significant amounts of the alcoholysis product, 2,4-dinitrophenetole, from this reaction. Unfortunately, this isolation experiment does not permit an unambiguous conclusion since, under the conditions of the experiment, 2,4-dinitrophenylpyridinium chloride undergoes alcoholysis to give 2,4-dinitrophenetole. With added pyridinium ion the alcoholysis of both the chloride and the quaternary ammonium salt is in part suppressed. In the absence of quantitative rate studies it is, therefore, not possible to assert that any of the 2,4-dinitrophenetole results from alcoholysis of the chloride rather than the quaternary ammonium salt.

Analysis of our rate data leads to an equally ambiguous result. The instantaneous rates are constant throughout the course of each run. The values in Table XI are, therefore, indistinguishable from the rates at zero time. At zero time, without added pyridinium ion, it can be assumed that the concentrations of ethoxide and pyridinium ion are equal, and it may be shown that

$$k_2(\text{pyridine})^{1/2} = k_1(\text{pyridine})^{1/2} + k_3K^{1/2} \quad (12)$$

where k_2 is the experimental second-order rate constant, k_1 is the rate with pyridine, k_3 the rate with ethoxide ion and K, the equilibrium constant for the reaction of pyridine with ethanol.

In accord with this equation a plot of $k_2(\text{pyridine})^{1/2}$ *vs.* $(\text{pyridine})^{1/2}$ is linear, and every point falls on the line. The intercept, however, is slightly negative, but if we were to draw a line with a slightly positive intercept, giving a reasonable value for $k_3K^{1/2}$, all of the points would still be on this alternate line within experimental error. The effect is thus too small and our results are insufficiently precise to permit a clear decision.

Finally, our results with added salts (Table XII) show that the reaction is subject to a positive salt effect but indicate no effect other than a neutral salt effect due to added pyridinium ion. Both this and the constancy of the instantaneous rate constants during the course of each run support an absence of any appreciable alcoholysis affecting the rate. Within the precision of our results, the best conclusion that can be drawn is that the reaction is truly bimolecular.

NORTH ADAMS, MASSACHUSETTS

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF NORTHWESTERN UNIVERSITY]

The Stereochemistry of Ketonization. IV[1]

BY HOWARD E. ZIMMERMAN

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Irreversible ketonization of the enol of 1-acetyl-2-phenylcyclohexane has been found to yield predominantly the *cis*-ketone. The degree of selectivity compared to closely related examples is rationalized with a concept of specific and non-specific steric hindrance. Acid-catalyzed bromination of *cis*-1-acetyl-2-phenylcyclohexane yields the expected 1-acetyl-1-bromo-2-phenylcyclohexane while *trans*-1-acetyl-2-phenylcyclohexane affords 1-bromoacetyl-2-phenylcyclohexane.

For a thorough understanding of the stereochemistry of the ketonization reaction of enols, previously shown to yield frequently the less stable of two stereoisomers,[2-4] a complete elucidation of the relation between molecular structure and both the direction and degree of stereoselectivity seems necessary. In particular, knowledge of the effect of small structural changes would be extremely useful.[5] The present paper relates details of a study of the 1-acetyl-2-phenylcyclohexane enol, this being one of a number of closely related systems studied in our laboratory with this objective in mind.

Of the two stereoisomeric 1-acetyl-2-phenylcyclohexanes requisite for this study, only one, m.p. 81°, had been reported. This seemed almost certainly to be the *trans* isomer, since it had been synthesized[6] from the 2-phenylcyclohexanecarboxylic acid shown more recently[7] to be *trans*. A synthesis by Kipping and Perkin[8] of the 81° ketone by treatment of ethyl 1-acetyl-2-phenylcyclohexanecarboxylate with alcoholic potassium hydroxide was not incompatible with this view, the drastic conditions sufficing for equilibration.[9]

However, two syntheses, which on mechanistic bases would be expected to lead to the *cis* stereoisomer, had been reported to result in formation of the same 81° 1-acetyl-2-phenylcyclohexane. The first involved hydrogenation of the Diels–Alder product from 1-phenylbutadiene and methyl vinyl ketone.[10-12] In the second[13] the 81° ketone was obtained from the conjugate addition of phenylmagnesium bromide to 1-acetylcyclohexene along with considerable 1,2-addition product. Since the product configuration in such a reaction is determined during enol ketonization,[2] by analogy with the stereochemistry of ketonization in similar systems[2-4] the *cis*-ketone would be predicted unless

(1) Part of this material was presented at the Sixth Reaction Mechanism Conference, held at Swarthmore College, September, 1956.

(2) H. E. Zimmerman, *J. Org. Chem.*, **20**, 559 (1955).

(3) H. E. Zimmerman, THIS JOURNAL, **78**, 1168 (1956).

(4) H. E. Zimmerman and H. J. Giallombardo, *ibid.*, **78**, 6259 (1956).

(5) *Cf.* the comparable use of substituent effects in studying resonance and polar factors.

(6) C. D. Gutsche and W. S. Johnson, THIS JOURNAL, **68**, 2239 (1946). This synthesis utilized the reaction of the acid chloride with the conjugate base of diethyl malonate followed by hydrolysis and decarboxylation. Isomerization to the *cis* series is unlikely.

(7) C. D. Gutsche, *ibid.*, **70**, 4150 (1948).

(8) F. S. Kipping and W. H. Perkin, *J. Chem. Soc.*, 304 (1890).

(9) The decarboxylation, which must proceed by way of the enol, would be anticipated to yield largely the *cis* product were it not for the isomerizing conditions.

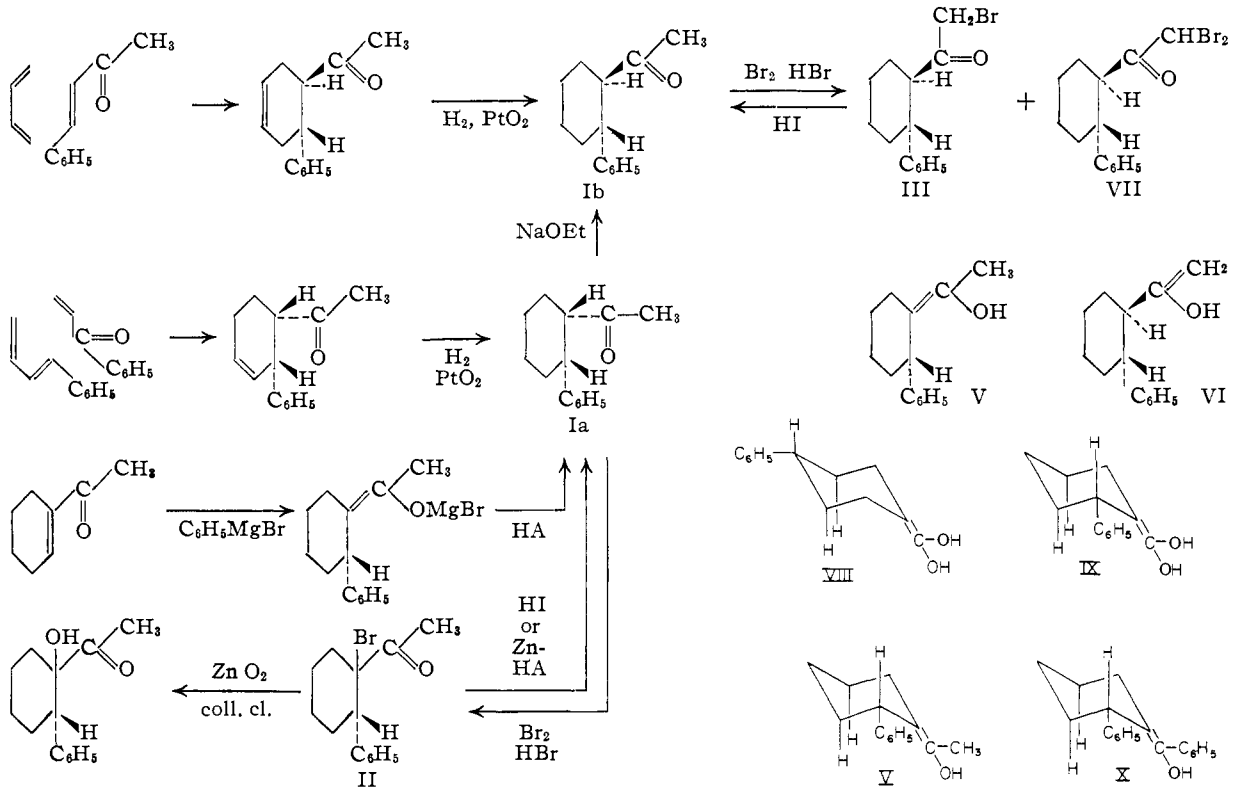
(10) G. A. Ropp and E. C. Coyner, THIS JOURNAL, **71**, 1832 (1949).

(11) L. Reich and E. I. Becker, *ibid.*, **71**, 1834 (1949).

(12) (a) Some evidence for a second Diels–Alder stereoisomer, in the form of a second semicarbazone, was reported in ref. 11; however, only the 81° hydrogenation product was isolated. (b) The *cis*-ketone is predicted by the Alder rule of maximum accumulation of unsaturation to result from *trans*-1-phenylbutadiene. *cis*-1-Phenylbutadiene has been reported to be unreactive in the diene synthesis by O. Grummitt and F. Cristoph, THIS JOURNAL, **73**, 3479 (1951).

(13) D. Nightingale, E. Milberger and A. Tomisek, *J. Org. Chem.*, **13**, 357 (1948).

CHART I



the reaction or isolation conditions were equilibrating.

Thus it was necessary to synthesize the unknown 1-acetyl-2-phenylcyclohexane stereoisomer and to clarify the configurational questions before proceeding with the study of ketonization.

trans-1-Acetyl-2-phenylcyclohexane (Ib), m.p. 81°, was prepared in quantity by catalytic hydrogenation of the Diels–Alder adduct[14] of butadiene and *trans*-benzalacetone[15]; this represents further support for the *trans* configuration of Ib, since the Alder rule predicts the *trans* adduct from the *trans* dienophile.

The adduct of 1-phenylbutadiene and methyl vinyl ketone on hydrogenation afforded a mixture of stereoisomers found on chromatographic separation to contain *ca.* 80% of the previously unreported *cis*-1-acetyl-2-phenylcyclohexane (Ia), m.p. 43°, the balance being the *trans*-ketone Ib. The configurational assignments received further confirmation from sodium ethoxide equilibration which showed the 81° ketone to be the more stable isomer.

Both isomers having been secured and configurations having been established, a study of the ketonization reaction of the enol was initiated. This began with a reinvestigation of the conjugate addition of phenylmagnesium bromide to 1-acetylcyclohexene. Due to hydroxylic and other contamination of the crude reaction product, quantitative infrared determination of the isomer ratio was not feasible; however, chromatographic separation indicated that the ketonic product was largely *cis*-1-acetyl-2-phenylcyclohexane (Ia) (*ca.* 80%) together with some *trans* isomer Ib.

Since reverse halogenation[16] of bromoketones with hydrogen iodide has proved[2,3] a convenient means of generating unstable enols, efforts were directed toward a synthesis of 1-acetyl-1-bromo-2-phenylcyclohexane (II). This ketone, m.p. 96°, was obtained unambiguously by the reaction of bromine with the magnesium enolate resulting from reaction of phenylmagnesium bromide with 1-acetylcyclohexene. The same bromoketone (II) was produced by direct acid-catalyzed bromination of *cis*-1-acetyl-2-phenylcyclohexane (Ia). The structure of 1-acetyl-1-bromo-2-phenylcyclohexane (II) was further demonstrated by the debromination experiments (*vide infra*) which yielded both *cis*- and *trans*-1-acetyl-2-phenylcyclohexane (Ia and Ib), a result consonant with the assignment of structure II to the bromoketone but not with a formulation of the bromoketone as 1-bromoacetyl-2-phenylcyclohexane (III).

Of great interest was the observation that bromination of *trans*-1-acetyl-2-phenylcyclohexane (Ib) led to a second bromoketone, m.p. 60°. Hydriodic acid debromination of this compound yielded the *trans*-ketone Ib as the sole product under conditions where the *cis* stereoisomer would have survived. It was clear that enol V was not a debromination intermediate; were this the case, a mixture of stereoisomers would have resulted as in debromination of 1-acetyl-1-bromo-2-phenylcyclohexane

(14) N. Natsinskaya and A. Petrov, *J. Gen. Chem.* (*U.S.S.R.*), **11**, 665 (1941).

(15) G. van Bree, *Bull. soc. chim. Belges*, **57**, 71 (1948).

(16) The mechanism of the analogous debromination with hydrogen bromide has been discussed by M. S. Newman, THIS JOURNAL, **73**, 4993 (1951).

(II). The new bromoketone, m.p. 60°, may thus be seen to be *trans*-1-bromoacetyl-2-phenylcyclohexane (III).

The formation of II rather than III in the acid-catalyzed bromination of Ia is not unexpected; Cardwell[17] has shown that with acid catalysis bromination of unsymmetrical ketones proceeds with attack at the more highly substituted α-position.[18,19] The formation of 1-bromoacetyl-2-phenylcyclohexane (III) in the acid catalyzed bromination of Ib is unusual and requires discussion.

Previously in studies of the 1-benzoyl-2-phenylcyclohexane and 2-methyl-3-phenylindanone systems it has been found that the *cis* stereoisomers undergo acid-catalyzed bromination much more readily than the corresponding *trans* isomers; in fact, *trans*-1-benzoyl-2-phenylcyclohexane is completely resistant to bromination. These observations have been attributed to the high energy of the transition state between *trans*-ketone and enol as well as to the lower energy ground state for the *trans*-ketones.

The abnormal bromination of *trans*-1-acetyl-2-phenylcyclohexane (Ib) may similarly be ascribed to the relatively high energy of the transition state interposed between Ib and the enol V; further evidence for this is seen in the reluctance of enol V to ketonize to Ib (*vide infra*). No such barrier exists, however, between Ib and the isomeric enol VI, and bromoketone III results.[20,21]

Debromination of 1-acetyl-1-bromo-2-phenylcyclohexane (II) was effected with hydriodic acid in acetone[2,3] to yield a mixture of the stereoisomeric 1-acetyl-2-phenylcyclohexanes shown by quantitative infrared analysis to contain 90.1% of the *cis* isomer. Complete reaction required less than two minutes, and it was shown that no isomerization of *cis*-1-acetyl-2-phenylcyclohexane occurred under reaction conditions during this time.[22]

Debrominations were also carried out using zinc and a proton donor. These results[23] are listed in Table I. While debromination in methanol, using collidinium chloride, proceeded smoothly without the use of a nitrogen atmosphere, the same reaction run in anhydrous benzene or collidine led to 1-acetyl-2-phenylcyclohexanol (IV).[24] When a nitrogen atmosphere was used, ketonization proceeded normally. This suggests that the bulky collidium chloride is an inefficient proton donor, allowing oxygen to compete successfully for the enol. When methanol is present, this acts as a proton carrier and allows rapid ketonization.

TABLE I

Run	Solvent	Proton source	*cis* isomer, %
1	Ether	Acetic acid	89.4
2, 3	Methanol	Collidinium chl.	92.4, 92.3
4	Methanol	Glycine	91.3
5	Methanol	Ammonium chl.	93.8
6, 7, 8	*t*-Butyl alc.[a]	Collidinium chl.	91.2, 90.8, 90.5
9	Acetonitrile[a]	Collidinium chl.	93.6
10	Benzene[a]	Collidinium chl.	88.8

[a] Nitrogen atmosphere.

It has been suggested previously[3] that the effect of non-specific steric hindrance, which hinders each side of the enolic double bond equally, is to amplify the effect of specific steric hindrance by enforcing a direct approach of the proton donor. Thus enol VIII ketonizes with only slight selectivity (50 to 61% *cis* depending on proton donor).[4] Enol IX shows enhanced selectivity[25] (61 to 73% *cis*) due to the non-specific hindrance offered by the 2-phenyl group which makes it more difficult for the proton donor to avoid interaction with the axial hydrogen atoms at carbons three and five. The enol V, presently investigated, is seen to be still more selective[26] while the enol X is virtually completely specific due to the non-specific effect of two phenyl groups.[2]

Experimental[27]

1-Acetylcyclohexene was prepared both by the method of English[28] and by the procedure of ref. 29; n^{25}D 1.4920 (reported[28] n^{20}D 1.4914).

Conjugate Addition of Phenylmagnesium Bromide to 1-Acetylcyclohexene.—To 0.12 mole of phenylmagnesium bromide in 45 ml. of ether was added 0.20 g. of cuprous chloride followed by 10-minute refluxing. Then 5.0 g. of acetylcyclohexene in 30 ml. of anhydrous ether was added dropwise during 20 minutes; an exothermic reaction took place. After refluxing for an additional 45 minutes, the reaction mixture was poured onto 200 g. of ice and 200 ml. of

(17) H. Cardwell and A. Kilner, *J. Chem. Soc.*, 2430 (1951).

(18) This may be attributed to an enhanced importance of hyperconjugative stabilization in the enolization transition state and a consequent facilitation by alkyl substituents despite an increase in steric hindrance. This contrasts with the orientation in base-catalyzed bromination where steric hindrance to proton removal is dominant with decreased importance of alkyl stabilization.

(19) *Cf.* C. Ingold in "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p. 557.

(20) This option was not available to *trans*-1-benzoyl-2-phenylcyclohexane with the resulting failure to brominate at all.

(21) Recently it has been proposed by M. Charpentier and B. Tchoubar, *Compt. rend.*, 1655 (1957), that the rate-determining step in the acid-catalyzed enolization of ketones is the formation of an enol π-complex from the ketone conjugate acid; this conclusion was drawn because of the success of the acid-catalyzed bromination of a hindered ketone contrasted with the failure of base-catalyzed bromination. It was asserted that acid-catalyzed bromination is not susceptible to steric hindrance to proton removal. Our results, both enolization (bromination) and ketonization, are best rationalized on the basis of a transition state involving not only a proton but also a proton carrier. Thus the selectivity of ketonization is not independent of the nature of the proton carrier as would be the case if only the proton appeared in the transition state.

(22) Thus enol is more rapidly formed from bromoketone by loss of bromine than from ketone by removal of a proton. In general, the transition state corresponding to the former situation is of lower energy than that for the latter. This is evidenced by the more rapid reaction of enols with bromine than with a proton (*i.e.*, the over-all rate of bromination of ketones is the rate of enolization).

(23) Because of the high stereoselectivity of ketonization in the present system even moderately large changes in selectivity effect only small changes in per cent. *cis* isomer. While the total spread indicated in Table I is larger than experimental error, smaller differences may not be significant.

(24) This structure was supported by carbon–hydrogen analysis, carbonyl and hydroxyl absorption in the infrared and mechanistic reasoning. The proven requirement of oxygen for the reaction as well as the known reaction of enols with oxygen to yield hydroperoxides suggest that the reaction involves formation and reduction of the α-hydroperoxide.

(25) Unpublished results with T. Cutshall.

(26) The higher selectivity exhibited by enol V compared to IX may be due to a later transition state for the latter as well as to increased non-specific hindrance in the former.

(27) All melting points were taken with a Fisher–Johns block checked with known compounds.

(28) J. English, Jr., and V. Lamberti, THIS JOURNAL, **74**, 1909 (1952).

(29) *Org. Syntheses*, **29**, 1 (1949).

saturated ammonium chloride solution, hexane extracted, washed and dried over sodium sulfate. Concentration of the extracts left a reddish oil which was chromatographed on silica gel (700 × 34 mm., packed with 10% ether in hexane and rinsed with hexane); 17 200-ml. fractions were collected, 1–5 with hexane, 6–14 with 10% ether in hexane and 15–17 with 20% ether in hexane. The weights obtained from these fractions were as follows: fraction 9, 0.18 g.; 10, 0.97 g.; 11, 1.21 g.; 12, 0.75 g.; 13, 0.45 g.; 14, 0.01 g.; 15, 0.26 g.; 16, 0.29 g.; 17, 0.36 g. Infrared spectra were run on all fractions. Fractions 12 and 13 were essentially pure *cis*-1-acetyl-2-phenylcyclohexane. One crystallization from methanol gave a m.p. of 37–39°. Two more crystallizations brought the m.p. to 41.0–41.5° without appreciable loss to the filtrates.

Anal. Calcd. for $C_{14}H_{18}O$: C, 83.12; H, 8.97. Found: C, 83.26; H, 8.72.

cis-1-Acetyl-2-phenylcyclohexane yielded a semicarbazone, m.p. 185.0–186.5°. Its infrared spectrum exhibited maxima at 13.04 and 13.30 μ.

Fractions 10 and 11 were seen from the infrared spectra to be *cis*-1-acetyl-2-phenylcyclohexane contaminated with small amounts of biphenyl. Fraction 15 was found to be pure *trans*-1-acetyl-2-phenylcyclohexane, m.p. 79.0–80.0°. Fraction 16 was the *trans*-ketone contaminated with a hydroxylic impurity.

***trans*-1-Acetyl-2-phenylcyclohex-4-ene.**—A three-neck flask was fitted with a gas inlet tube reaching below the surface of 100 g. of benzalacetone, a thermometer, air condenser and glass paddle stirrer. The flask contents were heated to 200° with rapid stirring and a slow stream of butadiene was passed through the benzalacetone for 12 hours. The reaction mixture was subjected to vacuum distillation giving: I, 16.69 g., b.p. 89–93° at 0.10 mm.; II, 33.21 g., b.p. 95–97° at 0.20 mm.; and III, 18.57 g., b.p. 98–100° at 0.20 mm. Fractions II and III completely solidified. Recrystallization of II from hexane gave 21.50 g. of 1-acetyl-2-phenylcyclohex-4-ene, m.p. 58–60°. Recrystallization of III gave 12.61 g., m.p. 59–61° (reported[14] m.p. 62.2–62.7°).

***trans*-1-Acetyl-2-phenylcyclohexane.**—A solution of 9.10 g. of *trans*-1-acetyl-2-phenylcyclohexene in 75 ml. of ethyl acetate was hydrogenated in a modified Parr apparatus with 50 mg. of platinum oxide catalyst. After the theoretical uptake, hydrogenation ceased. The filtered solution was concentrated and then the residue crystallized from hexane to yield 7.93 g. of *trans*-1-acetyl-2-phenylcyclohexane, m.p. 79.5–81.5° (reported 81–82°,[11] 78–79°,[8] 80–81°,[6] 78–78.5°,[10] 79–80°[13]).

Anal. Calcd. for $C_{14}H_{18}O$: C, 83.12; H, 8.97. Found: C, 82.99; H, 8.71.

trans-1-Acetyl-2-phenylcyclohexane formed a semicarbazone, m.p. 183–186°; its mixed m.p. with the corresponding *cis* derivative was depressed to 158–167°.

Diels–Alder Reaction of Methyl Vinyl Ketone with 1-Phenylbutadiene.—A mixture of 27 g. of 1-phenylbutadiene, 18 g. of methyl vinyl ketone, 30 ml. of benzene and 10 mg. of hydroquinone was refluxed under nitrogen for six hours. The solution was concentrated *in vacuo* and distilled to give: I, 4.82 g., b.p. 49–51° at 0.40 mm., $n^{25}D$ 1.5877; II, 23.50 g., b.p. 105–110° at 0.10 mm., $n^{25}D$ 1.5479; III, 6.84 g., b.p. 109–110° at 0.10 mm., $n^{25}D$ 1.5493. A modified claisen apparatus was used and the distillation required one hour. The material in fractions II and III, used directly in the following experiment, was a *cis–trans* mixture of 1-acetyl-2-phenylcyclohex-3-ene containing 80% *cis* isomer (*vide infra*); reported[10] $n^{25}D$ 1.5381.

***cis*-1-Acetyl-2-phenylcyclohexane.**—The combined fractions II and III of the preceding experiment were hydrogenated in a Parr apparatus in 100 ml. of ethyl acetate with 245 mg. of platinum dioxide. The filtered solution was concentrated. Ten grams of this material was chromatographed on silica gel (33 × 670 mm. packed with 10% ether in hexane and rinsed with hexane); 12 250-ml. fractions were collected, the first with hexane, the succeeding ten with 10% ether in hexane and the last with 20% ether. Fraction 5 contained 0.80 g., m.p. 39–40°; 6 contained 5.02 g., m.p. 42–43°; 7 yielded 2.06 g., m.p. 37–40°; 8 gave 1.19 g., m.p. 35–40°; 9 afforded 1.10 g., m.p. 66–70°; 10 gave 0.63 g., m.p. 69–72°; and 11 yielded 0.14 g., m.p. 69–72°. Crystallization of fractions 5 and 7 gave pure *cis*-1-acetyl-2-phenylcyclohexane, m.p. 41.5–43.0°; fraction 6 was already satisfactorily pure. Fractions 9, 10 and 11 represented impure *trans* isomer and crystallization from hexane brought the melting point to 79–80°. Chromatography of the remaining hydrogenation product gave similar results. Thus, *ca.* 80% of the product was the *cis* isomer.

1-Acetyl-1-bromo-2-phenylcyclohexane.—To a solution of 202 mg. of *cis*-1-acetyl-2-phenylcyclohexane in 10 ml. of acetic acid was added 176 mg. of bromine. Within 7 minutes the mixture was lemon yellow with evolution of HBr. The mixture was diluted with 100 ml. of water and extracted with 1:1 ether–pentane, washed, dried over sodium sulfate and concentrated *in vacuo* to leave an oil which solidified. Crystallization from hexane brought the m.p. to 86.5–92.0°. Another crystallization yielded 128 mg. of 1-acetyl-1-bromo-2-phenylcyclohexane, m.p. 93–94°.

In a second run 6.18 g. of *cis*-ketone in 100 ml. of acetic acid was treated with 5.12 g. of bromine to yield, by working up after 15 minutes, 8.51 g. of a solidifying oil. Crystallization from 60 ml. of hot hexane yielded 5.65 g., m.p. 91–93°. Another crystallization gave 4.74 g., m.p. 96.0–97.0°. The melting point did not change with further crystallization. Additional material was isolable from the filtrates.

Anal. Calcd. for $C_{14}H_{17}OBr$: C, 59.80; H, 6.09. Found: C, 60.17; H, 6.16.

To a solution of phenylmagnesium bromide in 50 ml. of ether, prepared from 22.0 g. of bromobenzene and 3.40 g. of magnesium was added 0.25 g. of cuprous chloride followed by refluxing for 15 minutes. To the mixture was then added 14.0 g. of 1-acetylcyclohexene in 20 ml. of anhydrous ether, the addition requiring 25 minutes. After refluxing for an additional hour and a half the mixture was cooled in ice, and 22.4 g. of bromine was added, with cooling over 15 minutes. Dilution with ice and water followed by ether extraction, washing with thiosulfate and water, drying over sodium sulfate and concentration left a dark oil. This was chromatographed on silica gel. Ten 100-ml. fractions were collected, the first three with hexane, the next four with benzene and the last three with ether. Fractions 4 through 7 contained a total of 7.62 g. of solid which on crystallization from hexane melted at 90–93°. Several crystallizations brought the m.p. to 95–96°. This material liberated iodine from hydriodic acid in acetone. Its infrared spectrum showed it to be identical with 1-acetyl-1-bromo-2-phenylcyclohexane obtained by direct bromination of *cis*-1-acetyl-2-phenylcyclohexane. Fractions 8–10 contained 3.16 g. of solid which on recrystallization from hexane yielded *trans*-1-acetyl-2-phenylcyclohexane, m.p. 78.0–78.5°.

Bromination of *trans*-1-Acetyl-2-phenylcyclohexane.—To a solution of 3.00 g. of *trans*-1-acetyl-2-phenylcyclohexane in 100 ml. of acetic acid was added 2.40 g. of bromine; 3 hours was required for decolorization. The mixture was then diluted with 500 ml. of water and ether extracted. The washed and dried extracts on concentration left an oily solid which was chromatographed on silica gel (19 × 400 mm., packed with 10% ether in hexane and rinsed with hexane). Nine 50-ml. fractions were collected, the first seven by elution with 5% ether in hexane, the last two with 20%. The contents of the fractions were as follows: 2, 0.71 g., m.p. 87–93°; 3, 1.08 g., m.p. 41–46°; 4, 1.39 g., m.p. 56–58°; 5, 0.19 g., slightly oily; 6, 0.07 g., oil; 7, 0.01 g., oil; 8, 0.02 g. of *trans*-1-acetyl-2-phenylcyclohexane, m.p. 77–78°; 9, 0.30 g. of the same, m.p. 77–78°. Recrystallization of fraction 2 from hexane yielded 0.47 g. of *trans*-1-dibromoacetyl-2-phenylcyclohexane, m.p. 97.0–97.5°, depressing the m.p. of 1-acetyl-1-bromo-2-phenylcyclohexane to 75°.

Anal. Calcd. for $C_{14}H_{16}OBr_2$: C, 46.70; H, 4.48. Found: C, 46.68; H, 4.21.

Recrystallization of fraction 4 from hexane gave 0.62 g. of *trans*-1-bromoacetyl-2-phenylcyclohexane, m.p. 59.5–60.5°. Similar material was obtained by extensive crystallization of fraction 3.

Anal. Calcd. for $C_{14}H_{17}OBr$: C, 59.80; H, 6.09. Found: C, 59.97; H, 5.92.

Debromination of *trans*-1-Bromoacetyl-2-phenylcyclohexane.—To 56.0 mg. of *trans*-1-bromoacetyl-2-phenylcyclohexane in 1.0 ml. of acetone was added 0.10 ml. of 47% hydriodic acid. An instantaneous liberation of iodine ensued. At the end of 1.5 minutes the mixture was poured into 10 ml. of aqueous sodium thiosulfate and the solid product was filtered and dried. Infrared analysis indicated it to be pure *trans*-1-acetyl-2-phenylcyclohexane.

In a second run 168 mg. of bromoketone in 5.0 ml. of acetone was treated with 0.50 ml. of 47% hydriodic acid for 2.5 minutes followed by dilution with 30 ml. of aqueous thiosulfate. The dried ether extracts were concentrated to leave 120.2 mg. of solid, m.p. 62–68°. Infrared analysis indicated this to be somewhat impure *trans*-1-acetyl-2-phenylcyclohexane uncontaminated with the *cis* isomer.

Debromination of *trans*-1-Dibromoacetyl-2-phenylcyclohexane.—To a solution of 56 mg. of dibromoketone in 1.0 ml. of acetone was added a solution of 0.10 ml. of 47% hydriodic acid in 1.0 ml. of acetone. At the end of 1.5 minutes the reaction product was worked up as described above. Infrared analysis indicated a mixture of *trans*-1-bromoacetyl-2-phenylcyclohexane and *trans*-1-acetyl-2-phenylcyclohexane. This mixture was treated in 2.0 ml. of acetone with 0.15 ml. of hydriodic acid. The product obtained as before melted at 63–68° and was seen from infrared analysis to be somewhat impure *trans*-1-acetyl-2-phenylcyclohexane uncontaminated with the *cis* isomer.

Stability of *cis*-1-Acetyl-2-phenylcyclohexane to Hydriodic Acid.—A solution of 50 mg. of *cis*-ketone and 0.10 ml. of 47% hydriodic acid in 2.0 ml. of acetone was allowed to stand at room temperature for 5 minutes and then was poured into 15 ml. of water and isolated as described in the debromination experiments (*vide supra*). The solid product was unchanged *cis*-ketone as indicated by quantitative infrared analysis.

Tetrabromination of *trans*-1-Acetyl-2-phenylcyclohexane and Debromination.—A solution of 404 mg. of *trans*-ketone and 0.20 ml. hydrobromic acid in 15 ml. of acetic acid was refluxed 1.75 hr. Dilution with water, ether–hexane extraction, washing, drying and concentration of the extracts led to isolation of a non-crystallizing oil. This was debrominated with 3.0 ml. of 47% hydriodic acid in 30 ml. of acetone. The crude solid product, isolated in the usual manner, was analyzed by infrared and found to be *trans*-1-acetyl-2-phenylcyclohexane uncontaminated with the *cis* isomer.

Infrared Analysis.—Essentially the same analytical technique described previously[3] was employed, this utilizing the relation $R = Q \times F$. Here R is the ratio of *cis* to *trans* isomer in a given mixture. $Q = \frac{D'D''_t - D''D'_t}{D''D'_c - D'D''_c}$. The D's, D_c's and D_t's are optical densities of a given mixture, pure *cis* and pure *trans*, respectively. The superscripts refer to the analytical wave lengths 13.04 and 13.19 μ. F was determined empirically from four known mixtures as shown in Table II. The average value of $F = 1.05$ was used in calculating the results in the last two columns of Table II. All spectra were taken at a total concentration of 40 ± 2 mg./0.30 ml. of CS_2. The calibration runs in Table II indicate an estimated maximum error of $\pm 0.8\%$ *cis* isomer due to infrared uncertainties.

Hydriodic Acid Debromination of 1-Acetyl-1-bromo-2-phenylcyclohexane.—To 56.0 mg. of bromoketone in 2.0 ml. of acetone was added 0.10 ml. of 47% hydriodic acid. Iodine was liberated instantaneously. At the end of 1.5 minutes the mixture was poured into 15 ml. of aqueous sodium thiosulfate and ether extracted. The dried extracts were concentrated to leave 46.3 mg., which on quantitative infrared analysis was found to contain 91.2% *cis*-1-acetyl-2-phenylcyclohexane. A run made four months earlier gave material analyzing as 91.0% *cis* isomer.

Zinc debrominations were carried out by magnetically stirring 56.0 mg. of 1-acetyl-2-phenylcyclohexane in the given solvent with 300 mg. of zinc dust and a proton source for sufficient time for complete reaction; nitrogen-dried with a train of Fieser solution, lead acetate; calcium chloride was used where indicated.

TABLE II

Actual % *cis* isomer	D'	D''	Q	Actual R	Calcd. F	Calcd. R	Calcd. % *cis* isomer
100.0	0.585	0.264	...	...	..	...	..
71.6	.468	.523	2.33	2.53	1.09	2.45	71.0
54.1	.432	.721	1.14	1.17	1.03	1.20	54.5
39.6	.398	.921	0.645	0.655	1.02	0.678	40.4
28.9	.314	.958	0.380	0.406	1.07	0.399	28.5
0.0	.171	1.097	...	...	..	...	..

Run 1 was made with 5 ml. of ether, 1.0 ml. of acetic acid for 14 hr.; run 2, 5 ml. of methanol, 300 mg. of collidinium chloride, 17 hr.; run 3, 10 ml. of methanol, 300 mg. of collidinium chloride, 10 hr.; run 4, 10 ml. of methanol, 300 mg. of glycine, 25 hr.; run 5, 10 ml. of methanol, 300 mg. of ammonium chloride, nitrogen atmosphere, 17 hr. Runs 6, 7 and 8, 10 ml. of *t*-butyl alcohol, 300 mg. of collidinium chloride, nitrogen atmosphere, 28 hr., 20 hr., and 22 hr. resp.; run 9, 10 ml. of acetonitrile, 300 mg. of collidinium chloride, nitrogen atmosphere, 22 hr.; run 10, 10 ml. of benzene, 300 mg. of collidinium chloride, nitrogen atmosphere, 24 hr.

Zinc Debromination of 1-Acetyl-1-bromo-2-phenylcyclohexane with Collidinium Chloride in Benzene.—When the debromination was run without a nitrogen atmosphere 1-acetyl-2-phenylcyclohexane did not result. The product infrared spectrum contained a strong OH stretching band at 2.80, 2.85 μ (doublet). From 112 mg. of bromoketone, in a preparative run, there was obtained 79 mg. of crude 1-acetyl-1-hydroxy-2-phenylcyclohexane, m.p. 78–82°. Recrystallization from hexane brought the melting point to 86.0–87.5°.

Anal. Calcd. for $C_{14}H_{18}O_2$: C, 77.01; H, 8.31. Found: C, 76.80; H, 7.95.

When collidine replaced benzene as the solvent the same result was obtained. When a nitrogen atmosphere was utilized only 1-acetyl-2-phenylcyclohexane stereoisomers resulted.

Equilibration.—To a sodium ethoxide solution prepared from 40 mg. of sodium and 5.0 ml. of ethanol was added 100 mg. of *cis*-1-acetyl-2-phenylcyclohexane. The clear solution was allowed to stand at room temperature for 8 hours and was then diluted with 40 ml. of water and filtered to yield 100.3 mg. of solid, m.p. 77–79°. A quantitative infrared analysis showed this to be a *cis–trans* mixture of the 1-acetyl-2-phenylcyclohexanes containing 13.1% of the *cis* isomer.

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