen-1-one is a mixture of the cis and trans isomers in an ~1 : 2 ratio. 2.4-Dinitrophenylhydrazone, mp 117-118° (ethanol). Found: C 62.68; H 7.47; N 14.00%. $C_{21}H_{30}N_4O_4$. Calculated: C 62.68; H 7.45; N 13.90%.

2-Methylcyclotetradecanone (Va). A solution of 7 g of (IVa) in 30 ml of ethanol was saturated with H_2 in the presence of 0.2 g of Pd / $BaSO_4$ and 1 ml of AcOH until the absorption ceased. The catalyst was filtered, and the solution was diluted with water and extracted with ether. The ether extract was washed with $NaHCO_3$ solution and dried over Na_2SO_4. Fractional distillation in vacuo gave 6.5 g of (Va) [5], bp 116-117° (1 mm); n_D^{20} 1.4790. 2,4-Dinitrophenylhydrazone, mp 110-111° (from ethanol). Found: N 13.79%. $C_{21}H_{32}N_4O_4$. Calculated: N 13.86%.

Ethyl-1-cyclotetradecanon-3-ol (IIIb). The reaction was carried out the same as in the preparation of (IIIa). For reaction we took 20 g of (I) in 30 ml of abs. $CHCl_3$, 15 g of abs. triethylamine, and 10.7 g of butyryl chloride in 20 ml of abs. $CHCl_3$. The residue from the separation of the triethylamine hydrochloride and removal of the solvent was treated with 3 g of $LiAlH_4$. Vacuum distillation gave 14.2 g of (IIIb), bp 145-155° (1 mm), and mp 42-43° (from petroleum ether). Found: C 75.74; H 11.83%. $C_{16}H_{30}O_2$. Calculated: C 75.59; H 11.80%.

2-Ethyl-2-cyclotetradecen-1-one (IVb). A solution of 4 g of (IIIb) and 0.1 g of p-toluenesulfonic acid in 50 ml of toluene was refluxed for 3 h. After workup we obtained 3.2 g of (IVb), bp 130-131° (1 mm); n_D^{20} 1.4965; d_4^{20} 0.9340. Found: C 80.84; H 11.87%. $C_{16}H_{28}O$. Calculated: C 81.32; H 11.86%. 2,4-Dinitrophenylhydrazone, mp 121-122° (ethanol). Found: C 63.06; H 7.64; N 13.40%. $C_{22}H_{32}N_4O_4$. Calculated: C 63.45; H 7.70; N 13.40%. Based on the GLC data, 2-ethyl-2-cyclotetradecen-2-one is a mixture of the cis and trans isomers.

2-Ethylcyclotetradecanone (Vb), A solution of 2 g of (IVb) in 20 ml of ethanol was saturated with hydrogen in the presence of 0.1 g of Pd / $BaSO_4$. We obtained 1.8 g of (Vb), bp 122° (1 mm); n_D^{20} 1.4818; d_4^{20} 0.9202. Found: C 80.44; H 12.58%. $C_{16}H_{30}O$. Calculated: C 80.65; H 12.60%. 2,4-Dinitrophenylhydrazone, mp 76-77° (ethanol). Found: C 63.01; H 8.04; N 13.19%. $C_{22}H_{34}N_4O_4$. Calculated: C 63.25; H 8.15; N 13.30%.

CONCLUSIONS

A method was proposed for the synthesis of the 2-methyl- and 2-ethylcyclotetradecanones from cyclododecanone via 1-morpholinocyclododecene.

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