

SHORT
COMMUNICATIONS

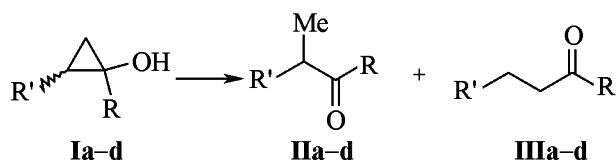
Preparation of α -Methyl-substituted Dialkyl Ketones by Alkaline Opening of 1,2-Dialkyl-substituted Cyclopropanols

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Substituted cyclopropanols are readily converted into the corresponding ketones when treated with acids or alkali and at heating [1]. With 1,2-cyclopropanols a problem exists concerning the regioselectivity of the ring opening. The opening of a three-membered cycle in cyclopropanols (**I**) can afford both branched **II** and unbranched **III** ketones.



R, R' = Me, Me (**a**); Me, Et (**b**); Et, Pr (**c**); Pr, Et (**d**).

Certain α -methylalkyl ketones are pheromones of insects and are active even as racemic mixtures. For instance, 4-methylheptane-3-one (**IIId**) is an alarm pheromone of leaf-cutting ants *Atta texana*. Both forming enantiomers are active, and the less active one, (R)-(-)-isomer of ketone, does not inhibit the more active (S)-(+)-isomer [2]. The regioselectivity of ring opening in diaryl-substituted cyclopropanols was previously investigated [1]. At the same time the transformations of 1,2-dialkyl-substituted cyclopropanols are poorly understood up till now [3].

In the present study was investigated the regioselectivity of ring opening in 1,2-dialkyl-substituted cyclopropanols effected by bases [4]. It was found that 1,2-dimethylcyclopropanol (**Ia**) on heating with KOH underwent isomerization into a mixture of 2-methylbutan-3-one (**IIa**) and penta-2-one (**IIIa**) in 20:1 ratio in the overall yield 65% (GLC, $^1\text{H NMR}$ [5]). The distillation of compound **Ia** on NaOH results in strong tarring.

The optimization of the ring opening was carried out by an example of 1-ethyl-2-methylcyclopropanol

(**Ib**). The reaction of cyclopropanol **Ib** with 20% water solution of potassium or lithium hydroxide in a mixture with dioxane along the procedure [6] gave rise to a mixture of ketones. For instance, in reaction of cyclopropanol **Ib** with aqueous LiOH in dioxane arises a mixture of 2-methylpentan-3-one (**IIb**) and hexan-3-one (**IIIb**) in 3:1 ratio (GLC). The water solutions of alkali (KOH, LiOH) in a mixture with the other solvents (DMF, DMSO, THF, MeOH, HMPA) afforded ketone mixtures with varying excess of the branched isomer. The highest selectivity was observed when KOH was applied.

As seen from table, the best results were obtained at the use of KOH powder in THF, MeOH, and pentane (runs nos. 2, 4, 5). According to GLC data in these cases the resulting mixture contained 2.5–6% of the initial cyclopropanol **Ib** and 0.5–1% of unbranched ketone isomer **IIIb**. In these solvents was carried out cyclopropanols isomerization taken in amount of 20–25 mmol (runs nos.6–8). Alcohols **Ib** and **Ic** in pentane and methanol when treated with KOH powder afforded ketones **IIb** and **IIc** containing ketones with straight chain **IIIb** and **IIIc** in 4 and 10% amount respectively, whereas compound **Id** in THF yielded pure ketone **IIId** ($^1\text{H NMR}$).

Thus by treating with KOH powder in THF from 1-ethyl-2-propylcyclopropanol was prepared 4-methylheptan-3-one in 75% yield. According to GLC data the ratio of 4-methylheptan-3-one (**IIId**) to octan-3-one (**IIIId**) was 200:1.

1,2-Dialkylcyclopropanols were prepared by reaction of the appropriate organomagnesium compounds with esters in the presence of titanium(IV) isopropoxide.

Isomerization of 1,2-dimethylcyclopropanol (Ia) in the presence of KOH (see table, run no.1). A mixture of 2 g of cyclopropanol **Ia** and 0.5 g of potass-

ium hydroxide in a Faworsky flask was placed into an oil bath preliminary heated to 120–130°C. The reaction product, 3-methylbutan-2-one (**IIa**) containing 4% of pentan-2-one (GLC), was distilled off in the course of reaction and collected. Yield 1.3 g (65%), bp 93–96°C (publ. bp 93°C [7]).

General procedure of cyclopropanols isomerization. To a solution of 3 mmol of substituted cyclopropanol in 4 ml of solvent was added 1 ml of 20% water solution or 0.2–0.4 g of alkali powder, and this mixture was stirred at room temperature. The reaction course was monitored by TLC. On completion of the reaction the organic layer was separated from alkali and analyzed by GLC under the following conditions: chromatograph LKhM-8MD, detector katharometer, carrier gas helium, columns 2000 \times 3 mm, stationary phases 5%OV-1 on Chromaton N-Super (0.16–0.20 mm) and 5% SE-30 on Inerton AW-HMDS (0.20–0.25 mm). ^1H NMR spectra were recorded from solutions in CCl_4 on spectrometer Tesla BS-467A (60 MHz), internal reference HMDS. Multiplicity and chemical shifts of the signals in the spectra of ketones obtained were consistent with the published data.

2-Methylpentan-2-one (IIIb) (see table, run no. 6). A mixture of 3.43 g of 1-ethyl-2-methylcyclopropanol (**Ib**) and 2.96 g of KOH powder in 35 ml of pentane was stirred for 24 h. The workup was as described above. After evaporation of the solvent the residue was distilled. Yield of 2-methylpentan-3-one (**IIIb**) containing 4% of hexan-3-one (**IIIb**) (GLC) 1.9 g (55%), bp 109–111°C (publ. bp 106–110°C [8]).

3-Methylheptan-4-one (IIIc) (see table, run no. 7). A mixture of 2.88 g of 1-propyl-2-ethylcyclopropanol (**Ic**) and 0.87 g of KOH powder in 28 ml of MeOH was kept for 24 h at room temperature and then worked up as above. We obtained 1.63 g (56%) of 3-methylheptan-4-one (**IIIc**) containing 10% of octane-4-one (**IIIb**) (GLC), bp 155–158°C (publ. bp 152–154°C at 740 mm Hg [9]).

4-Methylheptan-3-one (IIId) (see table, run no. 8). A mixture of 1.66 g of 1-ethyl-2-propylcyclopropanol (**Id**) and 0.75 g of KOH powder in 20 ml THF was stirred for 24 h, then filtered through silica gel bed, the latter was washed with ether, and after distilling off the solvent the residue was distilled. Yield of 4-methylheptan-3-one (**IIId**) 1.25 g (75%), bp 155–157°C (publ. 52–55°C at 25 mm Hg [10]).

Ratio of products obtained by cyclopropanols isomerization effected by potassium hydroxide

Run no.	Compd. no.	Solvent	Ratio of ketones (II):(III)	Yield, %
1	Ia	–	96:4	65
2 ^a	Ib	THF	99.5:0.5	
3 ^a	Ib	DMF	98:2	
4 ^a	Ib	MeOH	100:0	
5 ^a	Ib	Pentane	99:1	
6	Ib	Pentane	96:4	55
7	Ic	MeOH	90:10	56
8	Id	THF	99.5:0.5	75

^a Reaction mixtures were only analyzed by GLC.

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