CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA

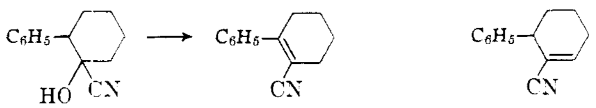
The Dehydration of 2-Phenylcyclohexanone Cyanohydrin: 6-Phenyl-Δ^1-cyclohexenecarbonitrile and 2-Phenyl-Δ^1-cyclohexenecarbonitrile

WILLIAM E. PARHAM, WILBUR N. MOULTON,[1] AND ALEXANDER ZUCKERBRAUN[1]

Received August 22, 1955

The dehydration of 1-hydroxy-2-phenylcyclohexanecarbonitrile (I), by reaction with thionyl chloride and pyridine, and by reaction with phosphorous oxychloride and pyridine, has been examined, and the principal product of these reactions has been shown to be 6-phenyl-Δ^1-cyclohexenecarbonitrile (III) instead of the previously reported 2-phenyl isomer (II). The course of the dehydration of I has been shown to be kinetically controlled, by the facile isomerization of the 6-phenyl isomer (III) to the more stable 2-phenyl isomer (II). A comparison of the chemical and physical properties of II and III, as well as derivatives of these nitriles, is described.

The purpose of this investigation was to determine whether or not the course of dehydration of 1-hydroxy-2-phenylcyclohexanecarbonitrile (I), by reaction with thionyl chloride and pyridine, and by reaction with phosphorus oxychloride and pyridine, is kinetically or thermodynamically controlled. These reactions have been previously reported[2-4]



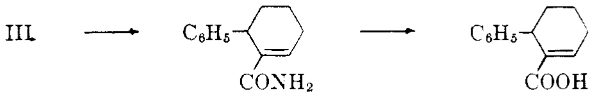
I II III

to give principally, 2-phenyl-Δ^1-cyclohexenecarbonitrile (II); however, the evidence for this structure is meager and is based primarily upon oxidative studies[3] of the single acid obtained by acid hydrolysis of II. Furthermore, the facile conversion of the nitrile function in II into bulkier groups such as carboxyl, carboxamide, and carbonyl, as reported by Veer and his co-workers,[2,3] appears somewhat unusual since molecular models of these derivatives indicate considerable steric crowding, particularly if the phenyl group, double bond, and functional group achieve the copolanar configuration required for maximum resonance interaction. These data suggested that the principal nitrile may indeed have the structure 6-phenyl-Δ^1-cyclohexenecarbonitrile (III).

The solid cyanohydrin I (95% yield from 2-phenylcyclohexanone) was separated into a solid isomer (m.p. 114–115°), and a liquid mixture of isomers by recrystallization from benzene. The dehydration reactions were carried out as previously described,[2-4] and it was found that high yields of the solid nitrile (II or III, m.p. 42–43°) were obtained from the solid cyanohydrin by dehydration with either thionyl chloride and pyridine or with phosphorus oxychloride and pyridine.

The solid nitrile (II or III) showed no absorption maximum in the ultraviolet region above 220 mμ ($\lambda_{252}E_{260}$), and failure of the nitrile to show peak absorption in this region is commensurate only with structure III.[5] Additional evidence for the structure of the nitrile was afforded by oxidation with alkaline permanganate. The acidic product (35% yield, m.p. 140°) was shown to be α-phenyladipic acid by comparison with an authentic sample.[6]

The unsaturated nitrile III was treated with hydrogen peroxide in aqueous acetone to give a 54% yield of amide IV. A 91% yield of the acid V was obtained from the amide by reaction with nitrous acid. The failure of the amide, acid, and corresponding ethyl ester to show appreciable absorption in the ultraviolet region above 220 mμ,[7] indicated that no isomerization of the double bond occurred during the conversion of III into these derivatives. The hydrolysis of III to V was also effected in 70–80% yield by reaction of one part nitrile with two parts of 50% sulfuric acid and two parts acetic acid, as described by Veer.[3] Veer stated



IV V

---

[1] From the Ph. D. Theses of Alexander Zuckerbraun, 1951, and Wilbur N. Moulton, 1954.

[2] S. Goldschmidt and W. L. C. Veer, *Rec. trav. chim.*, **67**, 489 (1948).

[3] W. L. C. Veer and P. J. A. Oud, *Rec. trav. chim.*, **72**, 1083 (1953).

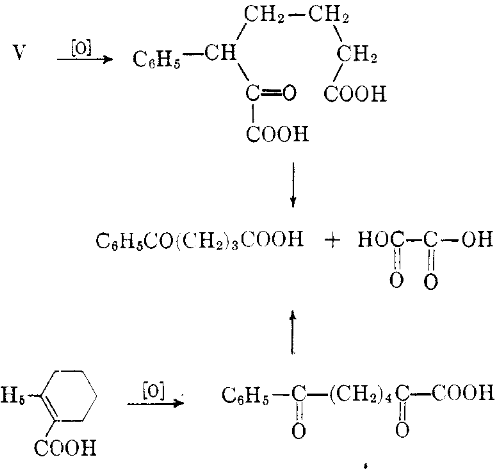
[4] V. Boekelheide and W. M. Schilling, *J. Am. Chem. Soc.*, **72**, 712 (1950).

[5] *cis*-Cinnamonitrile (b.p. 72–73° (0.6 mm.), n_D^{20} 1.5844 λ_{max}^{273} ε 16700) and *trans*-cinnamonitrile (b.p. 77°/0.5 mm.), n_D^{20} 1.6022 λ_{max}^{272} ε 23,100) were prepared as reference compounds by the method of J. Ghosez, *Bull. soc. chim. Belg.*, **41**, 477 (1932).

[6] F. H. Case, *J. Chem. Soc.*, 476 (1936), reports the melting point of 2-phenyladipic acid to be 132–133°. We observed a melting point of 142–143° (see experimental).

[7] *cis*-Cinnamic acid and *trans*-cinnamic acid absorb at λ_{max}^{261} ε 10,500 and λ_{max}^{272} ε 19,500, respectively. *cis*-Cinnamide (m.p. 87–88°) and *trans*-cinnamide (m.p. 149°) were found to absorb at λ_{max}^{254} ε 10,600 and λ_{max}^{273} ε 22,000, respectively. *cis*-Cinnamide was prepared by the reduction of phenylpropiolamide (m.p. 102–104°) with hydrogen in the presence of palladium on calcium carbonate. *Anal.* Calc'd for C_9H_9NO: C, 73.45; H, 6.16; N, 9.52. Found: C, 73.84; H, 6.42; N, 9.77. Ghosez (*Cf.* ref. 4) reports a melting point of 199–200° for *cis*-cinnamide.

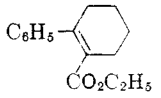
that the liquid nitrile, obtained from I, may be a mixture of II and III, but only one acid is obtained by its hydrolysis with sulfuric acid, and this has structure VI. Veer assumed that the position of the double bond in VI was established by oxidation to oxalic acid and γ-benzoylbutyric acid; however, this evidence may be discounted since either V or VI would be expected to give rise to these products upon oxidation.[8] In view of the structure of the starting nitrile III, the spectra of the acid and



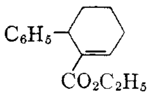
VI

its derivatives, and the data to be described subsequently in this report concerning VI, there can be no doubt that this acid, and the corresponding amide and ester, possess structures V, IV and IIIa, respectively.

Molecular models of 2-phenyl-Δ^1-cyclohexenecarbonitrile (II), and derivatives of this system such as IIa, indicated that considerable steric strain would be encountered if the phenyl group, double bond, and functional group achieved the copolanar configuration required for maximum resonance interaction. This effect would be at a minimum with the linear nitrile group (II), but should be of considerable moment with non-linear groups such



IIa



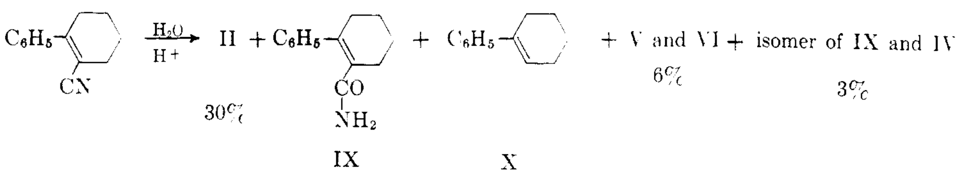
IIIa

as carboxyl, carbethoxy, or carbonyl. Attempts to isomerize the ethyl ester IIIa to IIa, with sodium ethoxide or sodium isopropoxide in hot alcohol, were indeed unsuccessful. The melting point of the crude acid (m.p. 140–155°), obtained from the reaction mixture subsequent to hydrolyses of the resulting ester, indicated the presence of some impurity, but pure 6-phenyl-Δ^1-cyclohexenecarboxylic acid V (m.p. 163°) was obtained in 75% yield after one recrystallization.

The isomerization of III to II, however, was readily achieved by the action of sodium isopropoxide in hot isopropyl alcohol. The product, II, had the same boiling point as the starting material III, could not be induced to crystallize, and showed peak absorption in the ultraviolet region at $\lambda^{251}_{\max}$ ϵ 9150.[5] The ultraviolet spectrum, the composition, and the infrared spectrum[9] of the new nitrile were in agreement with those expected for II. The reaction of the new nitrile with permanganate gave a 6% yield of benzoic acid and a 74% recovery of starting material. This result was not unexpected in view of the known resistance of completely substituted olefins, particularly those bearing electronegative substituents, to permanganate oxidation.[10] That the nitrile II was not contaminated with appreciable quantities of unchanged III was established by competitive hydrolysis experiments after it was learned that II is relatively stable to acid hydrolysis.

Samples of II and III were boiled for 24 hours, under identical conditions, in a solution of 50% acetic acid, 25% sulfuric acid, and 25% water. The hydrolysis of 6-phenyl-Δ^1-cyclohexenecarbonitrile (III) was rapid and gave a single acid (V) in 78% yield.

The results of the hydrolysis of 2-phenyl-Δ^1-cyclohexenecarbonitrile (II) were radically different; the principal products are shown in the following equation.



IX
11%

X
19%

The largest single component was unchanged II ($\lambda^{251}_{\max}$ ϵ 9350, compared to $\lambda^{251}_{\max}$ ϵ 9150 for starting material). Under the conditions of the experiment, the isomeric nitrile III would be rapidly removed; thus, it was apparent that the starting nitrile was essentially pure II, and that the original isomerization of III to II was complete.

The structure of the amide IX was established by chemical and spectral data. The infrared spectrum showed the characteristic amide bands at 3420, 3190, 1657, and 1640 cm.$^{-1}$; the ultraviolet

---

[8] Veer obtained a third acid (m.p. 132–133°) from the oxidation reaction. This acid was impure and was not identified; however, it may have been α-phenyladipic acid, which could only be obtained from V.

[9] II showed absorption at 2218 cm.$^{-1}$ which is characteristic of conjugated nitriles. R. E. Kitson and N. E. Griffith, *Anal. Chem.*, **24**, 334 (1952).

spectrum revealed peak absorption at $\lambda_{\max}^{240}$ ϵ 7000 (the spectra of reference compounds are discussed in footnote 7). Additional evidence for the structure of the amide was obtained by its reduction to *cis*-2-phenylcyclohexanecarboxamide (m.p. 81–82°, reported[11] m.p. 80–80.5°) by reaction with hydrogen over Raney nickel. 2-Phenyl-Δ^1-cyclohexenecarboxylic acid (VI, m.p. 133–134°) was prepared in 40% yield by the reaction of IX with nitrous acid.


VI

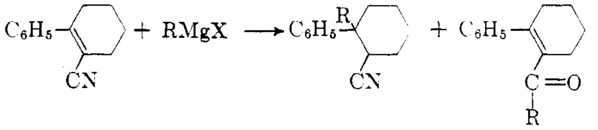
Since the acid VI was derived from IX, and was different from 6-phenyl-Δ^1-cyclohexenecarboxylic acid (V), as shown by spectral and mixture melting point studies, no further evidence for its structure was considered necessary. The acid VI showed peak absorption in the ultraviolet region at $\lambda_{\max}^{245}$ ϵ 7400 (see footnote 7 for reference compounds). The relative acid strengths of V, VI, *cis*-cinnamic acid and *trans*-cinnamic acid were measured and are discussed in the experimental section.

The acid catalyzed decarboxylation of 2-phenyl-Δ^1-cyclohexenecarboxylic acid (VI) would appear to be the most reasonable explanation for the formation of 1-phenylcyclohexene during the acid-catalyzed hydrolysis of II. It is apparent from the preceding data, concerning ultraviolet spectra, acid strengths, and from molecular models, that derivatives of the 2-phenyl-Δ^1-cyclohexene series are sterically hindered. It is also well known that hindered carboxylic acids decarboxylate readily in hot sulfuric acid solutions.[12]

It is apparent from the results described above that the dehydration of solid I, by the methods described, gives almost exclusively 6-phenyl-Δ^1-cyclohexenecarbonitrile (III). Since III is thermodynamically the least stable isomer, it would appear that the course of the dehydration is kinetically controlled, and that the structure of the product is a function of the stereochemistry of the cyanohydrin and of the stereochemistry of the reaction sequence. Since the reported methods of dehydration would be expected to involve replacement of the hydroxyl group by chlorine with inversion, followed by *trans*-elimination of hydrogen chloride, it is probable that the solid cyanohydrin is the epimer in which the cyano and phenyl groups bear a *trans* relationship. It is also probable that the liquid cyanohydrin (I) contains a considerable portion of the epimer in which the phenyl and cyano groups bear a *cis*-relationship. The formation of a mixture of II and III ($\lambda_{\max}^{252}$ ϵ 2900) by dehydration of liquid I is commensurate with this assumption.

It was to our interest to determine whether or not the nitriles II and III showed appreciable differences in their tendency to undergo 1,2- and 1,4-addition reactions with Grignard reagents.

The only product isolated from the reaction of II with phenylmagnesium bromide was a solid ketone (XI, R = C_6H_5, 45%, m.p. 110–111°).


II X XI

The product contained no nitrogen which would exclude the presence of small amounts of X. The ketone, which showed a sharp carbonyl band at 1682 cm.$^{-1}$, and strong absorption in the ultraviolet ($\lambda_{\max}^{242}$ ϵ 24,200), failed to react with 2,4-dinitrophenylhydrazine; only unchanged starting materials were recovered from such attempts. The failure of XI to give such a typical carbonyl derivative was not unexpected in view of the increased steric requirements of the hydrazone.

Similar results were obtained when II was allowed to react with benzylmagnesium chloride. The product (75% yield) contained carbon and hydrogen in amounts essentially as calculated for XI; however, in addition 1.26% nitrogen. The infrared spectrum revealed no absorption typical of saturated nitrile (2250 cm.$^{-1}$), but showed two absorption bands in the carbonyl region (1675 and 1700 cm.$^{-1}$). This product is obviously a mixture of either two ketones, or, more probably, of one ketone and its imine. The product reacted with 2,4-dinitrophenylhydrazine to give a gummy solid that hardened to a glass. This solid melted over a range and gave a low nitrogen analysis.

These results established that there was little, if any, tendency for II to give 1,4 adducts with these Grignard reagents. 6-Phenyl-Δ^1-cyclohexenecarbonitrile (III), on the other hand, gave both 1,2[3,13] and 1,4-adducts with Grignard reagents. The results are summarized in Table I.

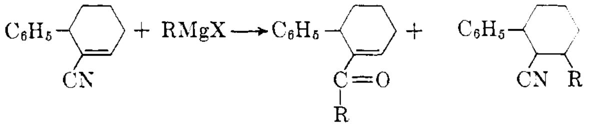

III XII XIII

TABLE I
REACTIONS OF 6-PHENYL-Δ^1-CYCLOHEXENECARBONITRILE WITH GRIGNARD REAGENTS

Reagent	Yield XII	Yield XIII
CH_3MgBr	56	0[a]
C_2H_5MgBr	62	ca. 3
C_6H_5MgBr	86	. .
$C_6H_5CH_2MgCl$	0[a]	42

[a] Not detected by isolation.

---

[10] S. M. McElvain, The Characterization of Organic Compounds, Macmillan Co., New York, N. Y., 1953, p. 83.

[11] C. D. Gutsche, *J. Am. Chem. Soc.*, **70**, 4150 (1948).

[12] *Cf.* W. M. Shubert, J. Donohue, and J. D. Gardner, *J. Am. Chem. Soc.* **76**, 9 (1954).

[13] The methyl ketone was previously prepared and reported to be XI (R = CH_3).

The ketones were characterized by conversion into the corresponding 2,4-dinitrophenylhydrazones, and the nitriles (XIII) by conversion into the corresponding acids. The ultraviolet spectra of the ketones and their derivatives were determined.

EXPERIMENTAL

1-Hydroxy-2-phenylcyclohexanecarbonitrile (I). The nitrile I was prepared from 2-phenylcyclohexanone by the method of Boekelheide and Schilling.[4] The tan solid (90–95% yield) was recrystallized from benzene-petroleum ether B to give a white solid (m.p. 108–110°, 44–46% yield). Further recrystallization of this solid raised the melting point to 114–115° (reported 117°,[4] 112°[2,3]). The mother liquor from the recrystallizations could be stripped to a brown oil, but no more solid could be obtained. Both the solid and liquid products were used in subsequent experiments.

The dehydration of I. The dehydration of I was carried out by the procedures of Boekelheide and Schilling,[4] and Goldschmidt and Veer.[2]

Reagent + pyridine	Cyanohydrin	Product	Yield, %	E at 252 mμ
$SOCl_2$	Solid	m.p. 33–35°	66*	1,250
$POCl_3$	Solid	m.p. 33–35°	77–83*	1,250
$SOCl_2$	Liquid	liquid	31	2,900
$POCl_3$	Liquid	liquid	42	. . .

* The spectra were determined on the crude product. The solid nitrile was easily purified by crystallization from petroleum ether, and was obtained pure, consistently, in yields >50% (E_{252} 260).

Oxidation of the solid nitrile (III). The solid nitrile (0.45 g.) was stirred for 48 hours with a solution prepared from potassium permanganate (1.2 g.), sodium carbonate (0.25 g.), water (100 ml.), and acetone (10 ml.). The reaction mixture was processed in the usual way, and the acidic product (35% yield) was recrystallized from chloroform-petroleum ether B. The product melted at 141–142°.

Anal. Calc'd for $C_{12}H_{14}O_4$: C, 64.86; H, 6.31; N.E., 111. Found: C, 64.99; H, 6.42; N.E., 112.5.

Found for authentic α-phenyladipic acid: C, 64.97; H, 6.38.

α-Phenyladipic acid has been reported to melt at 132–133°.[6] An authentic sample, prepared according to the procedure of Case,[1] melted at 142–143°. A mixture of these acids melted at 141–143°.

Derivatives of the nitrile III. Our work on this subject was completed in 1950–1951.[6] Since that time Veer and Oud[3] have reported some of the same derivatives, but assigned structures as derived from the isomer II.

6-Phenylcyclohexene-Δ¹-carboxamide (IV). A mixture of III (2.0 g., 0.1 mole), acetone (65 ml.), hydrogen peroxide (30 ml. of 10%), and aqueous sodium carbonate (5 ml. of 10%), was allowed to stand at 30–40° for two days. The resulting mixture was extracted with chloroform. From the chloroform extract there was obtained an oil which, upon crystallization from chloroform-petroleum ether (30–70°), gave 1.2 g. (54% yield) of white solid (m.p. 130–135°). This material was purified by sublimation, m.p. 141–142° (Veer[3] prepared this amide, m.p. 140–142°, from the acid chloride and assigned it structure IX).

Anal. Calc'd for $C_{13}H_{15}NO$: C, 77.58; H, 7.50; N, 6.96. Found: C, 77.30; H, 7.66; N, 6.95.

6-Phenylcyclohexene-Δ¹-carboxylic acid (V). (*a*). A solution of sodium nitrite (0.037 g., 0.00054 mole) in water (2 ml.) was added to a cold (0°) mixture prepared from the amide IV (0.117 g., 0.00054 mole), glacial acetic acid (8 ml.), and sulfuric acid (10 ml.). The resulting solution was heated at 60° until bubbling ceased, cooled to 0°, and treated with an additional solution of sodium nitrite (0.037 g., 0.00054 mole) in water (2 ml.). The mixture again was heated at 60° until bubbling ceased, and then was diluted with 60 ml. of water. The pale yellow solid (0.176 g., m.p. 162°, 100% yield) was sublimed to give the pure white acid melting at 163–164°.

Anal. Calc'd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.97. Found: C, 77.22; H, 7.17.

(*b*). The procedure described by Veer using nitrile and a hot mixture of acetic acid, sulfuric acid, and water gave the acid V in 78% yield. Veer[3] reported the acid to melt at 160–162°, and assigned to it structure VI.

Methyl 6-phenylcyclohexene-Δ¹-iminocarboxylate. The nitrile III (1.0 g., 0.0055 mole) was dissolved in anhydrous methanol (75 ml.) which was previously saturated with hydrogen chloride. Water (0.1 g.) was added, and the mixture was heated at the reflux temperature for 16 hours. During the period of reflux a slow stream of hydrogen chloride was passed through the liquid. The mixture then was diluted with water (200 ml.), and extracted with chloroform. The imino ester (38% yield), obtained from the chloroform, melted at 123–125°, and was purified by sublimation; m.p. 131–132°.

Anal. Calc'd for $C_{14}H_{17}NO$: C, 78.10; H, 7.96; N, 6.51. Found: C, 77.80; H, 7.63; N, 6.23.

Hydrolysis of the imino ester, by reaction with hot aqueous sodium hydroxide, gave 6-phenylcyclohexene-Δ¹-carboxylic acid (V, m.p. and mixture m.p. 161–163°).

2-Phenylcyclohexene-Δ¹-carbonitrile (II). 6-Phenyl-Δ¹-cyclohexenecarbonitrile (III, 91.6 g., 0.50 mole) was added to a hot solution prepared from sodium (11.5 g., 0.50 g.-atom) and dry isopropyl alcohol (500 ml.), and the resulting solution was heated at the reflux temperature for 24 hours. The resulting red solution was poured onto ice, neutralized with sulfuric acid (6 *N*), and extracted with ether. The yield of light orange oil, b.p. 120–130° (0.5 mm.), n_D^{25} 1.5709, was 67.4 g. (74%). A small sample was redistilled for analysis; b.p. 131° (1.8 mm.), n_D^{25} 1.5716, $\lambda_{\max}^{251}$ E 9,300 ± 300.

Anal. Calc'd for $C_{13}H_{13}N$: C, 85.20; H, 7.15; N, 7.64. Found: C, 84.83; H, 7.37; N, 7.63.

Acid hydrolysis of 2-phenylcyclohexene-Δ¹-carbonitrile (II). A mixture of II (18.3 g., 0.1 mole), sulfuric acid (18.3 g.), water (18.3 g.), and glacial acetic acid (36.6 g.) was heated at the reflux temperature for 24 hours. The resulting solution was poured onto ice (250 g.), and the resulting mixture was extracted with ether. The ether extract was extracted with aqueous sodium carbonate (3 *N*), and the two solutions were processed separately. A total of five products were isolated. The separation of these products are described in sections *A–E* below.

A. Acidic products. When the basic extract was acidified, a tan gum was obtained. Crystallization of this gum from benzene-petroleum ether B gave a white, solid, acidic product (1.20 g., 6% yield) which melted at 115–120°. The mixture of acids melted at 115–125° after one additional recrystallization from the same solvent.

Anal. Calc'd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98. Found: C, 77.15; H, 7.17.

This product was assumed to be a mixture of V and VI. The ultraviolet spectra suggested that V was the predominate isomer.

B. 2-Phenyl-Δ¹-cyclohexenecarboxamide (IX). Ether was removed from the ethereal extract, and the resulting brown oil partially crystallized. The solid was separated and washed with cold petroleum ether B. A tan solid (m.p. 139–141°) was obtained (2.25 g., 11%) which was subsequently shown to be IX. The tan solid was recrystallized from benzene to give a white solid melting at 144–145°.

Anal. Calc'd for $C_{13}H_{15}NO$: C, 77.58; H, 7.50; N, 6.96. Found: C, 77.38; H, 7.66; N, 6.80.

A mixture melting point of IX and IV (m.p. 142–143°) was 108–118°. The amide IX had a peak absorption in the ultraviolet at $\lambda_{\max}^{240}$ E 7,000.

The reduction of IX was effected in 95% ethanol using Raney nickel catalyst. The solid product (m.p. 69–70°, a hydrate), obtained from the ethanol, was dissolved in petroleum ether, and the resulting solution was dried with magnesium sulfate. The petroleum ether solution was evaporated, and fine white crystals (m.p. 81–82°, 59% yield) were obtained. Further recrystallization of the amide did not raise the melting point. *cis*-2-Phenylcyclohexanecarboxamide is reported[11] to melt at 80–80.5°.

Anal. Calc'd for $C_{13}H_{17}NO$: C, 76.81; H, 8.43. Found: C, 77.01; H, 8.78.

C. 1-Phenylcyclohexene (X). The filtrate and petroleum ether washing, from which IX had been separated, were concentrated and distilled. The low-boiling product (2.96 g., 19% yield) was identified as 1-phenylcyclohexene. A redistilled sample had the following properties: b.p. 69° (0.5 mm.), n_D^{25} 1.5663, λ_{max}^{247} 13,300. Authentic 1-phenylcyclohexene, prepared by the method of Nametkin and Iwanoff,[14] had the following properties: b.p. 69° (0.5 mm.), n_D^{25} 1.5695; λ_{max}^{247} 12,700. The infrared spectra of the two samples were essentially identical; however, the material obtained from II was contaminated by a small amount of impurity as evidenced by absorption at 1220 cm.$^{-1}$

Anal. Calc'd for $C_{12}H_{14}$: C, 91.08; H, 8.92. Found: C, 89.42; H, 9.01.

A sample of 1-phenylcyclohexene, obtained from II, was oxidized with potassium permanganate; γ-benzoylvaleric acid, m.p. 76–77°,[14] was obtained.

D. Recovery of II. The product obtained by distillation, subsequent to the removal of 1-phenylcyclohexene, was unchanged II (b.p. 80–103° (0.2 mm.), 5.50 g., 30%, n_D^{25} 1.5715). A sample was redistilled to give pure II, b.p. 113° (0.3 mm.), n_D^{25} 1.5725, λ_{max}^{251} E 9350.

E. The isomeric amide. The pot residue from the distillation (see *C* and *D*) partly crystallized. A gummy brown solid (1.52 g., 3%) was removed. The solid was recrystallized from benzene-petroleum ether B, and then from ethanol-water, and a white solid, m.p. 107–109° was obtained.

Anal. Calc'd for $C_{13}H_{15}NO$: C, 77.58; H, 7.50; N, 6.96. Found: C, 77.29; H, 7.66; N, 7.14.

The infrared spectrum of this amide was clearly different from that of IX and/or IV. The ultraviolet spectrum revealed a pronounced peak at λ_{max}^{242} (E 10,150). This data is consistent with the structure 2-phenyl-Δ^2-cyclohexenecarboxamide; however, the material was not examined further.

2-Phenylcyclohexene-Δ^1-carboxylic acid (VI). The amide IX was treated with nitrous acid by a procedure identical to that previously described for IV. The acid was obtained as a tan solid (0.20 g., 40% yield), and the color remained after one recrystallization from benzene-petroleum ether B, and two recrystallizations from ethanol-water. The acid melted at 133–134°. The color was removed by treating an aqueous solution of the sodium salt of the acid with charcoal. The white acid, thus obtained, melted at 133–134° (λ_{max}^{245} E 7,400).

Anal. Calc'd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98. Found: C, 77.43; H, 7.33.

REACTION OF II WITH GRIGNARD REAGENTS

A. Phenylmagnesium bromide. A solution of II (9.15 g., 0.05 mole) in ether (100 ml.) was added dropwise to a solution of phenylmagnesium bromide (31.4 g., 0.20 mole of bromobenzene and 4.86 g., 0.20 g.-atom, of magnesium) in ether (100 ml.), and the resulting solution was heated at the reflux temperature for 20 hours. The ether solution then was added slowly to dilute hydrochloric acid (300 ml., 3 *N*), and a solid separated that was insoluble in both water and ether. The ether then was removed by distillation, and the resulting aqueous mixture was heated for one hour at the reflux temperature. The solid slowly dissolved and an oil separated. The mixture was cooled and was extracted with ether. A mushy green solid was obtained by evaporation of the dried ether extract.

The product was recrystallized from petroleum ether to give 5.86 g. of pale green solid (45% yield, most of which melted at 106–108°). Recrystallization of the product from ethanol gave white crystals melting at 110–111°. The ultraviolet spectrum of the ketone (XI, R = C_6H_5) had a peak at λ_{max}^{242} E 24,200. The carbonyl band in the infrared spectrum was at 1682 cm.$^{-1}$

Anal. Calc'd for $C_{19}H_{18}O$: C, 86.98; H, 6.91. Found: C, 86.95; H, 7.18.

Attempts to prepare a 2,4-dinitrophenylhydrazone of XI resulted in the recovery of unchanged starting materials.

B. Benzylmagnesium chloride. The reaction of II (0.20 mole) with benzylmagnesium chloride was carried out as described above for phenylmagnesium bromide. The product (75% yield) was collected at 150–170° (0.03 mm.), n_D^{25} 1.5886. This material resisted crystallization.

Anal. Calc'd for $C_{20}H_{20}O$: C, 86.92; H, 7.29. Found: C, 86.44; H, 7.49; N, 1.26.

The infrared spectrum revealed two absorption bands in the carbonyl region (1675 and 1700 cm.$^{-1}$). The *2,4-dinitrophenylhydrazone* was recrystallized from ethanol to give orange needles that melted at room temperature (wet with solvent). When the ethanol was removed from the derivative a hard red glass was obtained (m.p. 45–58°, λ_{max}^{373} E 22,300).

REACTION OF III WITH GRIGNARD REAGENTS

These reactions were carried out by the usual procedure. The reaction complex in each case was decomposed with 3 *N* hydrochloric acid at 0°, and the mixture was extracted rapidly with cold ether. In this way unreacted starting material, together with 1,4-addition products, were removed from the water-soluble imine hydrochlorides, and a clean separation of 1,2- and 1,4-addition products was achieved. When the acidic aqueous solution was heated on the steam-bath for 45 minutes the ketones separated as oils, and were removed by ether extraction.

A. Methylmagnesium bromide. The preparation of XII (*R* = CH_3). From 12.5 g. (0.667 mole) of III there was obtained 7.5 g. (56.5% yield) of ketonic material. Most of this material, (XII, R = CH_3), boiled at 110° (1 mm.), n_D^{20} 1.5610, λ_{max}^{230} E 12,300.

Anal. Calc'd for $C_{14}H_{16}O$: C, 83.96; H, 8.05. Found: C, 83.50; H, 8.05.

The 2,4-dinitrophenylhydrazone of XII (*R* = CH_3), λ_{max}^{380} E 24,300, melted at 164° after recrystallization from ethanol-water.

Anal. Calc'd for $C_{20}H_{20}N_4O_4$: C, 63.14; H, 5.30. Found: C, 63.30; H, 5.62.

The oxime melted at 123.5–124° (reported m.p. 121–123.5°, but formulated as[3] the isomer derived from XI).

Anal. Calc'd for $C_{14}H_{19}NO$: C, 78.14; H, 7.90. Found: C, 78.20; H, 8.30.

No 1,4-adduct (XIII) was isolated.

B. Ethylmagnesium bromide. The preparation of XII (*R* = C_2H_5) *and the 1,4-adduct. 1,4-Adduct.* The ether extract was dried and concentrated to give 1.85 g. of a yellow oil. A mixture prepared from the oil, glacial acetic acid (20 ml.), and hydrobromic acid (10 ml.) was heated at the reflux temperature for 12 days. The resulting mixture was cooled and poured into cold water (200 ml.), and the resulting solution was made alkaline with potassium hydroxide and then extracted with chloroform. The alkaline solution was acidified (hydrochloric acid), and the resulting oil was extracted with chloroform. A solid acid was obtained from the chloroform extract which melted at 106° after crystallization from petroleum ether (60–68°). This acid tentatively has been assigned the structure 6-phenyl-2-ethylcyclohexane-1-carboxylic acid (derived from XIII, R = C_2H_5).

---

[14] S. Nametkin and N. Iwanoff, *Ber.*, **56**, 1805 (1923).

Anal. Calc'd for $C_{15}H_{20}O_2$: C, 77.60; H, 8.60; N. E., 232. Found: C, 77.90; H, 8.84; N. E., 228.

The ketone XII (*R* = C_2H_5). The ether extract, containing the ketone, was concentrated, and the residue (from which volatile material was removed) weighed 8.8 g. (62% yield). Most of this material distilled at 121° (2 mm.), n^{20}_D 1.5500, λ^{230}_{max} E 9100.

Anal. Calc'd for $C_{15}H_{18}O$: C, 84.06; H, 8.46. Found: C, 83.89; H, 8.60.

The 2,4-dinitrophenylhydrazone (λ^{380}_{max} E 24,600) melted at 160–161° after recrystallization from ethanol-chloroform.

Anal. Calc'd for $C_{21}H_{22}N_4O_4$: C, 63.90; H, 5.60. Found: C, 64.00; H, 5.64.

C. Phenylmagnesium chloride. The preparation of XII (*R* = C_6H_5). 6-Phenyl-1-benzoyl-Δ¹-cyclohexene (XII, R = C_6H_5) (3.65 g., 86% yield, m.p. 85–87°) was obtained as a tan solid from the ketone-containing ethereal extract. The ketone was obtained as white needles, λ^{246}_{max} E 10,000, m.p. 95–96°, by recrystallization from petroleum ether (60–68°).

Anal. Calc'd for $C_{19}H_{18}O$: C, 86.98; H, 6.91. Found: C, 86.96; H, 7.16.

The 2,4-dinitrophenylhydrazone (λ^{380}_{max} E 27,900) melted at 195° after recrystallization from ethyl acetate-petroleum ether (60–68°).

Anal. Calc'd for $C_{25}H_{22}N_4O_4$: C, 67.85; H, 5.01. Found: C, 67.90; H, 5.27.

D. Benzylmagnesium chloride. The preparation of XIII (*R* = $C_6H_5CH_2$—). No ketonic material was isolated. The dry ether extract, containing 1,4-adduct, was concentrated and distilled. The principal fraction (11 g., 67%) was collected at 160–190° (2 mm.). This material partially crystallized, and a total of 7.5 g. (42% yield) of solid (m.p. 70–74°) was obtained by crystallization from ethanol. The melting point of this product was raised to 74–75° by recrystallization from ethanol, with subsequent sublimation of the product at 140° (0.04 mm.).

Anal. Calc'd for $C_{20}H_{21}N$: C, 87.20; H, 7.60; N, 5.10. Found: C, 87.20; H, 7.69; N, 5.21.

The amide, derived from XIII (R = $C_6H_5CH_2$—), was prepared (94% yield, m.p. 185–187°) by reaction of the nitrile with hydrogen peroxide by a procedure similar to that previously described in this report. The product melted at 189–190° after recrystallization from chloroform-petroleum ether, with subsequent vacuum sublimation.

Anal. Calc'd for $C_{20}H_{23}NO$: C, 81.87; H, 7.90; N, 4.70. Found: C, 81.60; H, 7.86; N, 4.80.

The acid, derived from XIII (R = $C_6H_5CH_2$—), was prepared (95% yield, m.p. 139–141°) from the amide by reaction with nitrous acid by a procedure similar to that previously described in this report. The acid melted at 143–144° after sublimation at reduced pressure.

Anal. Calc'd for $C_{20}H_{22}O_2$: C, 81.59; H, 7.53; N. E., 294. Found: C, 81.50; H, 7.41; N. E., 292.

No ketonic material (XII) was isolated from this reaction.

Determination of acid strengths. Acid strengths were determined by titrations in aqueous ethanol, using a Beckman *p*H meter (Model G). Weighed samples of the acid, approximately 5 × 10^{-4} mole, were dissolved in 7.5 ml. of ethanol (95%). Water (2.5 ml.) was added and the resulting solution titrated with standard (0.0297 *N*) sodium hydroxide. The results are tabulated in the following table.

Acid	Sample wt. (gm.)	pK_a	Ka × 10^8	Neut. Equiv. Found	Neut. Equiv. Calcd
Benzoic	0.0627	6.29	51.4	122.5	122.1
Phenyl-propiolic	0.0678	4.00	10,000	147.0	146.1
cis-Cinnamic	0.0744	5.87	135	149.5	148.2
trans-Cinnamic	0.0703	6.27	53.8	148.3	148.2
V	0.1030	7.20	6.25	201.5	202.2
VI	0.0979	6.66	22.1	197.5	202.2

MINNEAPOLIS 14, MINN.