TABLE IV

REACTION CONSTANTS FOR THE GALLIUM BROMIDE CATALYZED ALKYLATION REACTIONS

Reaction	Reaction constants ρ_m	ρ_p	ρ
Methylation	−3.43	−3.61	−3.52 ± 0.09
Ethylation	−2.88	−2.62	−2.75 ± .13
Isopropylation	−2.49	−2.41	−2.45 ± .04
t-Butylation	−2.87	−2.75	−2.81 ± .06

with gallium bromide, caution should be observed. Such coördination will probably alter the activity of the catalyst and may change the reaction mechanism. It is not possible at this time to estimate the effect of such changes on the isomer distribution.

Experimental Part

Materials.—The purification and physical properties of all materials were reported in previous papers of this series.[9,20]

Isomer Distributions.—A 0.042 *M* solution of gallium bromide in toluene was prepared. To 25 ml. of this catalyst solution was added 0.0195 mole of methyl bromide in 25 ml. of toluene. The reaction was continued for 13 hours at 25° and by titration for hydrogen bromide it was ascertained that 58% reaction had occurred. In similar experiments 25 ml. of the catalyst solution was added to 25 ml. of toluene containing 0.0202 mole of ethyl bromide and reaction periods of 40 to 80 minutes were used. For the 40-minute reaction period, 55% reaction was observed, and in the 80-minute reaction period, 75–80% reaction was obtained. Toluene was treated with isopropyl bromide in a similar manner using 0.0205 mole of the halide. Complete reaction was obtained upon mixing. The reactions of isopropyl and *t*-butyl bromides in a flow apparatus were described previously.[9]

A pure sample of *p*-*t*-butyltoluene was passed through the flow reactor under the same conditions as the alkylations except that hydrogen bromide was added. It was analyzed in a similar manner as in other experiments.

All of the reactions were performed in toluene solution to correspond to the conditions used in the kinetic studies. The dried products were partially rectified in an efficient column with a small hold-up. Most of the excess toluene was removed. When the pot temperature began to rise, the rectification was discontinued. The column was washed down with toluene and the material remaining in the distillation flask was then analyzed by infrared analyses.[21] Since a considerable quantity of toluene remained in the sample, a "blanking out" technique was used for the analyses. Thus, as a double beam instrument was being used, toluene was added to the reference cell in order to compensate for that present in the sample. In this manner 70 to 90% of the absorption due to toluene in the sample was "blanked out."

The results of the infrared analyses were summarized in Table II.

Acknowledgment.—It is a pleasure to acknowledge our appreciation to the Bureau of Standards for providing the samples of pure hydrocarbons used as infrared standards and to Mr. P. Kinsey for his coöperation in determining the infrared spectra for this study.

(20) C. R. Smoot and H. C. Brown, THIS JOURNAL, **78**, 6245 (1956).

(21) For further details concerning the infrared analyses of alkyltoluenes, consult the Ph.D. thesis of C. R. Smoot, Purdue University Library.

LAFAYETTE, INDIANA

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF NORTHWESTERN UNIVERSITY]

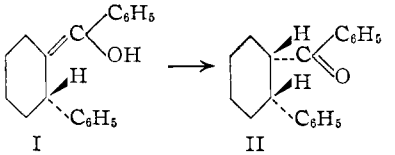
The Stereochemistry of the Ketonization Reaction of Enols. III[1,2]

BY HOWARD E. ZIMMERMAN AND HARRY J. GIALLOMBARDO

RECEIVED JUNE 5, 1956

A study has been made of the stereochemistry of decarboxylation of 4-phenylcyclohexane-1,1-dicarboxylic acid. Maximum specificity was observed in collidine where an average of 61% *cis*-4-phenylcyclohexanecarboxylic acid resulted. This is contrasted with 11% *cis*-isomer required for thermodynamic control.

Previously[3] it has been demonstrated that ketonization of exocyclic cyclohexane enols proceeds by prototropic attack from the less hindered side of the enolic double bond to yield the less stable stereoisomeric product. For example, ketonization of the enol I appeared to be completely stereospecific,



I II

leading to *cis*-1-phenyl-2-benzoylcyclohexane (II). In addition it was suggested[3] that decarboxylation of substituted cyclohexane-1,1-dicarboxylic acids involves such an enolic intermediate which ketonizes to yield the less stable isomer, in which the remaining carboxyl is axial. One case cited was the decarboxylation of 2-methylcyclohexane-1,1-dicarboxylic acid which had been reported by Perkin[4] and much more recently by Golmov[5] to yield *cis*-2-methylcyclohexanecarboxylic acid. In disagreement with this picture was the report by Perkin[6] that the decarboxylation of 2-phenylcyclohexane-1,1-dicarboxylic acid yielded 2-phenylcyclohexanecarboxylic acid of m.p. 104°, the isomer now known[7] to be *trans*.

It seemed clear that a quantitative study of decarboxylation of cyclohexane-1,1-dicarboxylic acids would not only clarify the situation but also would provide further examples of ketonization. To this end a study of the decarboxylation of the 2-phenyl and the 4-phenylcyclohexane-1,1-dicarboxylic acids was initiated. The present paper deals with the latter system.

The investigation of the 4-phenylcyclohexane-1,1-dicarboxylic acid (III) required first its synthesis,

(1) Paper II of this series: H. E. Zimmerman, THIS JOURNAL, **78**, 1168 (1956).

(2) Abstracted from the Master's thesis of Harry J. Giallombardo, presented to Northwestern University.

(3) H. E. Zimmerman, *J. Org. Chem.*, **20**, 549 (1955).

(4) W. Goodwin and W. Perkin, *J. Chem. Soc.*, 119 (1895).

(5) V. Golmov, *J. Gen. Chem.*, **23**, 1221 (1953).

(6) F. Kipping and W. Perkin, *J. Chem. Soc.*, 304 (1890).

(7) C. Gutsche, THIS JOURNAL, **70**, 4150 (1948).

secondly a preparation of the decarboxylation products and development of an analytical method for mixtures of these and finally an investigation of the decarboxylation itself.

Preparation of the hitherto unknown 4-phenylcyclohexane-1,1-dicarboxylic acid began with the Diels–Alder reaction of 2-phenylbutadiene with the reactive dienophile diethyl methylenemalonate[8] to yield diethyl 4-phenylcyclohex-3-ene-1,1-dicarboxylate (IV). The assignment of this structure to the adduct was supported not only by theory[9] but also by the ultimate conversion (*vide infra*) of IV to the known (*trans*-)4-phenylcyclohexanecarboxylic acid.

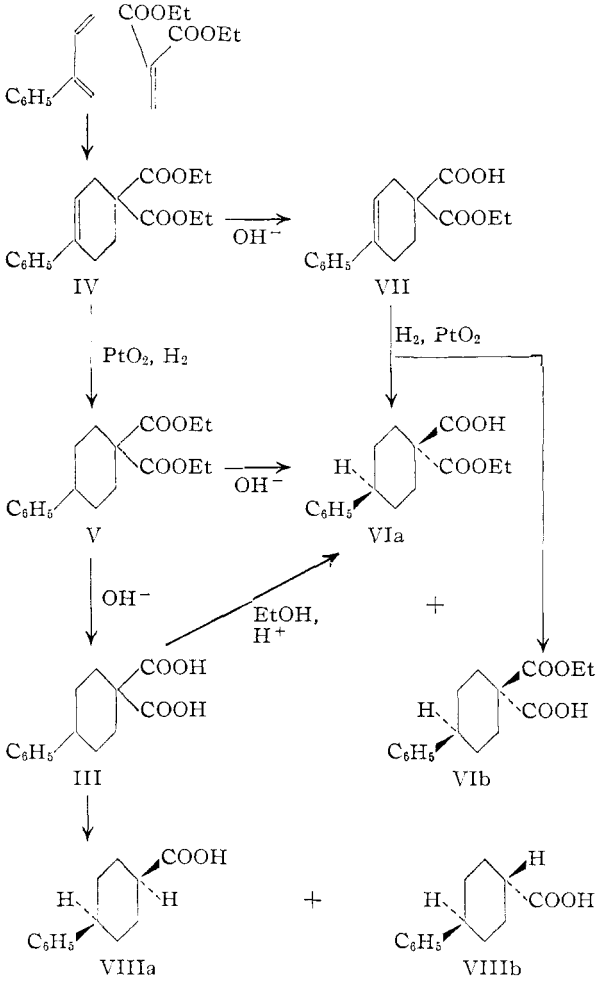
Hydrogenation of diethyl 4-phenylcyclohex-3-ene-1,1-dicarboxylate (IV) produced diethyl 4-phenylcyclohexane-1,1-dicarboxylate (V). Saponification of this compound gave the desired 4-phenylcyclohexane-1,1-dicarboxylic acid (III), m.p. 185–186° dec.

In an attempt to test the stereospecificity of the system diethyl 4-phenylcyclohexane-1,1-dicarboxylate (V) was subjected to partial saponification using a limited amount of base at room temperature. The major product, 1-carbethoxy-*trans*-4-phenylcyclohexanecarboxylic acid (VIb), was obtained in 53% yield while its stereoisomer, 1-carbethoxy-*cis*-4-phenylcyclohexanecarboxylic acid (VIa), was isolated in only 12% yield. The assignment of configuration VIb to the major product was based on the known[10] difficulty of saponification of axial carbethoxyl groups.

Both VIa and VIb were prepared by another route as well. Partial saponification of diethyl 4-phenylcyclohex-3-ene-1,1-dicarboxylate (IV), despite steric equivalence of carbethoxyl groups, led to 1-carbethoxy-4-phenylcyclohex-3-enecarboxylic acid (VII) in good yield; this result was not unexpected in view of the depression of the acid strength of a carboxyl group by a proximate carboxylate anion. Hydrogenation of VII resulted in formation of both 1-carbethoxy-*cis*-4-phenylcyclohexanecarboxylic acid (VIa) and its stereoisomer VIb. 1-Carbethoxy-*cis*-4-phenylcyclohexanecarboxylic acid (VIa) was also obtained in low yield by partial Fischer esterification of III.

Also requisite for a study of the decarboxylation of 4-phenylcyclohexane-1,1-dicarboxylic acid (III) was the preparation of the decarboxylation products, VIIIa and VIIIb. The stereoisomeric 4-phenylcyclohexanecarboxylic acids had been reported from the sodium–isoamyl alcohol reduction of 4-biphenylcarboxylic acid by Rassow[11] as melting at 113 and 202°. Fieser[12] reported that ozonization of the 202° isomer yielded *trans*-hexahydrophthalic acid and suggested that this compound was therefore *trans*. In agreement with this assignment was the report by Rassow[11] that vigorous acid treatment of the 113° isomer gave a mixture consisting largely of the 202° acid while the reverse isomerization was effected in only a 10% yield. The higher melting isomer had also been prepared by several investigators without comment regarding its configuration. Johnson and Offenhauer[13] obtained this compound by a modification of the method of Rassow as well as by the sodium hypobromite oxidation of 4-phenylhexahydroacetophenone, which in turn was prepared by the reaction of cyclohexene, benzene acetyl chloride and aluminum chloride. The latter method was employed by Nenitzescu[14] who also prepared the higher melting isomer from cyclohex-1-enecarboxylic acid, benzene and aluminum chloride. The formation of the 202° isomer under such drastic conditions seemed to support the *trans* assignment made by Fieser.[12]

CHART I



In the present investigation *trans*-4-phenylcyclohexanecarboxylic acid (VIIIb) was prepared by a modification of the method of Rassow[11] and of Johnson.[13] In agreement with the report of Rassow, isomerization of VIIIb with fuming hydrochloric acid at 185° did result in partial conversion to material of m.p. 116–117°. In view of the poor yield, the decarboxylation of 4-phenylcyclohexane-1,1-dicarboxylic acid (III) proved a more convenient source. However, it soon was apparent that the low melting isomer of Rassow was not homogeneous. Infrared analysis (*vide infra*) indicated it

(8) G. Bachman and H. Tanner, *J. Org. Chem.*, **4**, 493 (1939).
(9) B. Hudson and R. Robinson, *J. Chem. Soc.*, 715 (1941).
(10) D. Barton, *Experientia*, **6**, 316 (1950).
(11) R. Rassow, *Ann.*, **282**, 147 (1894).
(12) L. Fieser and co-workers, THIS JOURNAL, **70**, 3186 (1948).
(13) W. Johnson and R. Offenhauer, *ibid.*, **67**, 1045 (1945).
(14) C. Nenitzescu and I. Gavat, *Ber.*, **70**, 1883 (1937).

to contain *cis*- and *trans*-4-phenylcyclohexanecarboxylic acid in a two-to-one ratio. Chromatography of the decarboxylation product on silica gel afforded pure *cis*-4-phenylcyclohexanecarboxylic acid as needles, m.p. 129–130°.

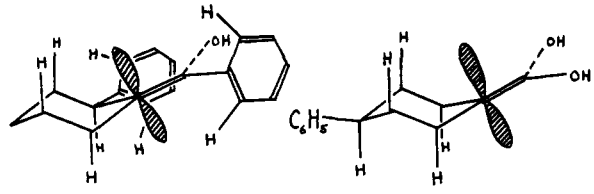
The required 4-phenylcyclohexane-1,1-dicarboxylic acid and its decarboxylation products having thus been prepared, it remained to devise a procedure for analyzing the decarboxylation mixtures. Slight modification of the infrared method used by us earlier[1] proved necessary, since *trans*-4-phenylcyclohexanecarboxylic acid was not sufficiently soluble in chloroform. The method described in the Experimental section was found to be convenient; most important was the fact that it did not require knowledge of the thickness or concentration of the potassium bromide pellets on which the spectra were run. The method proved to be accurate to ±3% *cis*-isomer. (Note Table II for known mixtures.) In addition, it was necessary to separate the decarboxylation products from unreacted 4-phenylcyclohexane-1,1-dicarboxylic acid before infrared analysis. This separation was effected by an eight funnel fractional extraction using ether and (*p*H 7) citrate buffer phases.

Decarboxylation was effected both by heating 4-phenylcyclohexane-1,1-dicarboxylic acid (III) without solvent and in mesitylene or collidine. Also, control experiments were run in which the stability of *cis*-4-phenylcyclohexanecarboxylic acid under various conditions of decarboxylation was examined. The results of the decarboxylation and control experiments are listed in Table I. It is clear from the control experiments (Table I; runs 6, 9, 10, 19, 20) that little or no isomerization of the initial decarboxylation product was occurring under reaction conditions. The conversion of *cis*-4-phenylcyclohexanecarboxylic acid to 89% *trans*-4-phenylcyclohexanecarboxylic acid by heating to 195° for 27 hr. (Table I, run 5) confirmed the assignment of configurations (*vide supra*).

Inspection of the results of decarboxylation shows that in all runs more *cis*-4-phenylcyclohexanecarboxylic acid resulted than anticipated on a thermodynamic basis. It is clear that the maximum stereospecificity was observed for runs made in collidine where an average of 61% *cis*-acid VIIIa was obtained. For each mode of decarboxylation—that is, use of collidine, mesitylene or no solvent—the deviation of the individual results from the average is only slightly greater than expected from the ±3 scatter observed in the infrared analysis of known mixtures and probably can be attributed to slight selective manipulative losses during purification. In any event, these deviations appear to be random and no correlation to the temperature or the time of the run is apparent.

Two points immediately present themselves. The first is the marked decreased stereospecificity in the present system, involving ketonization of IX, as opposed to the 1-phenyl-2-benzoylcyclohexane (II) case studied earlier[3,15]; the second is the decreased specificity for decarboxylation without added solvent compared with that in collidine.

Study of Fisher–Hirschfelder models indicates that the phenyl group at carbon 1 of the enol I of 1-phenyl-2-benzoylcyclohexane contributes only slightly more[16] hindrance to axial protonation than to equatorial attack. It is suggested that the presence of non-selective steric hindrance, con-



I IX

tributed by the C_1-phenyl group and also by the phenyl group on the exocyclic carbon atom, increases the importance of the selective steric effect of the axial hydrogen atoms at carbons four and six. Whereas in I the upper lobe of the p-orbital involved in bonding with a proton donor is hindered on all sides, this is not true of the enol IX of 4-phenylcyclohexanecarboxylic acid which lacks both the ring phenyl group as well as the phenyl group on the exocyclic carbon atom. Nevertheless, the equatorial attack is still somewhat preferred due to the hindrance offered by axial hydrogen atoms to axial attack.[17a,b]

The decreased stereospecificity of ketonization for decarboxylation as a melt compared to decarboxylation in collidine may be due to the smaller size of the proton donor in the former case, where it is most likely a carboxyl group; in collidine the proton donor might be expected to be conjugate acid of collidine, its ion pair equivalent or a hydrogen bonded collidine–carboxylic acid complex. Also, hydrogen bonding of the enolic hydroxyl hydrogen

(15) Unpublished work with T. Cutshall on the decarboxylation of 2-phenylcyclohexane-1,1-dicarboxylic acid indicates *ca.* 69% *cis*-2-phenylcyclohexanecarboxylic acid from runs without solvent (*i.e.*, 2.2 times as much *cis*-isomer per given amount of *trans*-isomer as in the 4-phenyl system).

(16) This is noted for the favored rotational conformation of the phenyl group about the C_1-phenyl bond; in this conformation one ortho-hydrogen atom lies between the enolic hydroxyl group and the C_6-axial hydrogen atom.

(17) (a) While the present study involves higher temperature conditions than used in the 1-phenyl-2-benzoylcyclohexane work, the absence of evidence for a dependence of stereospecificity on temperature in the ketonization of IX in collidine weakens arguments based on the intervention of boat forms at higher temperatures. The failure to observe such a temperature dependence may be due to masking by experimental errors. (b) It is of interest to note that of two *a priori* factors which might have been anticipated to control the stereochemistry of ketonization of exocyclic enols (for example I), steric hindrance to approach of the proton donor seems dominant. The other factor, the requirement for maximum p-orbital overlap, may be seen to be involved as follows. The four atoms on the enolic double bond of I (*i.e.*, the ground state for ketonization) are in one plane as required for overlap of the p-orbitals of the sp^2 hybridized carbon atoms. As a proton becomes bonded to carbon with a concomitant change in hybridization to sp^3 at this atom and with generation of a benzoyl group, overlap must continue, although the energetic importance of this overlap must gradually diminish until finally adjacent to the newly created benzoyl group is only a saturated sp^3 carbon atom. The overlap requirement during this process imposes a conformational requirement on the incipient benzoyl group. An inspection of models indicates that a continuation of overlap must be more difficult for formation of the observed axial benzoyl group than for an equatorial one. This is due to steric interaction between an axial benzoyl group and the neighboring axial hydrogen atoms when the proper conformation of the benzoyl group is attained. That these overlap considerations are not prevailing may be ascribed to the intervention of serious steric interaction between the benzoyl group and axial hydrogen atoms only after an essentially sp^2 hybridized transition state has been left.

TABLE I

SUMMARY OF RESULTS

Run	Reactant	Solvent	Temp.,[a] °C.	Time, min.	% *cis*
1	C_6H_5-$C_6H_9(COOH)_2$	None	194	5.0	51[c]
2	C_6H_5-$C_6H_9(COOH)_2$	None	194	9.0	48[c]
3	C_6H_5-$C_6H_9(COOH)_2$	None	225	0.3	56
4	C_6H_5-$C_6H_9(COOH)_2$	None	195	2.5	47[b]
5	*cis*-C_6H_5-C_6H_{10}-COOH	None	195	1620.0	11
6	*cis*-C_6H_5-C_6H_{10}-COOH	None	194	2.0	96
7	C_6H_5-$C_6H_9(COOH)_2$	Mesitylene	165	27.0	51
8	C_6H_5-$C_6H_9(COOH)_2$	Mesitylene	140	20.0	57[b,c]
9	*cis*-C_6H_5-C_6H_{10}-COOH	Mesitylene	175	60.0	95[c]
10	*cis*-C_6H_5-C_6H_{10}-COOH	Mesitylene	175	600.0	93[c]
11	*trans*-C_6H_5-C_6H_{10}-COOH	Mesitylene	175	600.0	0[c]
12	C_6H_5-$C_6H_9(COOH)_2$	Collidine	131	15.0	57[b,c]
13	C_6H_5-$C_6H_9(COOH)_2$	Collidine	130	3.0	62[b,c]
14	C_6H_5-$C_6H_9(COOH)_2$	Collidine	125	5.0	58[b,c]
15	C_6H_5-$C_6H_9(COOH)_2$	Collidine	115	5.0	53[b,c]
16	C_6H_5-$C_6H_9(COOH)_2$	Collidine	100	15.0	65[b,c]
17	C_6H_5-$C_6H_9(COOH)_2$	Collidine	89	60.0	66[b,c]
18	C_6H_5-$C_6H_9(COOH)_2$	Collidine	78	180.0	58[b,c]
19	*cis*-C_6H_5-C_6H_{10}-COOH	Collidine	130	12.0	100[c]
20	*cis*-C_6H_5-C_6H_{10}-COOH and $ClCH_2COOH$	Collidine	132	5.0	95[c]

[a] Bath temperature. [b] Purified by buffer procedure. [c] Purified by sublimation.

atoms with solvent collidine[18] would contribute to non-selective steric hindrance.

Experimental[19]

Diethyl Methylenemalonate.—This was prepared by the method of Bachman and Tanner.[20] It was found that this compound could be stored at 0° for long periods when a small portion of phosphorus pentoxide was added.

2-Phenylbutadiene.—This compound was prepared essentially by the method of Price.[21]

Diethyl 4-Phenylcyclohex-3-ene-1,1-dicarboxylate (IV).—To a mixture of 250 ml. of benzene and 78.7 g. (0.605 mole) of 2-phenylbutadiene in a 500-ml. round-bottom flask was added with swirling 104.2 g. (0.605 mole) of diethyl methylenemalonate. The addition required 10 minutes; the reaction mixture was then refluxed for 4.75 hr. The resulting solution was concentrated *in vacuo* to a pale yellow oil. Distillation of this residual oil under reduced pressure in a modified Claisen flask gave three fractions: I, mainly unreacted diethyl methylenemalonate, b.p. 26–163° at 0.5 mm.; II, 85.0 g. of a colorless oil, b.p. 162–164° at 0.7 mm., $n^{25}D$ 1.5292; and III, 213 g. of a colorless oil, b.p. 163–164° at 0.7 mm., $n^{25}D$ 1.5308. Fractions II and III were combined to give a total yield of 106 g. (58.5%) of diethyl 4-phenylcyclohex-3-ene-1,1-dicarboxylate. The compound rapidly decolorized 5% bromine in carbon tetrachloride. The infrared spectrum in chloroform showed carbonyl absorption at 5.75 μ and at 5.82 μ, as well as a maximum at 12.10 μ.

Anal. Calcd. for $C_{18}H_{22}O_4$: C, 71.50; H, 7.33. Found: C, 72.25; H, 7.32.

Diethyl 4-Phenylcyclohexane-1,1-dicarboxylate (V).—A solution of 90.0 g. (0.298 mole) of diethyl 4-phenylcyclohex-3-ene-1,1-dicarboxylate in 250 ml. of ethyl acetate was subjected to hydrogenation over 250 mg. of platinum oxide catalyst. After absorption of 0.331 mole of hydrogen, the catalyst was removed by filtration and the filtrate was then concentrated *in vacuo* to leave an oil. Distillation under reduced pressure using a modified Claisen flask gave three fractions: I, 9.2 g. of a colorless oil, b.p. 166–170° at 2.0 mm., $n^{25}D$ 1.4978; II, 57.4 g. of a colorless oil, b.p. 171–175° at 2.2 mm., $n^{25}D$ 1.5038; and III, 13.1 g. of a colorless oil, b.p. 175–176° at 2.2 mm., $n^{25}D$ 1.5081; fractions II and III were combined; the crude yield was 78.5%. A 45.0-g. sample was fractionated in a four-foot Piros-Glover spinning band column to give five fractions: I, 2.2 g. of a pale yellow oil, b.p. 175.0–192.1° at 2.8 mm., $n^{25}D$ 1.4935; II, 2.1 g. of a pale yellow oil, b.p. 136.8–142.8° at 0.10 mm., $n^{25}D$ 1.5000; III, 10.4 g. of a colorless oil, b.p. 144.8–145.1° at 0.15 mm., $n^{25}D$ 1.5041; IV, 11.5 g. of a colorless oil, b.p. 141.5–142.0° at 0.12 mm., $n^{25}D$ 1.5041; and V, 5.5 g. of a colorless oil, b.p. 142.1–146.8° at 0.12 mm., $n^{25}D$ 1.5138. The infrared spectra in chloroform of fractions III and IV were identical and showed a carbonyl band at 5.81 μ but no evidence of unsaturation at 12.1 μ. A sample of fraction III did not decolorize a solution of 5% bromine in carbon tetrachloride. The infrared spectrum of fraction V showed strong carbonyl absorption and an impurity of the unsaturated precursor.

Anal. Calcd. for $C_{18}H_{22}O_4$: C, 71.02; H, 7.95. Found: C, 71.58; H, 7.67.

4-Phenylcyclohexane-1,1-dicarboxylic Acid (III).—To a solution of 27 g. (0.482 mole) of potassium hydroxide in 100 ml. of 95% ethanol in a 250-ml. flask fitted with a reflux condenser was added 19.2 g. (0.0632 mole) of diethyl 4-phenylcyclohexane-1,1-dicarboxylate. The mixture was refluxed for 6 hr. During the reflux period the solution turned orange and a large amount of solid separated. The cooled mixture was diluted with 200 ml. of water and extracted with two 100-ml. portions of ether. The aqueous layer was acidified with 20% hydrochloric acid to a congo red end-point. A white solid separated and was extracted with ether. The ether solution was dried over sodium sulfate and was concentrated *in vacuo* leaving 14.97 g. of a pale yellow solid. Two crystallizations from ethyl acetate–ligroin (86–100°) afforded 7.4 g. of white crystals, m.p. 185–186° dec. From the filtrates were obtained two additional crops of the acid: 1.71 g., m.p. 185–186° dec.; 1.03 g., m.p. 181–183° dec., and 5.62 g. of an oily residue which only partially crystallized. Treatment of this last fraction with *n*-pentane and ethyl acetate gave an additional 1.20 g., m.p. 183–184° dec. The total yield of 4-phenylcyclohexane-1,1-dicarboxylic acid was 10.34 g. (68%). The infrared spectrum had a carbonyl maximum at 5.85 μ in potassium bromide.

Anal. Calcd. for $C_{14}H_{16}O_4$: C, 67.73; H, 6.50. Found: C, 68.00; H, 6.19.

1-Carbethoxy-*trans*-4-phenylcyclohexanecarboxylic Acid (VIb).—To a cooled solution of 0.92 g. (0.0164 mole) of potassium hydroxide and 12 ml. of 95% ethanol in a 25-ml. erlenmeyer flask was added 5.0 g. (0.0164 mole) of diethyl 4-phenylcyclohexane-1,1-dicarboxylate. The mixture was allowed to stand at room temperature for 2 days. It was then diluted with 50 ml. of water and extracted with ether. The aqueous residue was acidified with 20% hydrochloric acid to a congo red end-point and ether extracted. The combined ether extracts were washed once with water, dried over calcium chloride and then concentrated *in vacuo* to yield a white solid, 5.1 g., m.p. 131–135°. Two crystallizations from ethyl acetate afforded 1.5 g. of white needles, m.p. 149–150°, and a second crop of 0.89 g., m.p. 147–149°. The over-all yield of 1-carbethoxy-*trans*-4-phenylcyclohexanecarboxylic acid was 53%. The infrared spectrum of the product contained maxima at 5.76 μ and at 5.80 μ in chloroform.

Anal. Calcd. for $C_{16}H_{20}O_4$: C, 69.54; H, 7.30. Found: C, 69.51; H, 7.00.

The original ether extract was concentrated *in vacuo* to leave an oily residue. Crystallization from ligroin (86–100°) afforded the stereoisomer, 1-carbethoxy-*cis*-4-phenylcyclohexanecarboxylic acid (IVa), as white needles, m.p. 50–60°. Recrystallization gave 100 mg. of small, white needles, m.p. 76–78°. A mixed melting point with 1-carbethoxy-*trans*-4-phenylcyclohexanecarboxylic acid was depressed. The infrared spectrum was similar to that of its isomer below 7 μ, but above this wave length there were definite differences.

Anal. Calcd. for $C_{16}H_{20}O_4$: C, 69.54; H, 7.30. Found: C, 69.16; H, 7.15.

1-Carbethoxy-*cis*-4-phenylcyclohexanecarboxylic Acid (VIa).—To a mixture of 300 mg. (0.0012 mole) of 4-phenylcyclohexane-1,1-dicarboxylic acid and 5.0 ml. (0.85 mole) of absolute ethanol in a 25-ml. flask fitted with a reflux condenser was added 0.02 ml. of concentrated sulfuric acid. After refluxing for 1.5 hr., 50 ml. of water was added. The

(18) Since collidine–carboxyl interaction is expected for the ketonization product, some of this energy of interaction may be available in the transition state by collidine–incipient carboxyl bonding.

(19) All melting points were taken on a Fisher–Johns block whose thermometer was checked with known compounds.

(20) G. Bachman and H. Tanner, *J. Org. Chem.*, **4**, 493 (1939).

(21) C. Price, F. Benton and C. Schmidle, THIS JOURNAL, **71**, 2860 (1949).

solution was made basic with 10% sodium hydroxide and then ether extracted. The aqueous layer was acidified with 20% hydrochloric acid to a congo red end-point and then extracted with ether. The combined ether extracts were washed once with water, dried over sodium sulfate and concentrated *in vacuo* to give 362 mg. of a yellow oil, which would crystallize only partially. Chromatography on a 2.0 × 55.0 cm. silica gel (20–600 mesh) column using 1:3 ether–hexane yielded eleven 25-ml. fractions. A twelfth fraction was obtained by eluting with ether and found to contain a high melting solid. Fractions IV to XI gave a white solid, m.p. 74–78°. These were combined and crystallized from ligroin (86–100°) to yield 97.7 mg. of fine, white needles, m.p. 72–75°. Several further crystallizations afforded 20.4 mg. of white rods, m.p. 77–78°. From the filtrates a second crop, 7.8 mg., m.p. 77–79°, and a third crop, 31.2 mg., m.p. 75–76°, was obtained (yield 59 mg., 12%). A mixed melting point with 1-carbethoxy-*cis*-4-phenylcyclohexanecarboxylic acid obtained above showed no depression. The infrared spectrum was also identical with that of the earlier preparation.

1-Carbethoxy-4-phenylcyclohex-3-enecarboxylic Acid (VII).—To a solution of 0.927 g. (0.0166 mole) of potassium hydroxide and 12 ml. of 95% ethanol in a 50-ml. erlenmeyer flask was added 5.0 g. (0.0166 mole) of diethyl 4-phenylcyclohex-3-ene-1,1-dicarboxylate. After standing for 2 days at room temperature, the reaction mixture was diluted with 50 ml. of water and then ether extracted. The aqueous layer was acidified with 20% hydrochloric acid to a congo red end-point and extracted with ether. The ether extracts were washed once with water, dried over sodium sulfate and concentrated *in vacuo* to yield a pale yellow solid, 3.14 g., m.p. 115–125°. Three crystallizations from ethyl acetate gave 0.47 g. of white crystals, m.p. 131–132°. A second crop, 0.90 g., m.p. 130–131°, from the filtrate brought the yield to 1.37 g. (30%).

Anal. Calcd. for $C_{16}H_{18}O_4$: C, 70.05; H, 6.61. Found: C, 70.21; H, 6.36.

Hydrogenation of 1-Carbethoxy-4-phenylcyclohex 3-enecarboxylic Acid (VII).—A solution of 1.0 g. (0.00365 mole) of carbethoxy-4-phenylcyclohex-3-enecarboxylic acid in 15 ml. of ethyl acetate was hydrogenated at atmospheric pressure with 30 mg. of platinum oxide. The absorption of hydrogen was quantitative (108 ml. absorbed in 41 minutes). The catalyst was removed by filtration, and the filtrate was concentrated *in vacuo* yielding 876 mg. of a yellow oil which crystallized to a pale yellow solid, m.p. 58–70°. Fractional recrystallization of the crude product from ethyl acetate–ligroin (86–100°) yielded 119 mg. of pure 1-carbethoxy-*trans*-4-phenylcyclohexanecarboxylic acid (VIb), m.p. 149–150°, together with 36.7 mg. of less pure material. From the filtrates was obtained by recrystallization 86.5 mg. of its stereoisomer VIa, m.p. 78–80°.

***trans*-4-Phenylcyclohexanecarboxylic Acid (VIIIb).**—The following is a modification of the method of Johnson and Offenhauer.[13] To a Glas-col heated, refluxing solution of 5.0 g. (0.025 mole) of 4-biphenylcarboxylic acid in 500 ml. of isoamyl alcohol in a liter 3-neck flask equipped with a glass blade stirrer and reflux condenser there was added 35 g. sodium (1.52 moles) as quickly as possible with rapid stirring. The addition required 15 minutes. The mixture was then refluxed and stirred mechanically for 45 minutes. The product was isolated as described by Johnson and Offenhauer.[13] Crystallization of the crude product from aqueous acetic acid afforded 4.01 g. (78%) of *trans*-4-phenylcyclohexanecarboxylic acid as white, shining plates, m.p. 201–203° (reported, 203–204°,[13] 204°,[14] 202°[11]). The infrared spectrum in potassium bromide contained a carbonyl band at 5.90 μ.

Under the conditions of Johnson and Offenhauer[13] only starting material could be isolated.

Partial Conversion of *trans*-4-Phenylcyclohexanecarboxylic Acid (VIIIb) to *cis*-4-Phenylcyclohexanecarboxylic Acid (VIIIa).—The conversion was accomplished using the method of Rassow.[11] One gram (0.0049 mole) of *trans*-4-phenylcyclohexanecarboxylic acid and 10 ml. of fuming hydrochloric acid in a sealed tube were heated for 6 hours at 185°. The cooled reaction mixture was dissolved in 100 ml. of 10% sodium hydroxide and then filtered by gravity to remove insoluble tarry material. The filtrate was heated to boiling and cautiously acidified to a congo red end-point with 50% sulfuric acid. The hot mixture was then filtered free of crude *trans*-acid. On cooling the filtrate yielded 0.038 g. of material, m.p. 116–117°. Repeated extraction of the crude *trans*-acid with boiling water gave an additional 0.130 g., m.p. 115–116°. The undissolved solid consisted of 0.726 g. of crude *trans*-4-phenylcyclohexanecarboxylic acid (VIIIb), m.p. 190–195°. Infrared analysis of the 117° solid showed it to contain 66% *cis*-isomer. Recrystallization from ethyl acetate–ligroin did not change the melting point of this material.

***cis*-4-Phenylcyclohexanecarboxylic Acid (VIIIa).**—Seven 1-g. samples of 4-phenylcyclohexane-1,1-dicarboxylic acid were separately decarboxylated in a vacuum sublimation apparatus at 193° and 1.5 mm. for 12 minutes. The product sublimed during decarboxylation and a total of 5.2 g. (91%) was obtained. Recrystallization from ethyl acetate–ligroin (86–100°) gave 1.62 g. of *trans*-4-phenylcyclohexanecarboxylic acid (VIIIb), m.p. 202–203°. The combined filtrates were concentrated *in vacuo* and then subjected to chromatography on a 3.2 × 66.0 cm. silica gel (200–600 mesh) column. Sixty 40-ml. fractions were collected using 1:9 ether–hexane; five more 300-ml. fractions were obtained by eluting with 2:8 ether–hexane. The column was then rinsed with ether. Fractions 1–9 contained 0.094 g. of non-crystallizing oil. Concentration of fractions 10–14 yielded 0.223 g. of material with melting points in the range 100–129°; infrared analysis indicated that this material was 92% *cis*-4-phenylcyclohexanecarboxylic acid (VIIIa). Fractions 15–30 contained essentially pure *cis*-4-phenylcyclohexanecarboxylic acid, each fraction melting at 127–129°; the combined weight was 0.703 g. Recrystallization of this material from ethyl acetate–ligroin (86–100°) brought the melting point to 129.5–130.5° without appreciable loss of material. The infrared spectrum of this material was identical to that of *trans*-4-phenylcyclohexanecarboxylic acid below 7 μ but showed many differences above this wave length. Fractions 31–40 yielded 0.486 g. of solid, m.p. 124–128°, which was also essentially pure *cis*-isomer (infrared analysis). Concentration of the remaining fractions gave *cis*-isomer of lesser purity; the weights and infrared analysis were as follows: fractions 41–47, 0.286 g., 88% *cis*-acid; fractions 48–61, 0.639 g., 81% *cis*-acid; and fractions 62–66, 0.908 g., 14% *cis*-acid. Calculation indicated that of the decarboxylated material 48% was *cis*-acid.

General Procedures for Decarboxylation of 4-Phenylcyclohexane-1,1-dicarboxylic Acid (III). Without Solvent.—Two hundred milligrams of 4-phenylcyclohexane-1,1-dicarboxylic acid in a 5-ml. flask was placed in a preheated oil-bath at the desired temperature for a given length of time. The flask was allowed to cool, and the solid product was then analyzed by the infrared procedure. When the presence of undecarboxylated diacid was indicated, this was removed by the fractional extraction procedure described below. The results are summarized in Table I.

In Solution.—Two hundred milligrams of 4-phenylcyclohexane-1,1-dicarboxylic acid and 3.0 ml. of collidine or mesitylene in a 5-ml. flask equipped with a short air condenser was heated in an oil-bath at the desired temperature for a given length of time. The solution was cooled, taken up in ether and extracted with 10% sodium hydroxide solution. The basic aqueous solution was acidified to a congo red end-point with 20% hydrochloric acid and then was extracted with two 50-ml. portions of ether.

The undecarboxylated acid was removed by subjecting this ethereal solution to an eight-funnel fractional extraction essentially as described by Bush and Densen.[22] The two phases used were 50 ml. of ether and 50 ml. of a *p*H 7.0 buffer prepared by mixing 41.20 ml. of 0.2 *M* disodium phosphate and 8.80 ml. of 0.1 *M* citric acid as described by MacIlvaine.[23] The extraction was continued until each of eight funnels contained two phases. Each aqueous phase was then acidified with 20% hydrochloric acid to a congo red end-point. After thorough shaking, the buffer phases were removed. The ether phases were washed once with 50 ml. of water, dried over sodium sulfate and concentrated *in vacuo*. The monacid mixture was found in the first three funnels and the diacid in the last two. Only minute traces were found in the intermediate funnels.

In some cases sublimation of the decarboxylation product proved necessary to remove minute amounts of gummy material which made preparation of a clear potassium

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(23) T. MacIlvaine, *J. Biol. Chem.*, **49**, 183 (1921).

TABLE II

INFRARED DATA FOR KNOWN MIXTURES OF *cis*- AND *trans*-4-PHENYLCYCLOHEXANECARBOXYLIC ACID

Actual % *cis*	*D'*	*D''*	*D*	$\Delta D'$	$\Delta D''$	*Q*	Calcd. *F*	Approximated $R_{c/t}$	Calcd. % *cis*
0	0.662	0.063	0.022[a]	0.640	0.041	.....	...	....	..
6	.574	.040	.008[a]	.566	.032	.....	...	....	..
12	.492	.046	.008[a]	.484	.038	0.0266	5.06	0.128	12
16	.622	.091	.008[a]	.614	.083	0.127	1.49	0.228	18
20	.527	.079	.007[a]	.520	.072	0.133	1.92	0.221	17
30	.444	.119	.007[a]	.437	.112	0.347	1.21	0.486	33
50	.296	.154	.018[a]	.278	.136	0.780	1.27	0.990	50
73	.222	.285	.046[a]	.176	.239	2.50	1.09	2.65	72
76	.155	.246	.040[a]	.115	.206	3.42	0.920	3.46	78
84	.129	.230	.042[a]	.087	.188	4.25	1.20	4.21	81
86	.124	.285	.038[a]	.086	.247	5.99	1.01	5.75	85
89	.087	.292	.036[a]	.051	.256	12.4	0.610	10.7	92
90	.124	.392	.058[a]	.066	.334	12.7	0.695	10.9	92
95	.084	.350	.046[a]	.038	.304	26.0	0.735	21.7	96
100	.091	.433	.070[a]	.021	.360	.....	...	....	..
0	.662	.063	.060[b]	.602	.003	.....	...	....	..
6	.574	.041	.034[b]	.540	.007	.0108	6.15	.0657	6
12	.492	.046	.030[b]	.462	.016	.0424	3.17	.153	13
16	.622	.091	.031[b]	.591	.060	.149	1.28	.222	18
20	.527	.079	.027[b]	.500	.052	.143	1.78	.219	18
30	.444	.119	.018[b]	.426	.101	.354	1.18	.474	32
50	.296	.154	.000[b]	.296	.154	.819	1.21	.922	50
73	.222	.285	.020[b]	.202	.265	2.42	1.13	2.44	71
76	.155	.246	.008[b]	.147	.238	3.38	0.929	3.31	77
84	.129	.230	.009[b]	.120	.221	4.05	1.26	3.92	80
86	.124	.285	.000[b]	.124	.285	5.90	1.03	5.43	84
89	.087	.292	.000[b]	.087	.292	13.6	0.563	11.7	92
90	.124	.392	.001[b]	.123	.391	11.7	0.752	10.2	91
95	.084	.350	.000[b]	.084	.350	30.5	0.625	25.0	96
100	.091	.433	.009[b]	.082	.424	.....	...	....	..

[a] Reference wave length = 12.40 μ. [b] Reference wave length = 13.89 μ.

bromide pellet difficult. These mixtures were sublimed under oil pump vacuum of 120° and subjected to infrared analysis. Analysis before and after sublimation indicated no isomerization occurred during this process. The results are summarized in Table I.

Stability of the 4-Phenylcyclohexanecarboxylic Acids in Mesitylene.—A solution of 50 mg. of *cis*-4-phenylcyclohexanecarboxylic acid (VIb) in 3.0 ml. of mesitylene (b.p. 161–162°) in a 5-ml. flask equipped with a short air condenser was heated in an oil-bath at 176° for 1 hr. The hot solution was cooled and concentrated *in vacuo* to a pale yellow solid. This solid was dissolved in ether and extracted with saturated sodium bicarbonate solution. This extract was then acidified with 20% hydrochloric acid to a congo red end-point and ether extracted. The combined ethereal extracts were washed once with water, dried over sodium sulfate and concentrated *in vacuo* to yield 47 mg. of small, white needles, m.p. 95–120°, which were sublimed at 105–120° (2.5 mm.). Infrared analysis of the sublimate indicated that the product was 95% *cis*-4-phenylcyclohexanecarboxylic acid.

Essentially the same result was obtained when treatment was extended to 10 hr. at the same temperature.

When *trans*-4-phenylcyclohexanecarboxylic acid (VIIIb) was heated for 10 hr. under the same conditions, infrared analysis indicated that the product was unchanged *trans*-acid.

Stability of *cis*-4-Phenylcyclohexanecarboxylic Acid (VIIIa) in Collidine.—A solution of 35 mg. of *cis*-4-phenylcyclohexanecarboxylic acid in 3.0 ml. of collidine (b.p. 168°) in a 5-ml. flask equipped with a short air condenser was heated in an oil-bath at 130° for 12 minutes. The product, isolated as described above for the runs in mesitylene, melted at 125–127°. The usual infrared analysis indicated 100% *cis*-4-phenylcyclohexanecarboxylic acid.

When this experiment was repeated with the addition of 40 mg. of chloroacetic acid and with a heating time of five minutes, essentially unchanged *cis*-acid resulted.

Stability of *cis*-4-Phenylcyclohexanecarboxylic Acid (VIIIa) in the Absence of Solvent.—Thirty-five milligrams of *cis*-4-phenylcyclohexanecarboxylic acid in a 5-ml. flask was heated in an oil-bath at 195° for 2 minutes. On cooling, 35 mg. of small, white needles, m.p. 123–127°, was obtained. This was shown to be 96% *cis*-acid by the usual infrared analysis.

Isomerization of *cis*-4-Phenylcyclohexanecarboxylic Acid (VIIIa).—Forty milligrams of *cis*-4-phenylcyclohexanecarboxylic acid in a small test-tube was heated under nitrogen at 195° for 27 hr. The solid obtained on cooling melted at 107–192°. Infrared analysis showed the mixture to contain 11% *cis*-4-phenylcyclohexanecarboxylic acid.

Infrared Determination of Isomer Ratio.—The method described below is similar to that reported earlier[1] except that the spectra were run as potassium bromide pellets. In each case the unknown was prepared by concentrating a solution of the weighed sample (*ca.* 6 mg.) in 0.50 ml. ethyl acetate under a stream of nitrogen and grinding the residue with 100 mg. of potassium bromide. Seventy-five milligrams of the well ground mixture was placed under 22,000 lb. in a 1.10 cm. diameter casing.

It was found that *trans*-4-phenylcyclohexanecarboxylic acid exhibited a sharp maximum at 9.80 μ (optical density = 0.662; 6.0-mg. sample) while the *cis*-isomer had a minimum at this wave length (optical density = 0.091; 6.0-mg. sample). The spectrum of *cis*-4-phenylcyclohexanecarboxylic acid possessed a sharp maximum at 12.57 μ (optical density = 0.433; 6.0-mg. sample) while the *trans*-isomer had a minimum at this wave length (optical density = 0.063; 6.0-mg. sample).

The following form of the equation used earlier[1] was found more convenient

$$R_{c/t} = \frac{C_{cm}}{C_{tm}} = QF \qquad (1)$$

where

$$Q = \frac{\Delta D''_m \Delta D'_t - \Delta D'_m \Delta D''_t}{\Delta D'_m \Delta D''_c - \Delta D''_m \Delta D'_c}$$

TABLE III

INFRARED DATA FOR UNKNOWN MIXTURES

Run	D'	D''	D	$\Delta D'$	$\Delta D''$
1	0.218	0.126	0.018[a]	0.200	0.108
2	.268	.149	.014[a]	.254	.135
3	.319	.229	.028[a]	.291	.201
4	.305	.165	.041[a]	.264	.124
5	.328	.036	.027[b]	.301	.009
6	.114	.388	.022[b]	.092	.366
7	.360	.269	.143[a]	.217	.126
8	.229	.168	.012[b]	.217	.156
9	.078	.268	.008[b]	.070	.260
10	.108	.372	.004[b]	.104	.368
11	.568	.008	.003[a]	.565	.005
12	.261	.184	.004[b]	.257	.180
13	.292	.222	.004[b]	.288	.218
14	.202	.155	.000[b]	.202	.155
15	.244	.184	.002[b]	.242	.182
16	.301	.301	.008[b]	.293	.293
17	.261	.258	.006[b]	.255	.252
18	.245	.184	.008[b]	.237	.176
19	.095	.481	.000[b]	.095	.481
20	.131	.468	.008[b]	.123	.460

[a] Reference wave length = 12.40 μ. [b] Reference wave length = 13.89 μ.

and

$$F = \frac{C_c L_c}{C_t L_t}$$

$R_{c/t}$ is the ratio of *cis*-isomer to *trans*-isomer

$\Delta D'_c$ is the cor. optical density of pure *cis*-isomer at 9.80 μ
$\Delta D'_t$ is the cor. optical density of pure *trans*-isomer at 9.80 μ
$\Delta D'_m$ is the cor. optical density for the mixture of 9.80 μ
$\Delta D''_c$ is the cor. optical density of pure *cis*-isomer at 12.57 μ
$\Delta D''_t$ is the cor. optical density of pure *trans*-isomer at 12.57 μ
$\Delta D''_m$ is the cor. optical density for the mixture at 12.57 μ

All densities are corrected for errors in setting of zero density by subtraction of the optical density at a reference wave length, 12.40 μ.

C_{cm} is the concn. of the *cis*-isomer in the mixture
C_{tm} is the concn. of the *trans*-isomer in the mixture
C_c is the concn. of pure *cis*-isomer
C_t is the concn. of pure *trans*-isomer
L_c is the pellet thickness for pure *cis*-isomer
L_t is the pellet thickness for pure *trans*-isomer.

A large number of known mixtures were run in order to calibrate the method. For each of these runs the known value of $R_{c/t}$ and the determined values of the optical densities were inserted into equation 1, which was then solved for F. A plot of F *versus* per cent. *cis*-isomer (Fig. 1) was found to be linear in the range from 18–100%.

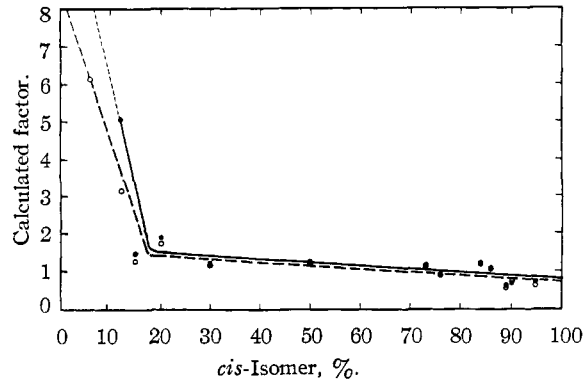

Fig. 1.—Calculated factor *vs.* % *cis*-isomer: ————, critical wave lengths = 12.57 and 9.80 μ, reference wave length = 12.40 μ; — — —, critical wave lengths 12.57 and 9.80 μ, reference wave length = 13.89 μ.

In the determination of unknown mixtures, F was assumed to be one as a first approximation. The per cent. *cis*-isomer obtained from equation 1 was used in conjunction with Chart II to obtain a more precise value of F and thus a more accurate per cent. *cis*-isomer. This procedure was continued until a limiting value of per cent. *cis*-isomer was obtained. Application of the method to further known mixtures indicated a probable accuracy of ±3 units of per cent. *cis*-isomer. Substitution of a different reference wave length (13.89 μ) gave substantially the same F *versus* per cent. *cis*-isomer curve.

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EVANSTON, ILLINOIS

[CONTRIBUTION FROM THE VENABLE CHEMICAL LABORATORY, UNIVERSITY OF NORTH CAROLINA]

Duality of Mechanism in the Reactions of Naphthyl Halides with the Sodium Amide–Piperidine Reagent[1]

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The reactions of seven of the eight monohalonaphthalenes with the sodium amide–piperidine reagent to form mixtures of III and IV go, to judge from product composition, entirely *via* "naphthalyne" intermediates (I and II). α-Fluoronaphthalene, however, reacts partly *via* α-naphthalyne (I) and partly by direct displacement of fluorine by a piperidino group. Direct displacement is also observed in the reactions of 1-fluoro-2-methylnaphthalene with sodium amide and piperidine to form 1-piperidino-2-methylnaphthalene, and of α- and β-naphthyl methyl sulfones with the same reagent to form III and IV, respectively. Thus this research is an exploration of the region of competition of the two mechanisms.

In a previous paper[3] it was shown that each of the two bromonaphthalenes reacts with sodium amide in refluxing piperidine to form a mixture of the two naphthylpiperidines in excellent yield. The mixture from α-bromonaphthalene contained 32% of α-naphthylpiperidine (III) and 68% of β-naphthylpiperidine (IV). The mixture from β-bromonaphthalene was 26% III and 74% IV. The formation of such product mixtures was explicable in terms of a

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(3) J. F. Bunnett and T. K. Brotherton, THIS JOURNAL, **78**, 155 (1956).