Preparation and Purification of 2-(1-Cyclohexenyl)cyclohexanone

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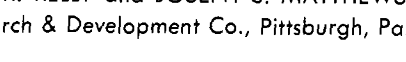
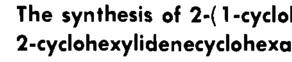
The synthesis of 2-(1-cyclohexenyl)cyclohexanone, together with its conjugated isomer 2-cyclohexylidenecyclohexanone, has been accomplished using anhydrides of phosphoric acid. The title compound has been separated from its conjugated isomer by low-temperature crystallization from a hydrocarbon solvent.

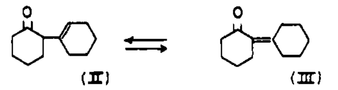
THE SELF-CONDENSATION product of cyclohexanone (I) was first made by Wallach (*12*) in 1896. Since then, numerous methods for the preparation of 2-(1-cyclohexenyl)cyclohexanone (II) have been reported. The most common early method of effecting condensation used strong mineral acids (*5*). More recently, ion exchange resins (*1*) and heterogeneous catalytic methods (*10*) have been used.

The use of the anhydrides of orthophosphoric acid as a reagent for this condensation is reported here for the first time. They include phosphorus pentoxide and pyrophosphoric acid, as in Equations 1 and 2.


(1)


(2)

The older literature indicates that only a single isomer is isolated for a given preparation. However, the work reported here shows that, in general, all known preparative methods result in a mixture of (II) with its conjugated isomer, 2-cyclohexylidenecyclohexanone (III), as in Equation 3.


(3)

All of these preparations are acid or base catalyzed. If purified 2-(1-cyclohexenyl)cyclohexanone (II) is contacted briefly with acidic or basic reagents, a mixture of the two ketone isomers results in approximately 90% (II) and 10% (III) in all cases. Since this shift in equilibrium takes place readily under conditions which would be encountered in all preparations of these condensation products, it follows that only mixtures of isomers will be obtained.

Cases where the condensation product was specifically identified as 2-cyclohexylidenecyclohexanone (III) list refractive indexes ranging from 1.4919 (*2*) to 1.5079 (*4*), while those claiming pure 2-(1-cyclohexenyl)cyclohexanone (II) gave values ranging from 1.5048 (*7, 11*) to 1.5070 (*1*). The refractive index of the purified 2-(1-cyclohexenyl)cyclohexanone (II) from this study is 1.5371. Therefore, the low values reported in the literature for this isomer would suggest that some 2-cyclohexylidenecyclohexanone (III) was also present. Duplication of a reported preparation (*8*), by which only pure (II) was supposedly obtained, yielded a mixture of ketone isomers with approximately the same product distribution as was obtained when the anhydrides of orthophosphoric acid were employed for this synthesis.

These isomers could not be separated by vacuum distillation, column chromatography or preparative gas-liquid chromatography. However, when this isomeric mixture was dissolved in an appropriate hydrocarbon solvent, such as *n*-pentane, and the temperature suitably depressed, 2-(1-cyclohexenyl)cyclohexanone selectively crystallized from solution. The hydrocarbon must be present in a range of 40 to 50 wt. % to effect separation. When the solvent concentration is less than 40%, crystallization of both isomers takes place, while above 55%, no crystallization takes place. The undiluted mixture forms a glass upon cooling. Complete separation requires three successive crystallizations (cycles), using 50 weight % *n*-pentane solutions in each step to give an 80.6% recovery of pure (II). The results of this separation, employing an isomer mixture synthesized using pyrophosphoric acid, are summarized in Table I. Ultraviolet spectroscopy was used to analyze the fractions (*3*). Examination of this purified material by infrared ($CHCl_3$) showed no absorption at 1685 cm.$^{-1}$ (conj. C=O) or 1638 cm.$^{-1}$ (conj. C=C), and the ultraviolet spectrum (MeOH) showed no absorption at 255 mμ, which indicates the completeness of separation.

Table I. Isomer Distribution during Purification Shown in Weight Per Cent of Composition

Isomer	Initial	Cycle 1	Cycle 2	Cycle 3
II	93.4	95.8	98.2	100.0
III	6.6	4.2	1.8	0.0

EXPERIMENTAL

Preparation of Ketone Mixture (II and III) Using Phosphorus Pentoxide. Cyclohexanone (500 grams, 5.1 moles) was placed in a Waring blender equipped with stainless steel cooling coils. Because of the high viscosity of the reaction mixture, conventional stirring equipment was not suitable.

Phosphorus pentoxide (123.5 grams, 0.87 mole) was added to the stirred cyclohexanone in three equal portions at half-hour intervals. The temperature was maintained at 50° C. throughout the three-hour total reaction time. An equal volume of ether was added, and the solution was washed with ice water to remove excess phosphorus pentoxide. The mixture was dried over $MgSO_4$ and the ether removed. Distillation gave 265.9 grams (58.7%) of the ketone mixture based on consumed cyclohexanone.

Preparation of Ketone Mixture (II and III) Using Pyrophosphoric Acid. Cyclohexanone (362 grams, 3.69 moles) was combined with 300 ml. of benzene in a blender equipped with cooling coils. Pyrophosphoric acid (329 grams, 1.85 moles) was added drop-wise to the stirred cyclohexanone solution over a four-hour period, and the resulting mixture was stirred a total of 24 hours. Benzene was removed, and the reaction mixture was continuously extracted with hexane for four hours. The extract was washed several times with water, dried over $MgSO_4$, and the hexane removed. Distillation gave 167 grams (81.6%) of the ketone mixture, based on consumed cyclohexanone.

Preparation of Ketone Mixture (II and III) Using Anhydrous Hydrogen Chloride (*4*). Cyclohexanone (98.1 grams, 1 mole) was placed in a 250-ml. graduated cylinder, cooled to ice bath temperature, and saturated with anhydrous hydrogen chloride for a three-hour period. This mixture was transferred to a 2-liter beaker, and one liter of cooled water was added with rapid mixing. A light yellow crystalline material which separated was filtered. This crude 2-(1-chlorocyclohexyl)cyclohexanone (IV) was washed three times with water to remove any residual acid, along with unreacted cyclohexanone (I). A total of 96 grams (90%) (IV) was obtained, with a melting point of 41–2° C.

To the 96 grams (0.450 mole) (IV) contained in a 1-liter beaker equipped with a magnetic stirrer was added 400 ml. of water. The beaker, with its contents, was submerged in an ice water bath and rapidly stirred. A sodium hydroxide solution (19.0 grams, 0.477 mole in 100 ml. of water) was added to this mixture at such a rate that the temperature did not exceed 40° C. After one hour, the mixture was transferred to a 1-liter separatory funnel, and the layers were separated.

The crude product was washed with water until the washings were neutral to pH paper. A sufficient quantity of diethyl ether was then added to dissolve the product. This solution was dried over $MgSO_4$, filtered, and the ether removed. The resulting material was distilled (117° C. at 4 mm.) to give 65.9 grams (82.4%) of the dimeric ketone mixture (II) and (III). Analysis of a methanolic sample of this mixture by ultraviolet spectroscopy (255 $m\mu$) showed that 9.7% 2-cyclohexylidenecyclohexanone was present in the ketone mixture.

Purification of 2-(1-Cyclohexenyl)cyclohenanone (II). A mixture containing 45.5 grams of (II) and 3.2 grams of (III) was dissolved in 48.7 grams of *n*-pentane and placed in a 1.5 × 8 inch test tube suspended from a controlled-rate lowering device (*6*). The tip of the tube was immersed in a cooling bath at −35° C. After the first crystals formed, the tube was lowered into the bath at the rate of 2 mm. per minute until 80% of the tube's contents was submerged. It was then withdrawn and the liquid portion decanted. The solid was redissolved in a sufficient quantity of *n*-pentane to reestablish a 50-50 wt. % solvent-ketone solution. This procedure was repeated two more times. The 36.7 grams of ketone (II) remaining after the third crystallization was completely free of (III). The melting point found for pure (II) was 7° C.; that reported for (III) is 57° C. (*9*).

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