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REACTION OF CYCLIC KETONES WITH KOH–DMSO

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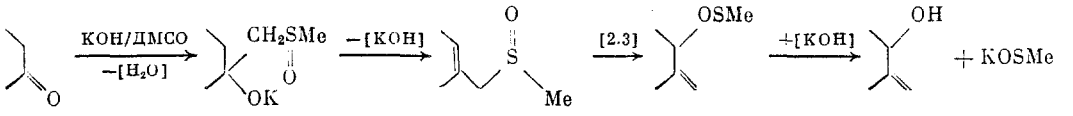
Upon reaction of cycloalkanones with a KOH-DMSO system 2-methylenecycloalkanols are formed, the yield (10-37%) of which decreases in the series: cyclohexanone > cycloheptanone > cyclooctanone > cyclododecanone.

It was shown [1-4] recently that the simple superbasic system KOH–DMSO can serve as a source of dimsyl anions for obtaining allyl alcohols from ketones by the sequence



In spite of moderate yields of allyl alcohols (XI)-(XV) (<40%), this reaction has obvious advantages over the known four-step method of obtaining allyl alcohols from ketones [5-7], based on the use of less accessible reagents (phenylsulfinylmethyllithium, trimethylsilylimidazole, lithium diisopropylamide, KH).

The goal of this work was to explore the possibility of using the above reaction for preparative synthesis of allyl alcohols and sulfoxides from cyclic and macrocyclic ketones, and especially the influence of ketone ring size on product yield. In the investigation the following ketones were used: cyclopentanone (I), cyclohexanone (II), 4-methylcyclohexanone (III), cycloheptanone (IV), cyclooctanone (V), and cyclododecanone (VI). It turned out (see Table 1) that with increase of the starting ketone ring size, beginning with cycloheptanone, the yield of the corresponding allyl alcohol decreases and in order to maintain it within 10-30% it is necessary to increase the relative amount of alkali and the reaction time. For example, under comparable conditions (110°C, starting ketone concentration: 0.5-0.6 mole/liter, KOH: 1.0-1.5 mole/liter) after 1 h the following amounts of ketones are found in the reaction mixture (GLC) (%): (II) traces, (IV) 46, (V) 67. The content of ketone (V) in the reaction mixture changes with time as follows: after 2 h 58%, after 4 h 50%. Apparently, addition of dimsyl anion to the carbonyl group is very sensitive to steric effects as is also the competing aldol condensation. From a preparative point of view, the best balance in favor of the first process is observed with six- and seven-membered cyclic ketones.

In the case of cyclopentanone (I) no 2-methylenecyclopentanol was observed in the reaction products. Instead a fraction was obtained (bp 98-101°C at 1 mm Hg), consisting mainly of 2-cyclopentylidenecyclopentanone (XVI) (IR, PMR) – the product of aldol condensation.

Kinetic experiments (Fig. 1) confirm the participation of ketones (II) and (IV) in a competing process. The rate of their disappearance [curves (II) and (IV)] exceeds significantly the formation rate of allyl alcohols (XI) and (XV). The concentration increase of the latter over 40-50 min stops at 35-40% of the theoretical value.

Curves *a* and b, constructed from the difference between the initial concentration of starting ketones (II) and (IV) (100%) and the sum of the current concentrations of these

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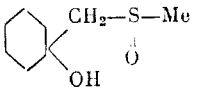
TABLE 1. Reaction Conditions* and Yield of Allyl Alcohols (XI)-(XV)

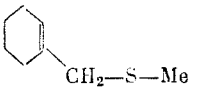
Ketone	Allyl alcohol	Ratio ketone: KOH:DMSO, mole	Time, h	Yield, %
(II)	2-methylenecyclohexanol (XI)	1:3.5:13.8	1	37 [3]
(III)	5-methyl-2-methylenecyclo-hexanol (XII)	1:2:18.8	1	19
(IV)	2-methylenecycloheptanol (XV)	1:2.9:28.9	2	30 [3]
(V)	2-methylenecyclooctanol (XIII)	1:5.7:23.1	11	28**
(VI)	2-methylenecyclododecanol (XIV)	1:5.2:32***	12	11

*Reaction temperature 110°C.
**According to GLC data.
***Reaction temperature 100°C.

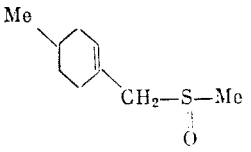
ketones and corresponding allyl alcohols (XI) and (XV), show a maximum, which indicates clearly a superposition of two processes: 1) formation of allyl alcohol precursors and 2) aldol condensation. As a matter of fact, stopping the reaction at point *a* of the curve maximum (after 10 min after mixing the reagents) allowed us to isolate the intermediates 1-(methylsulfinylmethyl)cyclohexanol (VII) and methyl-(1-cyclohexenylmethyl)sulfoxide (VIII) with yields of 4 and 27%, respectively, which was briefly reported [4, 8]. From 4-methylcyclohexanone (III) under the same conditions a mixture was obtained of isomeric (ratio 5:2, PMR) sulfoxides (IX) and (X) (total yield 25%).



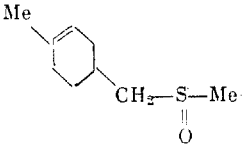
(VII)



(VIII)



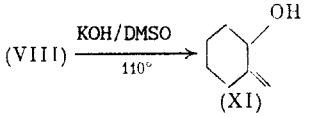
(IX)



(X)

Cyclopentanone (I) under the same conditions, according to GLC, IR, and PMR spectroscopy, gave only 6% of dimer (XVI).

Heating of allyl sulfoxide (VIII) (6 mmoles) under the reaction conditions (110°C, 12 mmoles KOH, 12 ml DMSO) leads to 2-methylenecyclohexanol (XI) with 67% yield, which confirms its participation in the process as an intermediate.



(XI)

EXPERIMENTAL

Chemically pure DMSO (~0.6% water) after dehydration with roasted Al_2O_3 and chemically pure KOH with water content ~15% was used (calculation per anhydrous preparation was not carried out). Commercially obtained ketones (I)-(VI) were distilled before use.

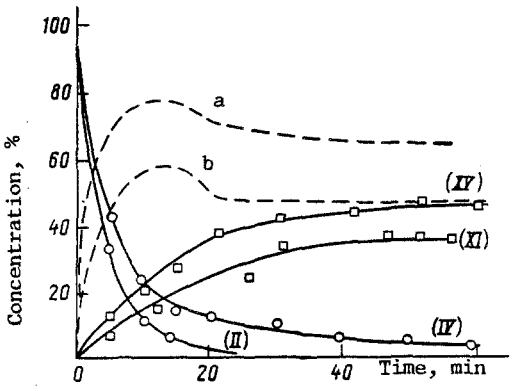


Fig. 1. Kinetic curves of expenditure for cyclohexanone (II) and cycloheptanone (IV) and formation of corresponding allyl alcohols (XI) and (XV). Curves *a* and b correspond to change of total concentrations of intermediate and secondary reaction products (according to GLC data). Reaction conditions: 110°C, ratio ketone:KOH:DMSO (mole) 1:1.92:27.2 [for curves of (II) and (XI)] (*a*), 1:3.9:28.2 [for curves (IV), (XV)] (b).

IR spectra were recorded on a Specord 751 R spectrometer (microlayer, KBr pellets). NMR spectra (^1H, ^{13}C) were taken on Bruker-200 SY (200 MHz for ^1H, 50.33 MHz for ^{13}C), Tesla BS-567A (100 MHz), and Jeol FX-90Q (22.49 MHz for ^{13}C) instruments with HMDS as standard in $CDCl_3$ and acetone-d_6. GLC was carried out on a LKhM-8MD chromatograph with a catharometer detector, a 3000 × 3 mm column with 5% DC-550 on Chromaton-N-AW-HMDS carrier at a column temperature of 80-180°C, programmed at 12°C/min. Detector and injector temperature was 200°C.

Kinetic curves were obtained by GLC using an internal standard (o-xylol). Samples of the reaction mixture (0.5 ml) were diluted with water 1:2, extracted with ether (1 ml), and analyzed.

Obtaining of alcohols (XI) and (XV) was described in [3].

1-(Methylsulfinylmethyl)cyclohexanol (VII) and Methyl-(1-cyclohexenylmethyl)sulfoxide (VIII). To a suspension heated to 110°C, consisting of 50 ml DMSO and 2.8 g (50 mmoles) KOH, 2.5 g (25 mmoles) of (II) was poured in and the mixture was stirred for 10 min, then quickly cooled to ~20°C. To the mixture there was added 2.6 g (48 mmoles) NH_4Cl, filtered, and DMSO was distilled under vacuum. The residue was extracted with CH_2Cl_2 (5 × 10 ml) and solvent was removed. By fractionation under vacuum there was obtained 1.5 g of a mixture of hydroxy sulfoxide (VII) and allyl sulfoxide (VIII), from which by preparative GLC (PAKhV-07, 1000 mm column, 15% PFMS on a Chromaton-N-AW-HMDS carrier, column temperature 180°C) there was isolated 0.16 g (yield 4%) of sulfoxide (VII) and 1.16 g [yield 27%, purity 99% (GLC)] of allyl sulfoxide (VIII), bp 95-96°C (2 × 10^{-2} torr), mp 29°C. PMR spectrum of compound (VII) ($CDCl_3$, δ, ppm): 3.61 br. s (1H, OH), 2.86 (2H, CH_2, AB-system, J = 13 Hz), 2.65 s (3H, Me), 1.90-1.35 m [10H, $(CH_2)_5$]. PMR spectrum of compound (VIII) ($CDCl_3$, δ, ppm): 5.74 br. s (1H, CH=), 3.33 two d (2H, CH_2, AB-system, J = 12.6 Hz), 2.52 s (3H, Me), 2.04 m and 1.6 m [8H, $(CH_2)_4$]. ^{13}C NMR spectrum of sulfoxide (VIII) ($CDCl_3$, δ, ppm): 129.60, 128.02, 63.77, 37.77, 28.78, 25.04, 22.17, 21.41. IR spectrum (microlayer, ν, cm^{-1}): 680, 800, 840, 920, 960, 1030, 1060, 1130, 1270, 1300, 1340, 1370, 1405, 1420, 1430, 1435, 1650, 1700, 2830, 2850, 2930, 2990, 3380-3440 (1700, 3380-3440, aldol microimpurity). Mass spectrum: $[M-H]^+$ 157. Found: C 60.66; H 8.84; S 20.00%. $C_8H_{14}OS$. Calculated: C 60.71; H 8.92; S 20.26%.

Methyl-(4-methyl-1-cyclohexenylmethyl)sulfoxide (IX). According to the method shown for synthesis of sulfoxides (VII) and (VIII), from 8.4 g (75 mmoles) of (III), [8.4 g (150 mmoles) KOH, 150 ml DMSO, 110°C, 10 min] there was obtained 3.25 g of an isomeric mixture of sulfoxides (IX) and (X) [yield 25%, purity of (IX) + (X) 99%] with bp of 96-97°C (2 × 10^{-2} torr). PMR spectrum (acetone-d_6, δ, ppm): 5.70 br. s (1H, CH=), 5.58 br. s [1H, CH= in isomer (X)], 3.32 two d [2H, $CH_2S(O)$, AB-system], 2.97 [2H, $CH_2S(O)$ in isomer (X)], 2.47 s (3H, Me), 2.08-1.1 m (7H, in ring), 0.94 m (3H, Me). Ratio of isomers (IX) and (X) 5:2. IR spectrum (microlayer, ν, cm^{-1}): 680, 940, 970, 1040, 1130, 1300, 1370, 1410,

1430, 1460, 1660, 1700, 2830, 2870, 2910-2930, 2950, 2980, 3030, 3370-3400 (1700, 3370-3400, aldol condensation product impurity). Found: C 63.24; H 9.30; S 17.34%. $C_9H_{10}OS$. Calculated: C 62.75; H 9.36; S 18.62%.

5-Methyl-2-methylenecyclohexanol (XII). To a suspension heated to 110°C, containing 8.4 g (150 mmoles) of KOH and 100 ml of DMSO, 8.4 g (75 mmoles) of (III) was added dropwise for 1 h, the mixture was cooled, diluted with water (1:2), extracted with ether (5 × 50 ml), washed with water (2 × 50 ml), and dried with Na_2SO_4. After removal of ether and distillation of the residue under vacuum there was obtained 1.78 g (yield 19%, 2.45 g of nondistilling residue) of 5-methyl-2-methylenecyclohexanol, bp 54-56°C (1.5 torr), n_D^{20} 1.4695, d_4^{20} 0.9235. PMR spectrum (acetone-d_6, δ, ppm): 4.95 br. s (1H, $=CH_2$), 4.66 br. s (1H, $=CH_2$), 3.96 m [2H, OH and CH(OH) in the ring], 2.25-2.39 m (2H, CH_2 in the ring at $=CH_2$), 1.90-2.03 m (1H, CH at Me), 0.93-1.90 m [4H, $(CH_2)_2$], 0.91 d (3H, Me). IR spectrum (microlayer, ν, cm^{-1}): 900, 990, 1000, 1030, 1080, 1130, 1140, 1200, 1330, 1370, 1430, 1640, 2850, 2860, 2910, 2940, 3070, 3320-3340. Found: C 74.74; H 11.05%. $C_8H_{14}O$. Calculated: C 76.14; H 11.18%.

2-Methylenecyclooctanol (XIII). To a suspension heated to 110°C, containing 2 g (36 mmoles) of KOH and 36 ml DMSO, 2.8 g (22 mmoles) of (V) was added and the mixture was stirred for 9 h, after which 5 g (90 mmoles) of alkali was added and heated for 4 h (according to GLC 20% of ketone remained), cooled, diluted with water (1:3), extracted with ether (5 × 20 ml), and dried with Na_2SO_4. After ether removal the residue (1.65 g, dark-brown liquid) was purified by preparative TLC (Al_2O_3, eluent ether–pentane 1:2). There was isolated 0.15 g of alcohol (XIII) [yield 6.8%, purity 89% (GLC)]. PMR spectrum (acetone-d_6, δ, ppm): 5.07 d (1H, $=CH_2$), 4.85 d (1H, $=CH_2$), 3.60 br. s (1H, OH), 4.11 m (1H, CH in ring), 2.10-2.35 m (2H, CH_2 at $=CH_2$ in ring), 1.30-1.90 m (10H, CH_2 in ring). IR spectrum (microlayer, ν, cm^{-1}): 900, 960, 990, 1030, 1050, 1110, 1140, 1300, 1345, 1390, 1440, 1460, 1470, 1630, 1680 (aldol condensation product), 2840, 2920, 2960, 3060, 3370-3400.

2-Methylenecyclododecanol (XIV) was obtained with 11% yield (purity 88%) from 4 g (22 mmoles) of cyclododecanone (VI) [4.4 g (79 mmoles) KOH, 50 ml DMSO, 110°C, 12 h, additionally 2 g (36 mmoles) of KOH was added over 10 h], mp 77-78°C. PMR spectrum (acetone-d_6, δ, ppm): 5.04 br. s (1H, $=CH_2$), 4.86 br. s (1H, $=CH_2$), 4.00 br. s (1H, OH), 4.09 m (1H, CH in the ring), 2.05-2.24 m (2H, CH_2 at $=CH_2$ in a ring), 1.00-1.90 br. m (16H in the ring). IR spectrum (KBr, ν, cm^{-1}): 730, 895, 905, 1020, 1040, 1060, 1090, 1140, 1240, 1310, 1350, 1450, 1470, 1640, 1680 (aldol condensation product), 1700 (starting ketone), 2840, 2900, 2910, 2930, 3070, 3380-3450.

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