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REACTION OF CYCLOHEPTANONE WITH CONCENTRATED SULFURIC ACID

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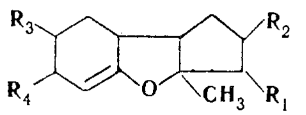
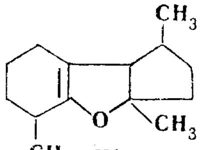
Treatment of cycloheptanone or 2-cycloheptylidenecycloheptanone with concentrated sulfuric acid, leads to self-condensation accompanied by intramolecular rearrangement and cyclization to give substituted tetrahydrofurans, viz. 2-methyl-2, 3-cyclohexano-4, 5-cyclohepteno-(Δ^5)-2, 3, 4, 5-tetrahydrofuran and 2-methyl-2, 3-cyclohexano-5-hydroxy-4, 5-cycloheptano-2, 3, 4, 5-tetrahydrofuran. Self-condensation of ketones with 6-membered rings under the action of concentrated sulfuric acid, proceeding via carbonium ions, and accompanied by contraction to a 5-membered ring, is also characteristic of cycloheptanone, the 7-membered ring of which isomerizes to a 6-membered one.

Recently the present authors showed [1] that treatment of cyclohexanone with concentrated sulfuric acid leads to self-condensation accompanied by ring contraction and formation of a substituted tetrahydrofuran, 2-methyl-2, 3-cyclopentano-4, 5-cyclohexeno-(Δ^5)-2, 3, 4, 5-tetrahydrofuran (I). Similar compounds (II, III, and IV) were also obtained by treating 4-, 3-, and 2-methylcyclohexanones with concentrated sulfuric acid [2].





IV

I: $R_1=R_2=R_3=R_4=H$; II: $R_1=R_3=CH_3$, $R_2=R_4=H$; III: $R_2=R_4=CH_3$, $R_1=R_3=CH_3$

We were interested in ascertaining whether ring contraction extends to other cyclic ketones, in particular to cycloheptanone. It should be mentioned that only one cycloheptanone self-condensation product, 2-cycloheptylidenecycloheptanone, is described in the literature [3], this being obtained by boiling cycloheptanone with potassium tert-butoxide.

The present paper is concerned with a study of the self-condensation of cycloheptanone under the action of sulfuric acid.

After cycloheptanone had been allowed to stand at room temperature for several days, a liquid product having the composition $C_{14}H_{22}O$ (V), and a solid product of composition $C_{14}H_{24}O_2$ (VI) were isolated.

Compound V is a dimer, formed by self-condensation of two molecules of cyclpheptanone with separation of a molecule of water. Hydrogenation shows this compound to be unsaturated, and to contain one C=C double bond. The product $C_{14}H_{22}O$ (V) was assumed to be 2-cycloheptylidenecyclopentanone, but a 2, 4-dinitrophenylhydrazone could not be prepared, although the authentic unsaturated bicyclic ketone of that formula gives a corresponding one [3].

The IR spectrum of V has a band at ν = 1708 cm^{-1}. The spectrum of 2-cycloheptylidenecycloheptanone itself has a band at ν = 1689 cm^{-1}, which is characteristic of a carbonyl group conjugated with a C=C double bond. The 1708 cm^{-1} band might be due to vibrations of a C=O group not conjugated with a C=C double bond, but in that case the IR spectrum of V should perhaps have exhibited a further band in the somewhat longer wavelength region, characteristic of the C=C isolated double bond. The IR spectrum of VII, the product of hydrogenating V, lacks the ν = 1708 cm^{-1} band, so that this band is to be ascribed to C=C valence vibrations. Compounds I, II, and IV have IR spectra with analogous bands 1693, 1701, 1703 cm^{-1}.

The data obtained, and analogy with compound I isolated from cyclohexanone-concentrated sulfuric acid reaction products, lead us to ascribe to V the structure of a substituted tetrahydrofuran, 2-methyl-2, 3-cyclohexano-4, 5-cyclohepteno-(Δ^5)-2, 3, 4, 5-tetrahydrofuran. However it is not impossible that reaction of cycloheptanone with concentrated sulfuric acid leads to a contraction of the 7-membered ring which does not stop at a 6-membered one, but extends to a 5-membered one.

Compound V gave a semicarbazone containing an OH group. I gives similar compounds (oxime, semicarbazone). The hydrolysis equation shows [1] that the OH group can only be at position 2. Evidently the 2, 4-dinitrophenylhydrazone of V could not be obtained because of steric hindrance.

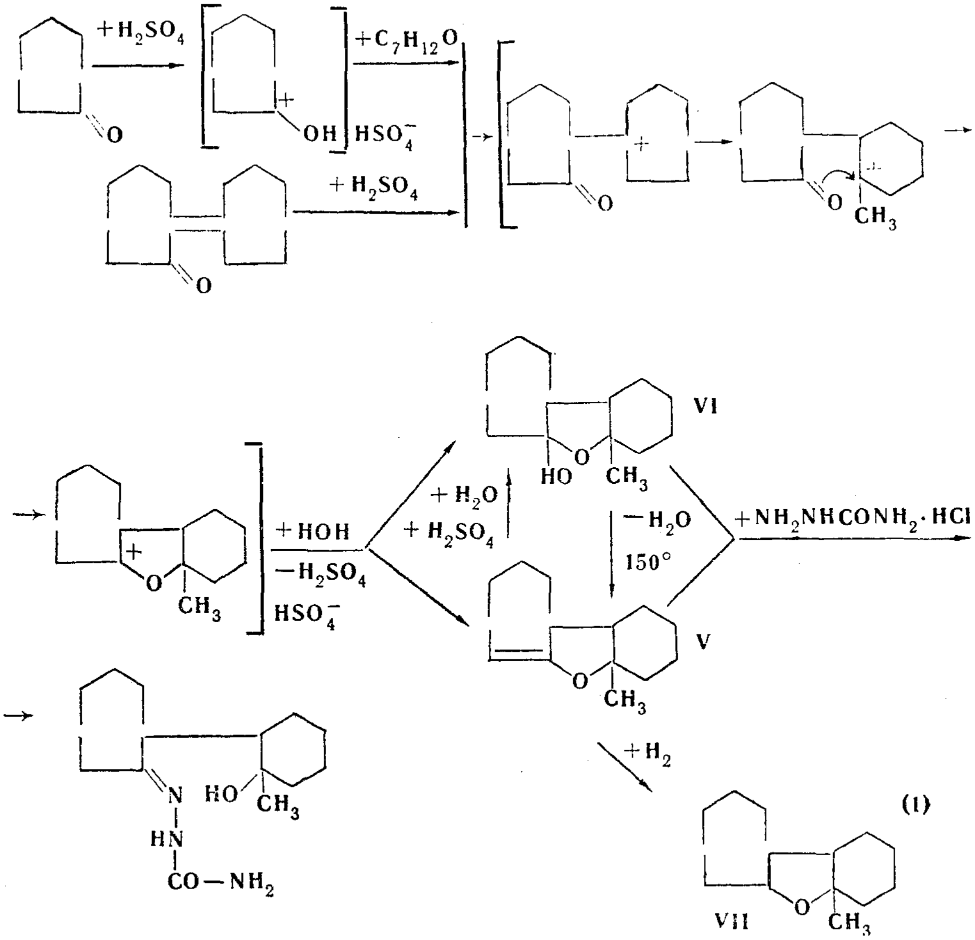
The position of the C=C double bond in V is confirmed by its PMR spectrum, which has a line at $\tau = 5.57$ ppm characteristic of protons linked to C=C carbon atoms [1]. The hydrogenation product VII has a PMR spectrum with a line at $\tau = 6.68$ ppm, due to the proton of the CH–O– group. According to the literature [4], such protons give $\tau = 6.46$ ppm.

The elementary analysis and molecular weight of VI shows that it contains one oxygen atom and two hydrogen atoms more than V. The IR spectrum of VI has a band at $\nu = 3360$ cm^{-1}, characteristic of the associated OH group (and in that connection, an enhanced molecular weight is found experimentally) and no bands characteristic of the C=O group. That VI contains an OH group is also confirmed by its PMR spectrum having a line at $\tau = 6.31$ ppm, characteristic of hydroxyl protons when there is association [5]. On melting, VI split off one molecule of water to give compound V. On the basis of the results obtained, VI was ascribed the structure of 2-methyl-2,3-cyclohexano-5-hydroxy-4,5-cycloheptano-2,3,4,5-tetrahydrofuran. Only this structure can split off water to give V. Compound VI gives a semicarbazone similar to the semicarbazone of compound V.

Unchanged V and a solid product VI were isolated from the products of reaction of V with concentrated sulfuric acid, while only VI was recovered from the products of reaction of VI with sulfuric acid.

Compounds V and VI are also obtained by treating 2-cycloheptylidenecycloheptanone with concentrated sulfuric acid.

The formation of V and VI from cycloheptanone and 2-cycloheptylidenecycloheptanone can be explained by formation of carbonium ions which undergo intramolecular rearrangement, and from which tetrahydrofuran derivatives are formed, in accordance with equations 1, on pouring into water. These equations show the reactions of V and VI with semicarbazide hydrochloride.



Thus treatment of cycloheptanone and 2-cycloheptylidenecycloheptanone, as well as of cyclohexanone, and 2-, 3-, and 4-methylcyclohexanones with concentrated sulfuric acid leads to self-condensation accompanied by ring contraction and formation of substituted tetrahydrofurans.

Experimental

Compounds I, II, and IV were synthesized as described in [1, 2]. The PMR spectra were also determined as described in [1, 2]. A UR-10 spectrophotometer was used to measure the IR spectra. The specimens were thin films of pure compounds between NaCl plates.

2-Methyl-2, 3-cyclopentano-4, 5-cyclohexeno-(Δ^5)-2, 3, 4, 5-tetrahydrofuran (I). Oxime mp 133° (ex benzene). Found: N 6.16%. Calculated for $C_{12}H_{23}O_2N$: N 6.66%. Semicarbazone mp 174°–175° (ex EtOAc). Found: N 16.90%. Calculated for $C_{13}H_{23}O_2N_3$: N 16.58%.

2-Cycloheptylidenecycloheptanone. A mixture of 47.5 g of cycloheptanone and 5 g KOH was refluxed for 40 min in a Dean and Stark apparatus. The reaction product was filtered off, and vacuum-fractionated to give 10 g (22%) 2-cycloheptylidenecycloheptanone, bp 127° (1 mm), n_D^{20} 1.5142, d_4^{20} 1.0008, MR_D 61.75 (calculated 61.99); the literature gives [3]: bp 130°–135° (0.9 mm), n_D^{20} 1.5212. Semicarbazone mp 167° (ex EtOH). Found: N 15.39%. Calculated for $C_{15}H_{25}N_3O$: N 15.95%.

2-Methyl-2, 3-cyclohexano-4, 5-cyclohepteno-(Δ^5)-2, 3, 4, 5-tetrahydrofuran (V), and 2-methyl-2, 3-cyclohexano-5-hydroxy-4, 5-cycloheptanotetrahydrofuran (VI). a) 23.8 g cycloheptanone was stirred, and 25 ml concentrated H_2SO_4 added over 2–3 min, so as to keep the temperature below 20° (the mixture turned red). After allowing the products to stand for 7 days at 20°, they were poured into 1 *l* water, and the precipitate filtered off, washed with water until neutral, and vacuum-dried. To extract V, the precipitate was washed with PrOH cooled to 0° (4 times with 25 ml each time), and the alcoholic filtrates evaporated and fractionally distilled under vacuum, to give 13 g (59.5%) V, bp 112° (1 mm), n_D^{20} 1.5130, d_4^{20} 1.008. Found: C 81.65; H 10.64%; Mol. wt. 211, (benzene); MR_D 61.18. Calculated for $C_{14}H_{22}O$: C 81.55; H 10.68%; mol. wt. 206; MR_D 61.43. V semicarbazone had mp 186°–187° (ex EtOH). Found: N 15.10%. Calculated for $C_{15}H_{25}N_3O_2$: N 14.94%. The precipitate remaining on the filter, 7.2 g (33%) was compound VI, mp 114°–115° (ex Me_2CO). Found: C 74.93, H 10.85%. Calculated for $C_{14}H_{24}O_2$: C 74.96; H 10.75%. VI semicarbazone had mp 186°–187° (ex EtOH). The mixed mp of semicarbazones V and VI was undepressed.

b) 5 ml concentrated H_2SO_4 was added to 5 g 2-cycloheptylidenecycloheptanone (20°–30°, 2 min), and the red mixture was allowed to stand for 7 days at 20°. The reaction products were worked up as described above, to give 2.6 g (52%) V and 1.5 g (28%) VI, identical with the V and VI prepared from cycloheptanone.

c) 0.1047 g VI was sealed in an evacuated tube, and heated at 180°–200° C for 5 hr, after which the reaction products were poured into 5 ml dry MeOH, and titrated with the Karl Fisher reagent: found 0.00842 g (100%) water. A parallel run involved heating 5 g VI, and vacuum-distillation of the reaction products gave 4.2 g (91%) V.

d) 1.3 g V was mixed with 5 ml concentrated H_2SO_4 (20°, 2 min), and the mixture left for 2 days at 20°. The products were worked up as described in (a) to give 1.3 g of the starting compound VI.

e) 4 g V was mixed with 4 ml concentrated H_2SO_4 (20°, 2 min), and the mixture left for 2 days at 20°. The products were worked up to give 0.8 g (18%) VI and 1.5 g (37%) V.

2-Methyl-2, 3-cyclohexano-4, 5-cyclopentano-2, 3, 4, 5-tetrahydrofuran (VII). In 5 hr 200 ml H_2 was passed into a mixture of 10 g V in 50 ml EtOH with 0.1 g Pd black which was stirred at 60°–70° C. The catalyst was filtered off, the alcohol removed, and the residue vacuum-fractionated, to give 9.9 g (98%) VII, bp 110° (1 mm), n_D^{20} 1.5050, d_4^{20} 1.0002. Found: C 80.68; H 10.79%; MR_D 61.52. Calculated for $C_{14}H_{24}O$: C 80.77; H 10.59%; MR_D 61.89.

In conclusion we wish to thank E. G. Pomerantseva for determining the IR spectra, and for discussing them.

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