[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND GEOLOGY, CLEMSON COLLEGE, AND THE SCHOOL OF CHEMISTRY GEORGIA INSTITUTE OF TECHNOLOGY]

# Stereochemistry of the Cycloheptane Ring. II.[1] *cis*- and *trans*-2-Phenylcycloheptanol

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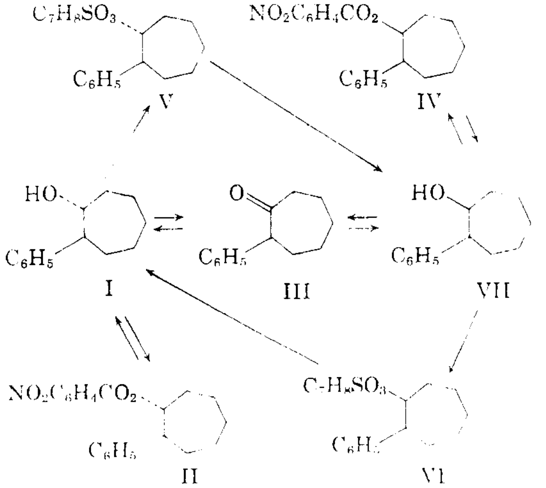
J. W. HUFFMAN[2a] AND J. E. ENGLE[2b]

*trans*-2-Phenylcycloheptanol (I) was prepared from phenyllithium and cycloheptene oxide. The *cis* isomer (VII) was prepared from the *p*-toluenesulfonate of I (IV), by reaction with basic alumina. VII was also prepared, by the lithium aluminum hydride reduction of 2-phenylcycloheptanone (III). VII was converted to I *via cis*-2-phenylcycloheptyl *p*-toluenesulfonate (VI). Both I and VII were dehydrated with phosphoric acid and with phosphorus oxychloride–pyridine to give mixtures of olefins, and other compounds. These mixtures were analyzed and the results discussed in terms of the conformations of the epimeric alcohols.

The steric course of several reactions in the cycloheptane series has been studied[1,3] and various conclusions have been drawn from these reactions, as well as from various theoretical considerations. However, there are apparently no examples of elimination reactions in the cycloheptane series. The classical work relating to the stereochemistry of a relatively simple organic reaction in a flexible ring system is the dehydration of *cis*- and *trans*-2-phenylcyclohexanol.[4] Although it has been shown by later workers that the dehydration of *trans*-2-phenylcyclohexanol does not proceed in the manner proposed by Price,[5] the conclusions drawn by the earlier workers retain their importance, because the work is one of the first examples which proves the general *trans* course of many elimination reactions. It was felt that the synthesis and dehydration of *cis*- and *trans*-2-phenylcycloheptanol would give insight into the effect of ring size on the course of elimination reactions.

The synthesis of *trans*-2-phenylcycloheptanol (I) followed the well known route used for the preparation of *trans*-2-phenylcyclohexanol.[6] Cycloheptene oxide[7] on treatment with phenyllithium gave I, although in low (25%) yield. I was characterized as the solid *p*-nitrobenzoate (II) m.p. 84–85°. With the stereochemistry of one of the isomeric alcohols known with certainty, the requirements for the synthesis of the *cis* alcohol were less rigid. The obvious synthetic route for the preparation of *cis*-2-phenylcycloheptanol was reduction by appropriate means of the readily available 2-phenylcycloheptanone (III).[8] Catalytic hydrogenation of the ketone, under the proper conditions, should proceed by addition of hydrogen from the catalyst surface to the least hindered side of the carbonyl group to afford the *cis* alcohol as the major product.[9] In our hands, however, 2-phenylcycloheptanone failed to yield any isolable alcohol. A number of reductions were carried out at room temperature and atmospheric pressure using various solvents and catalysts, and in no case, where the absorption of hydrogen proceeded at a reasonable rate, was exclusive reduction of the carbonyl group obtained.



As an alternate approach to the *cis* alcohol, the metal hydride reduction of 2-phenylcycloheptanone was investigated. It was anticipated that the reduction of the ketone with sodium or potassium boro-

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[1] J. W. Huffman and J. E. Engle, *J. Org. Chem.*, **24**, 1844 (1959) should be considered to be paper I of this series.

[2] (a) Department of Chemistry and Geology, Clemson College, Clemson, S. C. To whom all inquiries concerning this paper should be directed. (b) Redstone Arsenal Research Division, Rohm & Haas Co., Huntsville, Ala.

[3] (a) J. J. Sicher, J. Jonas, M. Svoboda, and O. Knessl, *Collection Czechoslov. Chem. Communs.*, **23**, 2094 (1958). (b) J. Sicher and M. Svoboda, *Collection Czechoslov. Chem. Communs.*, **23**, 2094 (1958). (c) N. L. Allinger, *J. Am. Chem. Soc.*, **81**, 5727 (1959). (d) R. Pauncz and D. Ginsburg, *Tetrahedron*, **9**, 40 (1960).

[4] C. C. Price and J. V. Karabinos, *J. Am. Chem. Soc.*, **62**, 1159 (1940).

[5] H. J. Schaeffer and C. J. Collins, *J. Am. Chem. Soc.*, **78**, 124 (1956).

[6] J. W. Cook, C. L. Hewett, and C. A. Lawrence, *J. Chem. Soc.*, **71** (1936).

[7] P. B. Talukdar and P. E. Fanta, *J. Org. Chem.*, **24**, 555 (1959).

[8] C. D. Gutsche, *Org. Synthesis*, **35**, 91 (1951).

[9] W. Hückel and R. Neidlein, *Ber.*, **91**, 1391 (1958).

hydride would afford a sizeable percentage of the less stable *cis* isomer.[10] However, attempted reduction by this method gave only a small amount of reduced material and we turned to the more vigorous reducing agent, lithium aluminum hydride. Reduction of III, afforded a mixture of the epimeric alcohols and unreduced ketone. Treatment of the crude reaction mixture with *p*-nitrobenzoyl chloride afforded a solid ester, m.p. 92–93°, which was isomeric with II and must be *cis*-2-phenylcycloheptyl *p*-nitrobenzoate (IV). Vapor phase chromatography and infrared measurements showed that the crude reaction mixture consisted of 64% *cis* alcohol, 13% *trans* alcohol, and 19% unreduced ketone. The formation of a preponderance of the unstable epimer in a lithium aluminum hydride is somewhat unusual. However, the failure of borohydride reductions and hydrogenation of the ketone attest to the hindered nature of the carbonyl group, and the formation of the less stable isomer in the reduction of hindered ketones is not unprecedented.[10] It was possible to isolate a small quantity of the *p*-toluenesulfonate ester (V) of the *trans* alcohol from this reaction mixture, by virtue of the fact that the *trans*-tosylate is some twenty times less soluble in the recrystallization medium (cyclohexane) than is the *cis*-tosylate (VI).

The *p*-toluenesulfonates were converted to the epimeric alcohols by treatment with basic alumina.[11] The *cis*- and *trans*-*p*-nitrobenzoates could be saponified to the corresponding *cis* and *trans* alcohols (VII and I, respectively), and the gross structures of these alcohols were proven by their oxidation to 2-phenylcycloheptanone.

An attempt was made to prepare *trans*-2-phenylcycloheptanol by the reduction of 2-phenylcycloheptanone with lithium aluminum hydride–aluminum chloride, conditions which have been shown to afford a preponderance of the more stable isomer.[12] Although it was not possible to isolate a pure derivative from this reaction, vapor phase chromatography showed that the reaction produced 13% *cis* alcohol, 52% *trans*, 22% recovered ketone, and 13% of five unidentified compounds. It was found in contrast to the results of Eliel and Rerick[12] that reduction of 2-phenylcycloheptanone with lithium aluminum hydride for several hours gave significantly more *trans* alcohol than the short term reduction which gave largely *cis* alcohol. Although the products of the long term reduction were not analyzed in detail, the only product isolable from this reaction was the *trans* alcohol.

In order to have a sample available for a reference compound for vapor phase chromatography, phenylcycloheptane was prepared by the reduction of a mixture of *cis*- and *trans*-2-phenylcycloheptyl-*p*-toluenesulfonates. 1-Phenylcycloheptene was prepared for the same purpose by the dehydration of 1-phenylcycloheptanol, prepared by the reaction of phenylmagnesium bromide and cycloheptanone.[13]

The classical dehydration reactions in the cyclohexane series[4] were carried out by treating the alcohols with hot 85% phosphoric acid. Although Price contended that the dehydration of *trans*-2-phenylcyclohexanol gave largely 3-phenylcyclohexene, it has been shown[5] that this reaction gives a mixture of the three possible phenylcyclohexenes, benzylcycloheptene, and benzalcyclopentane, with 3-phenylcyclohexene comprising only 9% of the total material. The results obtained by Price in the *cis* case were shown to be qualitatively correct.

Dehydration of the *cis*-2-phenylcycloheptanol with phosphoric acid gave 50% of conjugated olefin as determined by ultraviolet spectroscopy. Vapor phase chromatography of the reaction mixture showed that 35% of 1-phenylcycloheptene was formed, in addition of 25% of 3-phenylcycloheptene. The balance of the reaction mixture was composed of varying amounts of five other products. Acid treatment of the *trans* alcohol under the same

TABLE I

ANALYSIS OF DEHYDRATION MIXTURES OF *cis*- AND *trans*-2-PHENYLCYCLOHEPTANOL

| Alcohol | Dehydration Agent | Product | % by Weight |
|---|---|---|---|
| *cis* | $H_3PO_4$ | A | 29 |
| | | 3-Phenylcycloheptene | 25 |
| | | 1-Phenylcycloheptene | 35 |
| | | B | trace |
| | | C | 6 |
| | | D | trace |
| | | E | 3 |
| *cis* | $POCl_3$ | 3-Phenylcycloheptene | 8 |
| | | 1-Phenylcycloheptene | 41 |
| | | X | 7 |
| | | *trans*-2-Chlorophenylcycloheptane | 42 |
| | | *cis*-2-Chlorophycycloheptane | 3 |
| *trans* | $H_3PO_4$ | A | 65 |
| | | 3-Phenylcycloheptene | 27 |
| | | 1-Phenylcycloheptane | 10 |
| | | B | trace |
| | | C | 3 |
| | | D | trace |
| *trans* | $POCl_3$ | 3-Phenylcycloheptene | 32 |
| | | 1-Phenylcycloheptene | 2 |
| | | X | 1 |
| | | Y | 1 |
| | | *trans*-2-Chlorophenylcycloheptane | 2 |
| | | *cis*-2-Chlorophenylcycloheptane | 62 |

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[10] (a) W. G. Dauben, C. J. Fonken, and D. S. Noyce, *J. Am. Chem. Soc.*, **78**, 2579 (1956). (b) D. M. S. Wheeler and J. W. Huffman, *Experientia*, **16**, 516 (1960).

[11] (a) G. H. Douglas, O. S. Ellington, G. D. Meakins, and R. Swindells, *J. Chem. Soc.*, 1720 (1959). (b) F. C. Chang and R. T. Blickenstaff, *Chem. & Ind.* (*London*), 590 (1958).

[12] E. C. Eliel and M. N. Rerick, *J. Am. Chem. Soc.*, **82**, 1367 (1960).

[13] G. Baddely, J. Chadwick, and H. T. Taylor, *J. Chem. Soc.*, 45 (1956).

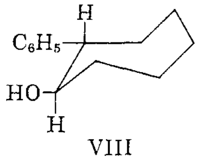
conditions gave the same seven compounds, but in varying amounts. Ultraviolet measurements showed that about 25% of conjugated olefins were formed. These results were also confirmed by vapor phase chromatography, the results of which are summarized in Table I.

The usefulness of the results of the dehydrations with phosphoric acid are suspect, however, in view of the fact that a sample of a dehydration mixture containing no conjugated olefin is rapidly converted to a mixture containing 25% of conjugated material, which is presumed to be 1-phenylcycloheptane. Schaeffer and Collins have also obtained evidence of the instability of 3-phenylcyclohexene under the conditions of the dehydrations.

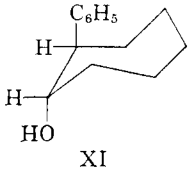
In view of the ambiguities involved in the acid catalyzed dehydrations we turned our attention to dehydration conditions where rearrangement of the olefins produced is precluded. Mild, stereospecific, dehydrating agents which have found use in the steroid and related fields are phosphorus oxychloride and thionyl chloride. Although the detailed mechanism of these reactions is not known[14] there appear to be a sufficient number of precedents in the steroid field to indicate that the dehydrations with inorganic acid chlorides and pyridine proceed to give nearly exclusive *trans* elimination of water.[15]

Attempted dehydration of the phenylcycloheptanols with thionyl chloride–pyridine gave dark colored liquids which showed no absorption in the ultraviolet. Treatment of the alcohols with phosphorus oxychloride–pyridine afforded nearly colorless oils which were analyzed by a combination of infrared and ultraviolet spectroscopy, and vapor phase chromatography. The details of these analyses are discussed in the experimental section and the results are listed in Table I.

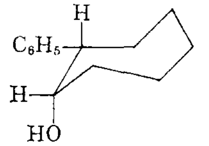
In a completely qualitative manner it is apparent from the production of only 2% 1-phenylcycloheptene from the dehydration of *trans*-2-phenylcycloheptanol that the geometry of the cycloheptane ring is such that dehydrations in the cycloheptane series occur *via* a normal *trans* elimination as in the case of cyclohexane derivatives. The results in the dehydration of the *cis* alcohol also bear out this conclusion, in that one obtains a mixture of both 1- and 3-phenylcycloheptane. If one assumes, as seems likely, that substituents on a cycloheptane ring occupy, a quasi-equatorial conformation then the preferred comformation of the *trans* alcohol will be VIII, while one can consider that the *cis* alcohol will be a mixture of IX and X.



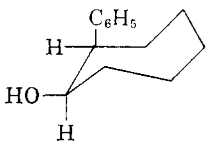
VIII



XI



IX



X

Since the elimination of water from an alcohol by means of phosphorus oxychloride pyridine proceeds by a normal anti-parallel mechanism,[14] then the conformational isomers responsible for the production of olefins will be IX and XI, for the *cis* and *trans* alcohols respectively. In the case of the *trans* alcohol the di-quasi-axial form, XI would be assumed to be of negligible importance, at least in the starting alcohol, however, from the analysis of the dehydration mixture, it is evident that at least 32% of the alcohol reacts in this form. The bulk of the material appears to react in the more stable form, VIII, as is evidenced by the production of 62% *cis*-2-chlorophenylcycloheptane.[16] In the case of the *cis* compound, virtually half of the alcohol reacts in each form (IX and X) as is shown by the formation of 49% of olefins and 42% of *trans*-2-chlorocycloheptane.[16] This is the expected result if it is observed that in both IX and X one group is quasi-axial, and the other quasi-equatorial.

While the formation of a large percentage of chloro compound under the conditions of these dehydrations is somewhat unusual in the cyclohexane series, occurring in only certain sterically hindered alcohols, such as 7β-hydroxycholestanyl acetate,[17] in view of the greatly enhanced reactivity of cycloheptane derivatives to nucleophilic substitution re-

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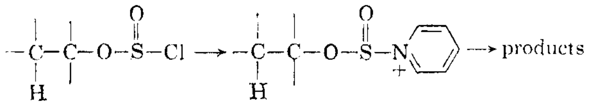
[14] It would seem that the first step in these dehydrations is the same as that in the reaction whereby an alcohol treated with thionyl chloride in pyridine forms the chloride of opposite configuration, *i.e.*, initial formation of a chlorosulfite (or phosphite) ester which then reacts with pyridine to give the appropriate pyridinium salt. This may then undergo either nucleophilic ($S_N2$) displacement by chloride, or a concerted (probably $E_1$)[15] elimination to give the olefin, sulfur dioxide, and pyridine hydrochloride. A similar mechanism must prevail with phosphorus oxychloride in pyridine. For a discussion of the displacement reactions of chlorosulfite esters see J. Hine, *Physical Organic Chemistry*, McGraw-Hill, New York, 1956, 114–115.



$$-\underset{H}{\overset{|}{\underset{|}{C}}}-\overset{|}{\underset{|}{C}}-O-\overset{O}{\overset{\|}{S}}-Cl \longrightarrow -\underset{H}{\overset{\vdots}{\underset{|}{C}}}-\overset{|}{\underset{|}{C}}-O-\overset{O}{\overset{\|}{S}}-\underset{+}{N} \longrightarrow \text{products}$$

[15] L. F. Fieser and M. Fieser, *Steroids*, Reinhold, New York, 1959, give a number of examples of dehydrations in the steroid field.

[16] Although we have no experimental evidence that the conversion of the alcohols to the corresponding chlorides proceeds with inversion, a consideration of the mechanism of these reactions (see Ref. 14) indicates that inversion certainly occurs. The identity of the small quantity of isomeric chloro compound is based on a comparison of the retention times from the vapor phase chromatographic analysis.

[17] W. Buser, *Helv. Chim. Acta.*, 30, 1379 (1947).

actions, as compared to cyclohexanes[18] the production of large percentages of chloro compounds from *cis*- and *trans*-2-phenylcycloheptanol does not appear particularly unusual.

## EXPERIMENTAL[19]

*trans-2-Phenylcycloheptanol.* (a) *trans*-2-Phenylcycloheptanol was prepared according to the method whereby Cook, Hewett, and Lawrence prepared *trans*-2-phenylcyclohexanol. Phenyllithium was prepared by the addition of small pieces of freshly cut lithium to a solution of bromobenzene in ether maintained at ice bath temperature. The reaction mixture was stirred for 1 hr.; approximately two thirds of the lithium had dissolved. To the cold solution of phenyllithium, an ether solution of cycloheptene oxide (a quantity equivalent to the theoretical amount of phenyllithium) was added dropwise with stirring. The reaction mixture was maintained at ice bath temperature for about thirty minutes and then boiled under reflux for 2 hr.; excess aqueous ammonium chloride was added, and the organic material isolated by extraction with ether. The ether extract was washed with sodium bicarbonate, dried and concentrated on the steam bath at reduced pressure. The resulting oil was distilled at 113–114° (0.5 mm.) to yield 25% of *trans*-2-phenylcycloheptanol.

The *p*-nitrobenzoate ester was prepared by reaction of the alcohol in dry pyridine with *p*-nitrobenzoyl chloride. Crystallization from 95% ethanol afforded pale yellow crystals, m.p. 84.0–85.0°.

*Anal.* Calcd. for $C_{20}H_{21}NO_4$: C, 70.78 H, 6.24; N, 4.13. Found: C, 70.62; H, 6.01; N, 4.24.

(b) Sodium hydroxide (2.6 g., 0.065 mole) was added to a mixture of 3.87 g. of (0.0114 mole) *trans*-2-phenylcycloheptyl *p*-nitrobenzoate, 45 ml. of dioxane, and 19 ml. of water. The *p*-nitrobenzoate ester was derived from the crude product of an extended reduction (*vide infra*) of 2-phenylcycloheptanone with lithium aluminum hydride.

The mixture was heated under reflux for 9 hr. The dioxane was removed at reduced pressure as the dioxane–water azeotrope, 100 ml. of water added, and the mixture extracted with three portions of chloroform. The extracts were washed twice with water, dried, and the chloroform removed *in vacuo* yielding 2.04 g., 94% of colorless oil. Short path distillation afforded 1.448 g., 67% of *trans*-2-phenylcycloheptanol, $n_D^{25}$ 1.5415.

Vapor phase chromatography of the distilled *trans* alcohol showed it to be homogeneous.

(c) A solution of 805 mg. (2.34 mmoles) of *cis*-2-phenylcycloheptyl *p*-toluenesulfonate in 4 ml. of dry benzene was applied to a column (2 × 20 cm.) of 67.5 g. of basic alumina prepared in dry benzene. After standing at room temperature for 59 hr. elution with 300 ml. of dry benzene afforded 256 mg., 64% of olefinic material. Further elution with 300 ml. of 5% methanol in ether yielded 104 mg., 23% of *trans*-2-phenylcycloheptanol.

The *p*-nitrobenzoate ester was prepared, m.p. 83.0–84.4°, mixed melting point with authentic *trans*-2-phenylcycloheptyl *p*-nitrobenzoate, 83.3–84.6°.

*trans-2-Phenylcycloheptyl p-toluenesulfonate.* *trans*-2-Phenylcycloheptanol (1.107 g., 0.006 mole) was dissolved in 20 ml. of dry pyridine, cooled in ice, and 1.52 g. (0.008 mole) of *p*-toluenesulfonyl chloride was added in one portion. The mixture was allowed to stand in a melting ice bath and then at room temperature for 3 days. Excess saturated sodium bicarbonate solution and water were added. The precipitated *trans*-2-phenylcycloheptyl *p*-toluenesulfonate was collected, washed well with water, and air dried yielding 1.23 g., m.p. 96.0–96.4°. The melt was heterogeneous at the melting point. The aqueous portion of the reaction mixture was extracted several times with chloroform which was washed with hydrochloric acid, dried, and concentrated at reduced pressure yielding solid material. Crystallization from cyclohexane gave 0.15 g. of white crystals. This portion was combined with that obtained directly giving a total yield of 1.38 g., 69%. Crystallization from cyclohexane afforded 1.00 g., 50% of *trans*-2-phenylcycloheptyl *p*-toluenesulfonate, m.p. 82–83°[20] (heterogeneous at the melting point).

*Anal.* Calcd. for $C_{20}H_{24}O_3S{\cdot}2H_2O$: C, 63.13; H, 7.42. Found: C, 63.92; H, 6.82.

In the case of both the *cis*- and *trans*-*p*-toluenesulfonates it was not found possible to obtain good analytical results.

Drying of a portion at 80° for 14 hr. at oil pump pressure caused extensive decomposition to occur resulting in a brown gum with only a 2.5% loss in weight. The gum, extracted exhaustively with cyclohexane, yielded a glass.

*Reduction of 2-phenylcycloheptanone:* (a) *Short reaction time* A slurry of 12.2 g. (0.32 mole) of lithium aluminum hydride in 375 ml. of dry ether was prepared and stirred for *ca.* 5 min. The flask was cooled in an ice bath, and a solution of 30 g. (0.16 mole) of 2-phenylcycloheptanone in 200 ml. of dry ether was added dropwise over a period of 15 min. The reaction was maintained at ice bath temperature and stirred for 70 min. One hundred milliliters of ethyl acetate was added dropwise, followed by 60 ml. of water and 250 ml. of 6*N* hydrochloric acid, the layers were separated, and the aqueous phase extracted twice with ether; the ether portions were combined, washed with dilute sodium bicarbonate, dried, and the ether removed at the water pump. The remaining ethyl acetate was removed with a stream of dry air yielding *ca.* 30 g. of oil. Analysis of the reaction mixture by a combination of vapor phase chromatography, and infrared spectroscopy showed the oil contained 64% *cis* alcohol, 13% *trans*, and 19% unreduced ketone.

A 6.6-g. portion of the crude product was dissolved in 25 ml. of dry pyridine, cooled in ice, and 12.0 g. (0.061 mole) of *p*-toluenesulfonyl chloride was added in one portion. The mixture was swirled for a few minutes, allowed to stand in a melting ice bath, and then at room temperature for 3 days. Excess saturated sodium bicarbonate solution was added with cooling, and the mixture extracted with several portions of chloroform. The chloroform was washed well with dilute hydrochloric acid, and removed (below 50°) at reduced pressure to yield 8.9 g. of oil which did not solidify upon refrigeration overnight. The oil was dissolved in 150 ml. of petroleum ether (b.p. 30–60°), and the crystals which formed after several hours of refrigeration were collected and washed with petroleum ether, yield 1.40 g., m.p. 81.5–106°. The melt became heterogeneous suddenly at 117°. Recrystallization four times from cyclohexane, not exceeding 60°, yielded 132.3 mg., 1.1% (if all starting material were alcohol) of *trans*-2-phenylcycloheptyl *p*-toluenesulfonate, m.p. 83.5–84°.

Another 5.0-g. portion of the crude product was dissolved in 20 ml. of dry pyridine and treated with 9.25 g. (0.05 mole) of *p*-nitrobenzoyl chloride at room temperature. The mixture was allowed to stand without cooling for 1 hr. Water was added, and the mixture extracted with chloroform. Washing of the chloroform extract with sodium bicarbonate and dilute hydrochloric acid, drying, and removal of the solvent gave an oil. The oil was taken up in 200 ml. of 95% ethanol, filtered, and concentrated to 50 ml. on a steam bath. After refrigeration the solid was collected and air dried yielding 2.57 g., m.p. 81–88°. Eight crystallizations from hot 95% ethanol

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[18] J. Hine, *Physical Organic Chemistry*, McGraw-Hill, New York, 1956, p. 160.

[19] Analyses were performed by Galbraith Laboratories, Knoxville, Tenn. Infrared spectra were carried out in chloroform solution or as liquid films on a Perkin-Elmer model 137 spectrophotometer. Ultraviolet spectra were carried out in 95% ethanol on a Beckman model DK-1 spectrophotometer. Melting points were determined on a Fisher-Johns block and are uncorrected.

[20] S. J. Cristol and F. R. Stermitz, *J. Am. Chem. Soc.*, 82, 4692 (1960) have reported similar melting point behavior on recrystallization of 2-phenylcyclohexyl tosylates.

afforded 0.996 g., 11% of *cis*-2-phenylcycloheptyl *p*-nitrobenzoate, m.p. 92.0–93.2°.

*Anal.* Calcd. for $C_{20}H_{21}NO_4$: C, 70.78; H, 6.24; N, 4.13. Found: C, 71.00; H, 6.08; N, 4.16.

(b). *Extended reaction time.* A solution of 25.0 g. (1.33 moles) of 2-phenylcycloheptanone in 100 ml. of dry ether was added, during 1 hr., with stirring to 9.9 g. (0.26 mole) of lithium aluminum hydride in 100 ml. of dry ether. The reaction mixture was kept cold for 1.5 hr., boiled under reflux for 9 hr., and stirred at room temperature overnight. Seventy milliliters of ethyl acetate was added followed by 100 ml. of water and 200 ml. of 6*N* hydrochloric acid. The layers were separated, and the aqueous phase extracted with two portions of ether. The combined ether extracts were washed with sodium bicarbonate solution, dried, and concentrated on a steam bath at reduced pressure, yield 24.3 g., 96%.

Preparation of the *p*-nitrobenzoate ester with *p*-nitrobenzoyl chloride in pyridine afforded an oil which was crystallized from 95% ethanol giving a 67% yield, m.p. 78–87°. Several recrystallizations gave 3.76 g., of *trans*-2-phenylcycloheptyl *p*-nitrobenzoate; m.p. and mixed m.p. 82–84°.

*Reduction of 2-phenylcycloheptanone with lithium aluminum hydride–aluminum chloride.* To 400 ml. of dry ether cooled in an ice bath was added slowly, with stirring, 53.4 g. (0.400 mole) of aluminum chloride followed by 3.79 g. (0.100 mole) of lithium aluminum hydride. This mixture was allowed to stir at ice bath temperature for 1 hr., at which time 38.25 g. (0.203 mole) of 2-phenylcycloheptanone dissolved in 100 ml. of dry ether was added during the 25 min. The ice bath was removed and the mixture was boiled under reflux with continued stirring for 12 hr. Forty-five milliliters of water was added, followed by 300 ml. of 10% sulfuric acid; the layers were separated, and the aqueous phase was extracted with two portions of ether. The ethereal layer was washed with one portion of 5% sodium bicarbonate, dried, and concentrated on the steam bath at reduced pressure yielding 38.1 g. of crude product. Although no solid derivative could be obtained in this run, vapor phase chromatography showed the mixture to consist of 13% *cis* alcohol, 52% *trans* alcohol, 22% ketone, and 13% of five unidentified products.

*cis-2-Phenylcycloheptanol* (a) *trans*-2-Phenylcycloheptyl *p*-toluenesulfonate (1.506 g., 4.32 mmoles) dissolved in 8.0 ml. of dry benzene was applied to a column of basic alumina, (127 g., 4.5 × 18 cm.) prepared in dry benzene, and washed once with eight 1-ml. portions of dry benzene. The column was allowed to stand at room temperature for 6 hr. Elution with 300 ml. of benzene gave 373 mg., 50% of colorless oil. The next 400 ml. of benzene eluate was discarded as was the initial 100 ml. of methanol-ether eluate. Further elution with 200 ml. of 5% methanol in ether gave 332 mg., 40% of *cis*-2-phenylcycloheptanol as a colorless oil.

The *p*-nitrobenzoate was prepared in the usual way, m.p. 91.5–93.5°, mixed melting point with authentic *cis*-2-phenylcycloheptyl *p*-nitrobenzoate, *vide supra* 91.8–93.2°.

(b) The saponification of *cis*-2-phenylcycloheptyl *p*-nitrobenzoate derived from short reduction of 2-phenylcycloheptanone with lithium aluminum hydride was carried out in the same way as for *trans*-2-phenylcycloheptyl *p*-nitrobenzoate. *cis*-2-Phenylcycloheptanol was obtained after saponification as a colorless oil; distillation afforded a fraction boiling at 98.5–102.5°/0.25 mm., yield 72%, $n_D^{25}$ 1.5436.

*cis-2-Phenylcycloheptyl p-toluenesulfonate.* To a cold solution of 1.66 g. (8.73 mmoles) of *cis*-2-phenylcycloheptanol in 8 ml. of dry pyridine was added 2.49 g. (13.10 mmoles) of *p*-toluenesulfonyl chloride. The mixture was allowed to stand in a melting ice bath and then at room temperature for 3 days. The flask was chilled in ice and excess sodium bicarbonate solution was added. The mixture was extracted with chloroform and the extracts washed with dilute hydrochloric acid, dried, and concentrated below 50°, under reduced pressure, to yield 2.40 g., 80% of *cis*-2-phenylcycloheptyl *p*-toluenesulfonate as an oil which crystallized fully on standing at room temperature. The white solid was crystallized three times from cyclohexane, maintained below 60°, to yield 830 mg., 28% of small white crystals, m.p. 91.7–93.0°. The melt became heterogeneous at 104°.

*Anal.* Calcd. for $C_{20}H_{24}O_3S{\cdot}2H_2O$: C, 63.13; H, 7.42. Found: C, 63.64; H, 6.91.

*Phenylcycloheptane.* A mixture of *cis*- and *trans*-2-phenylcycloheptyl *p*-toluenesulfonates (3.49 g., 0.0101 mole) in the minimum amount of dry ether to effect solution (*ca.* 200 ml.) was added to a slurry of 0.38 g. (0.01 mole) of lithium aluminum hydride in 30 ml. of dry ether at room temperature. After boiling under reflux for 20 hr., an additional 0.3 g. (0.008 mmole) of lithium aluminum hydride was added, and boiling continued for another 21 hr. One hundred milliliters of water was added slowly with ice bath cooling followed by 100 ml. of 6*N* hydrochloric acid. The layers were separated; the aqueous phase was extracted with one portion of ether, and the combined ethereal extracts were washed with one portion of sodium bicarbonate, dried, and concentrated on a steam bath, yielding 1.73 g., 98%, of crude phenylcycloheptane.

The crude product was chromatographed on 150 g. (3.2 × 17.0 cm.) of acid washed alumina prepared in, and eluted with petroleum ether. The first 150 ml. of eluate containing 80.9 mg. of oil was discarded. The next 100 ml. of eluate was collected and evaporated to yield 1.330 g., 76%, of colorless oil. Further elution with 150 ml. of petroleum ether produced 135 mg. of residue. The middle fraction was distilled through a short path to apparatus yield 0.728 g., 41%, of phenylcycloheptane, $n_D^{25}$ 1.5254.[21]

*1-Phenylcycloheptene.* Phenylmagnesium bromide, prepared from 14.9 g. (0.095 mole) of bromobenzene in 75 ml. of dry ether was treated with 10.0 g. (0.089 mole) of cycloheptanone according to Baddeley, Chadwick, and Taylor,[13] in the usual Grignard fashion. Completion of the reaction yielded crude 1-phenylcycloheptanol. Dehydration and fractional distillation afforded 7.04 g., 46%, of 1-phenylcycloheptene, b.p. 74.5–76.5/0.3 mm., $n_D^{25}$ 1.5575, $\lambda_{max}$ 247 m$\mu$, $\epsilon$, 14,000. The reported boiling point is 113–115°/8 mm. and $n_D^{20}$ 1.5624.[22] The $\lambda_{max}$ reported is 247 m$\mu$ ($\epsilon$ 11,500).[13] Vapor phase chromatography showed the product to be homogeneous.

*2-Phenylcycloheptanone.* (a) Kiliani's reagent, prepared according to Sato and Ikekawa,[23] was added dropwise to 244 mg. (1.29 mmoles) of *trans*-2-phenylcycloheptanol in 2 ml. of redistilled acetone until a greenish-orange color was permanent. During the addition a very dark oil separated and settled. Water was added, and then 5% sodium hydroxide until the mixture was alkaline. Extraction with chloroform and removal of the solvent gave a yellow oil which was taken up in 95% ethanol and treated with 2,4-dinitrophenylhydrazine reagent. The yellow precipitate was collected, washed with 95% ethanol, and dissolved in *ca.* 6 ml. of ethyl acetate which was filtered and evaporated to 0.5 ml. Ethanol was added, whereupon crystallization occurred immediately. The flask was cooled, and the 2-phenylcycloheptanone 2,4-dinitrophenylhydrazone collected, m.p. 168.5–171.5°. mixed melting point with the same derivative of authentic 2-phenylcycloheptanone showed no depression.

(b) *cis*-2-Phenylcycloheptanol (268 mg., 1.14 mmoles) was dissolved in 2 ml. of redistilled acetone. Kiliani's reagent was added dropwise until a greenish-orange color was permanent. Water (25 ml.) and sodium hydroxide (25 ml.) were added and the mixture extracted with four 10-ml. portions of chloroform. The extract was dried and the solvent removed under reduced pressure yielding 211 mg., 79%, of 2-phenylcycloheptanone.

The 2,4-dinitrophenylhydrazone was prepared, m.p. 170.8–171.3°, mixed melting point with authentic 2-phenylcycloheptanone 2,4-dinitrophenylhydrazone, 171.0–172.5°.

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(21) A. C. Cope, and A. A. D'Addreco, *J. Am. Chem. Soc.*, **73,** 3419 (1951) give $n_D^{25}$ 1.5287.

(22) H. Pines, A. Edeleanu. and V. N. Ipatieff, *J. Am. Chem. Soc.*, **67,** 2193 (1945).

(23) Y. Sato and N. Ikekawa, *J. Org. Chem.*, **24,** 1367 (1959).

*Dehydration of cis-2-phenylcycloheptanol with phosphorus oxychloride pyridine.* *cis*-2-Phenylcycloheptanol (122 mg., 0.64 mmole) was dissolved in 2.0 ml. of dry pyridine. Phosphorus oxychloride (0.15 ml.) was added slowly, and the solution, protected with a calcium chloride tube, was warmed on a steam bath for 1 hr. The clear, colorless solution was cooled, diluted with 3 ml. of water, and extracted with four 1-ml. portions of ether. The extract was washed with three 1-ml. portions of 6*N* hydrochloric acid, dried, and the ether was removed under a stream of dry nitrogen, yielding 103 mg., 93%, of clear, virtually colorless oil. A combination of vapor phase chromatography, and infrared and ultraviolet spectroscopy showed the product to consist of 8% 3-phenylcycloheptene, 41% 1-phenylcycloheptene, 42% of *trans*-2-chlorophenylcyclohexane, and 8% of two unidentified products.

*Dehydration of trans-2-phenylcycloheptanol with phosphorus oxychloride in pyridine.* The same procedure was followed as for *cis*-2-phenylcycloheptanol yielding 89% of a clear, colorless oil.

Analysis of the product, as in the case of the *cis* alcohol showed the product to be composed of 32% 3-phenylcycloheptene, 2% 1-phenylcycloheptene, 62% *cis*-2-chlorophenylcycloheptane, and 4% of three unidentified products.

*Dehydration of cis-2-phenylcycloheptanol with phosphoric acid.* A mixture of 121 mg. (0.640 mmole) of *cis*-2-phenylcycloheptanol and 206 mg. of 85% phosphoric acid was maintained at 150–200° for 3 hr. The mixture was cooled, diluted with 2 ml. of water, and extracted with four 2-ml. portions of ether. The ether extract was washed with two 2-ml. portions of 5% sodium hydroxide, dried, and concentrated under a stream of dry air to yield 101 mg., 92% of yellow oil. The analysis of this material showed it to contain 35% 1-phenylcycloheptene, 25% 3-phenylcycloheptene and varying percentages of five other products.

*Dehydration of trans-2-phenylcycloheptanol with phosphoric acid.* The same procedure was followed as for *cis*-2-phenylcycloheptanol, yielding 84% of yellow oil. Analysis of this oil showed it to contain 10% 1-phenylcycloheptene, 2% 3-phenylcycloheptene, and varying percentages of five other compounds.

*Treatment of 3-phenylcycloheptene with phosphoric acid.* The crude product, 38.3 mg., obtained from the dehydration of *trans*-2-phenylcycloheptanol with phosphorus oxychloride was heated in 76.7 mg. of 85% phosphoric acid in a manner similar to the phosphoric acid dehydration. Isolation of the ether-soluble fraction provided 30.2 mg. of brown oil. Ultraviolet spectroscopic measurement using the extinction at 247 mμ showed that the product contained *ca.* 25% 1-phenylcycloheptene.

*Analysis of mixtures.* The dehydration mixtures in solution with dry benzene were filtered through a short column of acid-washed alumina. The gas chromatographic analyses were conducted on a 6 ft. × 4 mm. glass column packed with General Electric silicone gum (SE30) coated on 80–100 mesh Chromosorb W (*ca.* 3% silicone by wt.). The column was maintained at 153° with an inlet pressure of 16.5 p.s.i. of argon. The flow rate of gas under these conditions was *ca.* 30 ml./min.

The percentage of 1-phenylcycloheptene was determined by comparing peaks and retention time with that of synthetic 1-phenylcycloheptene and by means of the ultraviolet maximum at 247 mμ which agreed well with the percentages determined by vapor phase chromatography. 3-Phenylcycloheptene was determined by hydrogenation of the dehydration product of *trans*-2-phenylcycloheptanol with phosphorus oxychloride–pyridine and this figure agreed well with the maximum assigned in the vapor phase chromatographic analysis. The chlorophenylcycloheptanes were detected from an examination of the infrared spectrum of the dehydration mixtures, (no hydroxyl, carbonyl, or phosphate ester bands) and comparison of these spectra with those of an authentic sample.

*cis-2-Chlorophenylcycloheptane.* This material was prepared from *cis*-2-phenylcycloheptanol by the general method of Frazer[24] *et al.* To a chilled solution of 1.0 g. (5.25 mmoles) of *cis*-2-phenylcycloheptanol in 50 ml. of dry ether was added 0.715 g. (6.00 mmoles) of thionyl chloride and 0.475 g. (6.00 mmoles) of dry pyridine. The reaction was allowed to warm to room temperature and then to stand 15 min. The pale yellow solution was filtered, and the solvent removed at reduced pressure. To the yellow residual oil was added 0.25 g. (3.12 mmoles) of thionyl chloride and the reaction heated 3 hr. on the steam bath, cooled, and diluted with ether. The ethereal solution was washed well with water, dilute sodium hydroxide, dried, and the solvent removed *in vacuo* to give 0.49 g. of brown oil. This oil was distilled at 0.7 mm. pressure to give a small quantity of colorless liquid, b.p. 90–105° (bath temperature).

*Anal.* Calcd. for $C_{13}H_{17}Cl$: C, 74.80; H, 8.21; Cl, 17.03. Found: C, 75.07; H, 8.30; Cl, 16.69.

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CLEMSON, S. C.

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