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[CONTRIBUTION FROM ABBOTT LABORATORIES]

An Improved Synthesis of Cyclopropyl Phenyl Ketone and Related Substances

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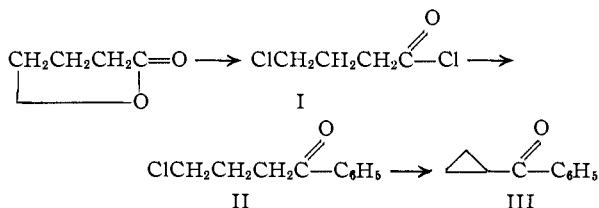
The synthesis of cyclopropyl phenyl ketone (III) in 75% yield from γ -butyrolactone is given. It is shown that the intermediate γ -chlorobutyryl chloride can be used to prepare other cyclopropyl aromatic ketones. Several new products derived from III are described.

In recent years there has been an increased interest in the study of compounds containing the cyclopropyl group. This is due in large part to the unique electronic nature of this arrangement of atoms; it is well known that the cyclopropane ring often possesses a large measure of unsaturated character.

Work with cyclopropane derivatives has been hampered by the relative unavailability of key intermediates. We have found a convenient method of preparing cyclopropyl phenyl ketone (III) which appears to be applicable to many other aromatic ketones and hence provides an entering wedge for the synthesis of numerous derivatives.

III has been prepared by a variety of methods. The most generally used procedures have utilized a γ -halogenated butyronitrile as the common intermediate.¹⁻³ The cost of this substance and the relatively low over-all yields have made it difficult to obtain large quantities of the ketone.

The availability of butyrolactone suggested to us a simpler and far cheaper process for obtaining III. The lactone, by successive treatment with hydrochloric acid and thionyl chloride, is converted to γ -chlorobutyryl chloride (I) in 88% yield. I is then condensed with benzene to give the chloro-ketone II, which is cyclized to III in the usual way with methanolic potassium hydroxide. The over-all yield from the lactone is 75-77%.



The use of a Friedel-Crafts reaction with a simple γ -halogenated acid chloride is apparently new. α -Halogenated acid chlorides have been used in this type of reaction, and it has been found that only the acyl halide enters into the reaction.⁴ It

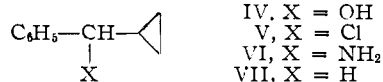
has been reported⁵ that either one or both of the halogen atoms in β -chloropropionyl chloride can be made to react with aromatic hydrocarbons in the presence of aluminum chloride. Hale and Britton⁶ were able to obtain a reaction exclusively at the acid halide function with this substance.

Mayer and Fischbach⁷ studied the Friedel-Crafts reaction of 2-(bromomethyl)-benzoyl bromide, which may be considered a special case of a γ -halogenated acid halide. They found that both the acyl and alkyl halide entered the reaction with the production of either a disubstituted derivative or an anthrone.

In our own case it was difficult to eliminate completely replacement of the γ -chloro group; however, when the reaction was carried out rapidly at moderately low temperatures ($< 20^\circ$), the amount of by-product formed was minimal.

Presumably, the reaction sequence outlined can be followed with any aromatic compound which normally undergoes a Friedel-Crafts substitution. Toluene, chlorobenzene, phenetole and naphthalene were treated with I, and the expected products were obtained in all cases. No attempt was made to determine optimum operating conditions in these preparations.

Having on hand substantial quantities of III, we prepared several related compounds, many of which have not been described previously. Reduction of III with lithium aluminum hydride gave α -cyclopropylbenzyl alcohol (IV). The carbinol was converted to the carbamate in good yield by the method of McLamore⁸; it yielded an allophanate in poor yield when treated with cyanic acid.



An earlier attempt to prepare the carbamate by the phosgene-ammonia method resulted in the for-

(1) J. B. Conant, J. B. Segur and W. R. Kirner, *THIS JOURNAL*, **46**, 1882 (1924).

(2) R. P. Mariella and R. R. Raube, *ibid.*, **74**, 521 (1952).

(3) H. R. Henze and C. W. Gayler, *ibid.*, **74**, 3615 (1952).

(4) A. Collet, *Bull. soc. chim.*, [3] **17**, 66 (1897).

(5) F. Mayer and L. van Zütphen, Dissertation, Frankfurt (1923); reported in ref. 7.

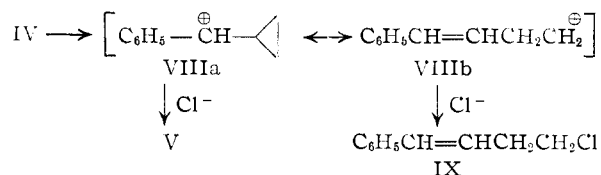
(6) W. J. Hale and E. C. Britton, *THIS JOURNAL*, **41**, 841 (1919).

(7) F. Mayer and W. Fischbach, *Ber.*, **58**, 1251 (1925).

(8) W. M. McLamore, S. Y. P'an and A. Bawley, *J. Org. Chem.*, **20**, 1379 (1955).

mation of water. Since it appeared very unlikely that simple dehydration to a cyclopropylidene derivative would occur under these conditions, the products of this reaction were examined in more detail. It was found that treatment of IV with phosgene led to a mixture which contained a large amount of halogenated material. A small amount of a highly reactive halide was present; this was not isolated but was shown to be V by conversion to the corresponding amine VI. The majority of the halide was isomeric with V. It was an unreactive, stable substance which was shown to contain an ethylenic linkage. The infrared spectrum suggested that the substance was 4-chloro-1-phenyl-1-butene (IX). Confirmation of this structure was obtained through ozonolysis.

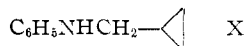
The formation of V and IX can be rationalized easily as shown. In the presence of a trace of hydrogen chloride (from the phosgene) the carbenium ion VIIIa is produced.⁹ VIIIa reacts with the chloride anion to produce V; VIIIb leads to IX. Each mole of water produced in the reaction is capable of yielding two moles of hydrogen chloride by reaction with phosgene; hence, water may accumulate as was observed experimentally.



Since the chloride V was of greater interest to us than IX, we sought to prepare this substance by the reaction of phosphorus trichloride on the carbinol. Even though the reaction was carried out at a low temperature, the only product which could be isolated was IX.

The ketone III was converted in good yields to the known oxime and semicarbazone. The former was reduced catalytically in satisfactory yield to VI. VI was converted to the corresponding urea as well as to methyl N-(α -cyclopropylbenzyl)-carbamate.

Reduction of the oxime with lithium aluminum hydride gave a mixture of VI and a second, isomeric amine, which, being a weaker base, was easily separated. Reasoning by analogy with the behavior of other alkyl aryl ketoximes under similar conditions,^{10,11} we suggest that the by-product is N-(cyclopropylmethyl)-aniline (X).



Reduction of III by means of the Huang-Minlon modification of the Wolff-Kishner reaction resulted in an excellent yield of the hydrocarbon VII.

Acknowledgments.—The author is indebted to Mr. William Washburn for the infrared data, to Mr. Elmer Shelberg and his staff for the microanalyses and to Mr. Morris Freifelder and Mr. George Stone for the catalytic hydrogenation.

(9) Cf. J. D. Roberts and R. H. Mazur, *THIS JOURNAL*, **73**, 2509 (1951).

(10) D. R. Smith, M. Maienthal and J. Tipton, *J. Org. Chem.*, **17**, 294 (1952).

(11) R. E. Lyle and H. J. Troscianiec, *ibid.*, **20**, 1757 (1955).

Experimental

γ -Chlorobutyryl Chloride (I).— γ -Butyrolactone (500 g., 5.81 moles) was distributed among five pressure bottles.¹² The vessels were placed in a Dry Ice-acetone bath during the addition of 46–51 g. (10–20% excess) of anhydrous hydrogen chloride to each. The bottles were stoppered and allowed to stand at room temperature for two to three weeks.

The contents of the bottles were combined and placed in a two-liter flask fitted with a condenser and hydrogen chloride trap. Thionyl chloride (759 g., 6.38 moles) was added and the solution was refluxed for 1 hr. Fractionation yielded 718 g. (88%) of product boiling at 55–60° (10 mm.). n_D^{20} 1.4590.¹³

Cyclopropyl Phenyl Ketone (III).—Anhydrous aluminum chloride (423 g., 3.17 moles) was suspended in 2115 cc. of dry benzene in a five-liter flask fitted with a stirrer, dropping funnel, thermometer and hydrogen chloride trap. The mixture was cooled in ice to 15°, and 423 g. (3 moles) of I in 423 cc. of dry benzene was added at such a rate as to maintain the temperature at 15–20°. About 20 minutes was required for the addition.¹⁴ The ice-bath was removed and stirring was continued for 20 minutes.

The reaction mixture was poured into ice-water. The benzene layer was separated, dried over Drierite and concentrated under reduced pressure. The residue of crude chloroketone II was not purified but was treated with 297 g. (4.5 moles) of 85% potassium hydroxide pellets dissolved in 1188 cc. methanol. The mixture, which became hot, was shaken frequently while standing for 30 minutes. It was then cooled and filtered. Most of the methanol was removed under reduced pressure; the residue was taken up in ether and water. The ether layer was separated, washed with water, dried over Drierite and concentrated. Distillation yielded 372–385 g. (85–88%), b.p. 109–110° (10 mm.), n_D^{25} 1.5515. Mariella and Raube² reported b.p. 102° (7 mm.), n_D^{25} 1.5514.

γ -Phenylbutyrophenone appeared as a high-boiling residue from the distillation of the product. The amount of this by-product was increased if the reaction time was prolonged or if the temperature was allowed to rise above 20°. The material distilled at 170–172° (1.0 mm.). Crystallization in Skellysolve B yielded a solid melting at 53–56°.¹⁵

The oxime of III was prepared by heating 58.4 g. with 56 g. of hydroxylamine hydrochloride in 100 cc. of pyridine and 100 cc. of absolute alcohol for 16 hr. on a steam-bath. The solvents were removed under reduced pressure. When the residue was treated with ice-water, 61 g. (95%) of product, m.p. 81–92°, separated.

It was difficult to obtain a sharp melting point by recrystallization; some improvement could be made by long drying in a vacuum oven at 50°. By extensive purification, material melting at 99–101° was obtained.¹⁶ The lower melting material was considered to be a mixture of *syn* and *anti* forms and was used without purification in the reduction experiments.

The semicarbazone was prepared by dissolving 29.2 g. of III in 150 cc. of alcohol and adding water to the point of incipient precipitation. The solution was treated with 33.6 g. of semicarbazide hydrochloride together with 41 g. of sodium acetate. The reaction mixture was refluxed for 15 minutes, diluted with water and cooled. Filtration yielded 37.3 g. (92%) m.p. 183–185°. Conant¹ reported m.p. 182–183°.

Cyclopropyl *p*-Tolyl Ketone.—A procedure essentially the same as that described for III was followed on a smaller scale with the substitution of toluene for benzene. The

(12) "Citrate of Magnesia" bottles with a capacity of 300 cc. were found well suited to handle the small pressures involved.

(13) R. Leimu, *Ber.*, **70**, 1040 (1937), reported b.p. 55–56° (12 mm.), n_D^{20} 1.4616. F. F. Blicke, W. B. Wright, Jr., and M. F. Zienty, *THIS JOURNAL*, **63**, 2488 (1941), reported b.p. 60–61° (12 mm.).

(14) Occasionally a considerable induction period was observed at the start of the reaction. This has been attributed to (1) too scrupulously dry aluminum chloride and (2) poor stirring. No more than one-fourth of the acid chloride should be added until it is obvious that reaction is occurring (generation of heat, evolution of hydrogen chloride and dissolution of aluminum chloride).

(15) R. Stoermer and Fr. Schenck, *Ber.*, **61**, 2312 (1928), reported m.p. 56–57°.

(16) Conant (ref. 1) reported m.p. 90–94°. T. K. Marshall and W. H. Perkin, *J. Chem. Soc.*, **59**, 853 (1891), reported m.p. 90–92°. The latter authors also had difficulty in obtaining sharply melting material.

temperature was kept at 10–15° during the addition of 56.4 g. of the acid chloride over a period of 15 minutes. The mixture was hydrolyzed after five additional minutes at 10–15°. The product was obtained as an oil, b.p. 124–127° (9 mm.), which readily crystallized. Recrystallization from Skellysolve B yielded 34.5 g., m.p. 49–51°, and 19.5 g., m.p. 46–51°, for a total of 54 g. (84%).¹⁷

Anal. Calcd. for C₁₁H₁₂O: C, 82.5; H, 7.6. Found: C, 82.2; H, 7.4.

***p*-Chlorophenyl Cyclopropyl Ketone.**—The procedure described above was followed with chlorobenzene. The acid chloride (56.4 g.) was added over a ten-minute period at 25–30°, and the mixture was maintained at 25–30° for an additional 30 minutes. Distillation yielded 57.5 g. (80%), b.p. 132–133° (10 mm.), *n*_D²⁵ 1.5683. A 12" packed column was used during the distillation in an attempt to separate any *ortho* isomer, if present. None was observed.

Anal. Calcd. for C₁₀H₉ClO: C, 66.5; H, 5.0. Found: C, 66.5; H, 5.0.

Cyclopropyl *p*-Ethoxyphenyl Ketone.—Aluminum chloride (56.4 g., 0.42 mole) was suspended in 225 cc. of carbon disulfide in a one-liter flask fitted with a stirrer, dropping funnel, thermometer and hydrogen chloride trap. The mixture was cooled to 10° and a solution of 48.8 g. (0.4 mole) of phenetole in 56.4 g. (0.4 mole) of I was added at such a rate as to maintain the temperature at 10–15°. Fifteen minutes was required for the addition. Stirring at the same temperature was continued for 10 minutes.

The intermediate chloroketone was converted to the cyclic ketone as described for III. The product solidified; dilution with Skellysolve B and filtration yielded 54 g. (71%), m.p. 68–70°. An analytical sample, m.p. 68–70°, was prepared from Skellysolve B.

Anal. Calcd. for C₁₂H₁₄O₂: C, 75.8; H, 7.4. Found: C, 76.2; H, 7.6.

Cyclopropyl β -Naphthyl Ketone.—Aluminum chloride (56.4 g., 0.42 mole) was dissolved in 225 cc. of nitrobenzene. The solution was cooled to 10° and treated with a solution of 51.2 g. (0.4 mole) of naphthalene, 56.4 g. (0.4 mole) of I and 56 cc. of nitrobenzene. There was no vigorous reaction and little evolution of hydrogen chloride. The dark reaction mixture was warmed very slowly to 50° and maintained at that temperature for 1 hr. (total reaction time, 3 hr.).

The chloroketone was isolated and converted to the cyclic ketone in the usual way. Most of the product precipitated with the potassium chloride during the treatment with methanolic potassium hydroxide. Washing the precipitate with water and methanol left 40.4 g., m.p. 117–120°. An additional 10.0 g., m.p. 117–120°, was obtained from the methanolic filtrate. The total yield was 50.4 g. (64%). An analytical sample, m.p. 119–120°, was prepared from ethanol.

Anal. Calcd. for C₁₄H₁₂O: C, 85.7; H, 6.2. Found: C, 85.8; H, 6.3.

The oxime was prepared in the same manner as the oxime of III. The melting point was constant at 103–106° after several recrystallizations from isopropyl ether.

Anal. Calcd. for C₁₄H₁₃NO: N, 6.6. Found: N, 6.6.

In order to prove the position of substitution on the naphthalene nucleus, a Beckmann rearrangement was carried out on the oxime following the procedure given by Horning.¹⁸ Hydrolysis of the resulting amide gave 2-naphthoic acid.

α -Cyclopropylbenzyl Alcohol (IV).—Fifty grams (0.34 mole) of III was added dropwise to a stirred solution of 5.0 g. (0.13 mole) of lithium aluminum hydride in 150 cc. of dry ether. After 15 minutes, the product was isolated in the usual way. Distillation yielded 47.4 g. (93%), b.p. 121° (12 mm.), *n*_D²⁵ 1.5390.

Anal. Calcd. for C₁₀H₁₂O: C, 81.0; H, 8.2. Found: C, 81.0; H, 8.0.

The allophanate was prepared in the usual way¹⁹ from 5 g. of the carbinol. The solution was allowed to stand several

days but no solid separated. A small amount of alcohol and Skellysolve B were then added. After the solution had stood for several weeks in the cold room, some crystalline material separated; this was found to be a mixture of ethyl allophanate and the desired product. Separation yielded about 0.2 g., m.p. 138–140° (gas).

Anal. Calcd. for C₁₂H₁₄N₂O₃: N, 12.0. Found: N, 12.1.

α -Cyclopropylbenzyl Carbamate.—The procedure as given by McLamore and co-workers⁹ was followed with 13.4 g. of IV. Prismatic crystals separated from the ethereal solution after the ammonia had evaporated. Filtration yielded 7.0 g., m.p. 104–112°. By processing the filtrate, an additional 4.8 g., m.p. 111–115°, was obtained, bringing the total crude yield to 11.8 g. (69%). An analytical sample, m.p. 114–115°, was obtained from isopropyl ether and alcohol.

Anal. Calcd. for C₁₁H₁₃NO₂: N, 7.3. Found: N, 7.4.

Reaction of IV with Phosgene. Conversion to 4-Chloro-1-phenyl-1-butene (IX).—The carbinol (14.8 g., 0.1 mole) was added to 14.4 g. (0.15 mole) of phosgene dissolved in 60 cc. of dry toluene and cooled in ice. The temperature rose to 15° and water separated within a few minutes. The reaction mixture was kept in ice for 1 hr., then at room temperature for 2 hr. The toluene layer was decanted, dried over Drierite and concentrated under reduced pressure. Distillation gave 13.9 g., b.p. 115–130° (12 mm.), *n*_D²⁵ 1.5422–1.5612, which was collected in several fractions. All fractions decolorized bromine and permanganate solutions. All fractions gave an immediate precipitate with alcoholic silver nitrate.

The lower boiling fractions (7.3 g.) were combined and allowed to stand overnight in 25 cc. of concentrated ammonium hydroxide with occasional shaking. The organic material was extracted with ether and separated into basic and neutral fractions by means of dilute hydrochloric acid. The basic fraction yielded 1.0 g. of amine hydrochloride, m.p. 220–224°. Recrystallization brought the m.p. to 235–236°, which was not depressed when the substance was mixed with the hydrochloride of VI. The salt was converted to the urea by means of potassium cyanate. The melting point was 143–146°, undepressed by admixture with authentic (α -cyclopropylbenzyl)-urea.

The neutral material was fractionated. The majority boiled at 131–135° (15 mm.), *n*_D²⁵ 1.5616. A purer sample of this substance was obtained from the combined higher boiling fractions (6.0 g.) by treatment with ammonia as described above. About 100 mg. of additional VI hydrochloride was obtained from this treatment. The neutral material yielded 3.4 g., b.p. 132–135° (16 mm.), *n*_D²⁵ 1.5632, when distilled. This substance still decolorized bromine and permanganate solutions; however, it reacted with alcoholic silver nitrate only after heating for 10 minutes. The infrared spectrum gave no evidence of an intact cyclopropyl group; although possible bands at 3.23 and 3.32 μ (3096 and 3012 cm.⁻¹) were obscured by the C–H stretching vibration of the phenyl group, there was no significant absorption in the 9.75–10 μ (1026–1000 cm.⁻¹) region. The compound was transparent in the 7.2–7.3 μ (1390–1370 cm.⁻¹) and 6–6.15 μ (1667–1626 cm.⁻¹) regions, indicating, respectively, the absence of a terminal methyl and a terminal ethylenic linkage. A strong band at 10.36 μ (965 cm.⁻¹) indicated a *trans* double bond. Absorption at 6.31 μ (1585 cm.⁻¹), on the long wave length side of the >C=C< stretching vibration of the benzene ring, suggested that the double bond was conjugated with the phenyl group.

The only structure consistent with the above data is IX. The location of the olefinic linkage was demonstrated through ozonolysis, which led to a copious precipitate of benzoic acid. The location of the halogen atom must be as shown to account for the absence of a terminal methyl group. In addition, 1-, 2- and 3-chloro-1-phenyl-1-butenes are known compounds²⁰ which differ from the substance isolated here.

Anal. Calcd. for C₁₀H₁₁Cl: C, 72.0; H, 6.7; Cl, 21.3. Found: C, 72.3; H, 6.9; Cl, 20.9, 20.8.

(20) K. von Auwers, *Ber.*, **45**, 2781 (1912); I. E. Muskat and M. Herrman, *This Journal*, **53**, 260 (1931); I. E. Muskat and K. A. Huggins, *ibid.*, **56**, 1239 (1934); A. Zaki and Y. Iskander, *J. Chem. Soc.*, 68 (1943).

(17) H. Wohlgemuth, *Ann. chim.* [9], **3**, 141 (1915), reported m.p. 48°.

(18) E. C. Horning and V. L. Stromberg, *This Journal*, **74**, 2680 (1952).

(19) M. A. Spielman, J. D. Barnes and W. J. Close, *ibid.*, **72**, 2520 (1950).

Reaction of IV with Phosphorus Trichloride. Attempted Preparation of α -Cyclopropylbenzyl Chloride.—The carbimol (5.6 g.) was dissolved in 50 cc. of dry ether and cooled in Dry Ice-alcohol. The solution was stirred during the dropwise addition of 2.6 g. of phosphorus trichloride in 10 cc. of dry ether. The solution was stirred for 1 hr. in the cold; the bath was then removed and the mixture was allowed to stand 2 hr.

Water was added and the layers were separated. The organic layer was washed with sodium bicarbonate solution and dried over Drierite. The product boiled over a wide range (120–140° at 16 mm.), and there was an appreciable amount of non-volatile residue. Through redistillation a small amount of liquid boiling at 135° (19 mm.), n_D^{20} 1.5620, was obtained. The infrared spectrum indicated that the substance isolated was crude IX.

α -Cyclopropylbenzylamine (VI). A. By Catalytic Reduction.—Cyclopropyl phenyl ketoxime (16.1 g., 0.1 mole) was dissolved in 200 cc. of absolute alcohol containing 0.25 mole of dry hydrogen chloride. Hydrogenation was carried out with 2.0 g. of 5% palladium on charcoal at a pressure of 30 lb. In 2 hr., the mixture was filtered; the filtrate was concentrated to about 50 cc. and diluted with dry ether. Twelve grams (65%) of product, m.p. 237–238°,²¹ was obtained.

B. By Reduction with Lithium Aluminum Hydride.—The oxime (30 g., 0.19 mole) was dissolved in 150 cc. of dry ether and added dropwise to 14.1 g. (0.37 mole) of the hydride in 150 cc. of dry ether. The mixture was refluxed for two days.

The product was processed in the usual way. Distillation yielded 22.8 g., b.p. 103–115°, n_D^{20} 1.5390–1.5492. Since the product was obviously a mixture, it was combined with similar material from an earlier run (total, 32 g.) and dissolved in a slight excess of dilute hydrochloric acid. The solution was extracted with ether to remove any neutral substance, and then it was neutralized to a methyl red end-point. The oil which separated was extracted with ether (solution A). The aqueous solution was now made basic and again extracted with ether (solution B).

Both solutions were dried over potassium hydroxide and treated with dry hydrogen chloride. Solution B yielded 25.9 g. of the hydrochloride of VI, m.p. 224–226°. The melting point was raised to 233–234° by recrystallization

(21) N. Kizhner, *J. Russ. Phys. Chem. Soc.*, **43**, 1163 (1911) [*C. A.*, **6**, 597 (1912)], reported m.p. 220–221°.

from ethanol-ether. Solution A yielded 10.0 g., m.p. 173–176°. Several recrystallizations from alcohol did not change the melting point. From a consideration of the weakly basic character of the amine and the analogous rearrangements observed by others,^{10,11} the substance is assigned the structure of N-(cyclopropylmethyl)-aniline hydrochloride (X·HCl).

Anal. Calcd. for $C_{10}H_{13}N\cdot HCl$: C, 65.4; H, 7.7; N, 7.6. Found: C, 65.5; H, 7.8; N, 7.7.

(α -Cyclopropylbenzyl)-urea.—The amine hydrochloride (9.2 g., 0.05 mole) was dissolved in 40 cc. of water and treated with 4.9 g. (0.06 mole) of potassium cyanate in 20 cc. of water. After several hours, the product was separated by filtration; the yield was 8.0 g. (85%), m.p. 143–146°. An analytical sample prepared from alcohol melted at 145–146°.

Anal. Calcd. for $C_{11}H_{14}N_2O$: N, 14.7. Found: N, 14.9.

Methyl N-(α -Cyclopropylbenzyl)-carbamate.—A Schotten-Baumann reaction was carried out with 18.4 g. of VI hydrochloride and 14.3 g. of methyl chloroformate. Filtration yielded 16.2 g. (79%), m.p. 88–90°.

Recrystallization from dilute alcohol gave an analytical sample melting at 88–90°.

Anal. Calcd. for $C_{12}H_{15}NO_2$: N, 6.8. Found: N, 6.8.

Benzylcyclopropane (VII).—The ketone III (29.2 g., 0.2 mole), 24 g. (0.4 mole) of 85% hydrazine hydrate, 26.4 g. (0.4 mole) of 85% potassium hydroxide and 150 cc. of diethylene glycol were refluxed in an oil-bath at 120° for 1 hr. The condenser was then set for distillation and the temperature was gradually raised to 200°. The product steam distilled during this time. After 1 hr. at 200°, the reaction mixture was cooled somewhat and treated with 20 cc. of water. The steam distillation was then continued for an additional hour.

The oil was separated from the water by means of ether. The dried ether layer was concentrated and distilled, yielding 22 g. (83%), b.p. 188°, n_D^{20} 1.5140. A portion was redistilled over sodium for analysis; all came over at 83–84° (20 mm.), n_D^{20} 1.5130.

Anal. Calcd. for $C_{10}H_{12}$: C, 90.9; H, 9.2. Found: C, 90.9; H, 9.2.

NORTH CHICAGO, ILLINOIS

[CONTRIBUTION NO. 2131 FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY]

Mechanisms for Liquid Phase Hydrolyses of Chlorobenzene and Halotoluenes¹

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A study of the rearrangements which occur during the high temperature liquid phase hydrolyses of the halotoluenes has shown that the extent of rearrangement is a sensitive function of temperature, base strength and the nature of the halogen. These hydrolyses involve either a benzyne (elimination-addition) mechanism, which gives both rearranged and unrearranged products, or an SN_2 -type mechanism. The SN_2 -type mechanism was found to be favored at lower temperatures, in the presence of weaker bases and with the more easily ionizable halogens. By suitable choice of conditions, one or the other reaction could be made to occur almost exclusively. Chlorobenzene-1-¹⁴C, with 4 *M* sodium hydroxide solution at 340°, gave 58 ± 1% phenol-1-¹⁴C and 42 ± 1% phenol-2-¹⁴C, which indicates that under these conditions the benzyne mechanism predominates but is not the exclusive reaction path.

It has been known for many years that the individual chlorotoluenes are hydrolyzed with sodium hydroxide solution at temperatures above 300° to yield mixtures of cresols.^{3,4} The extent and character of these rearrangements bear a marked simi-

larity to what would be expected if a "benzyne" (elimination-addition) mechanism⁵ were operative. Thus, the entering hydroxyl group has never been found farther than one carbon away from the leaving chlorine, and the chlorotoluenes and cresols (as sodium cresolates) are apparently not isomerized

(1) Presented in part at the National Academy of Science Meeting in Pasadena, California, November 4, 1955; J. D. Roberts, A. T. Bottini and D. A. Semenov, *Science*, **122**, 881 (1955).

(2) National Science Foundation Predoctoral Fellow, 1954–1957.

(3) V. E. Meharg and I. Allen, Jr., *THIS JOURNAL*, **54**, 2920 (1932).

(4) R. N. Shreve and C. J. Marsel, *Ind. Eng. Chem.*, **38**, 254 (1946).

(5) (a) J. D. Roberts, H. E. Simmons, Jr., L. A. Carlsmith and C. W. Vaughan, *THIS JOURNAL*, **75**, 3290 (1953); (b) J. D. Roberts, D. A. Semenov, H. E. Simmons, Jr., and L. A. Carlsmith, *ibid.*, **78**, 601 (1956); (c) J. D. Roberts, C. W. Vaughan, L. A. Carlsmith and D. A. Semenov, *ibid.*, **78**, 611 (1956).