[CONTRIBUTION FROM THE WALKER LABORATORY THE RENSSELAER POLYTECHNIC INSTITUTE]

The Behavior of Cyclopropyl Ketones in the Schmidt Reaction[1]

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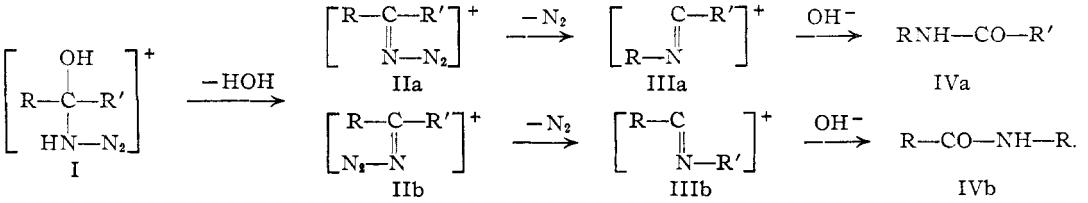
The reactions of five cyclopropyl ketones and two 1-phenylcyclopropyl ketones with equivalent amounts of hydrazoic acid have given mixtures of amides. The products resulting from migration of the cyclopropyl group were N-cyclopropylamides; no isomerization to ethylenic or heterocyclic derivatives could be detected. The relative migrations of the groups in the unsymmetrical ketones differ from those predicted from steric considerations; predominant migration of the cyclopropyl group was observed only in the reactions of the 1-phenylcyclopropyl ketones.

Previous papers from this Laboratory have described the rearrangement of cyclopropyl ketimines and the corresponding ketimmonium chlorides to give the isomeric pyrrolines or pyrrolinium chlorides.[2-5] Other work[6-8] has recorded the rearrangement of cyclopropyl compounds to ethylenic and to cyclobutyl derivatives. Such considerations have led to studies of the Beckmann rearrangement of aryl cyclopropyl ketoximes[9] and of the reactions of cyclopropyl ketones with hydrazoic acid.

The reaction of equivalent amounts of hydrazoic acid with ketones in the presence of strong acids, the Schmidt reaction, is known to give amides.[10]

$$R{-}CO{-}R + HN_3 \longrightarrow R{-}CO{-}NHR + N_2$$

The mechanism for this rearrangement suggested by Smith[11] involves the formation of an intermediate which, by loss of nitrogen and migration of an alkyl or aryl group to the electron deficient nitrogen, gives the amide.



The present work on the behavior of some cyclopropyl ketones in this reaction was undertaken in order to ascertain whether any of the possibilities for rearrangement within the cyclopropyl group itself, attendant on migration of that group, might be realized. It was considered possible that, in migration, the cyclopropyl group might remain unchanged, that it might isomerize to the corresponding ethylenic derivative, or that the ring might open so that one portion attacked the positive nitrogen. In the last case, the product might be a 2-alkyl or aryl pyrrole. Fundamental carbon-skeletal rearrangements have been noted in the reactions with hydrazoic acid of triethylacetic acid[12] and of 2-methyl-2-phenylhexanoic acid.[13] That migration of the cyclopropyl group without structural change within the group was to some extent possible had been indicated in investigations of the Beckmann rearrangement of ketoximes[9,14] and in the preparation of cyclopropylamine in low yield from cyclopropanecarboxylic acid.[15]

The reactions of five cyclopropyl ketones and of two 1-phenylcyclopropyl ketones with equivalent amounts of hydrazoic acid in chloroform solution, catalyzed by moderate amounts of sulfuric acid, have now been studied. The products were, in general, mixtures of amides which might be expected as products of the normal Schmidt reaction on unsymmetrical ketones. Table I summarizes the results of these reactions and of hydrolysis studies conducted to determine the relative amounts of the two isomeric amides present in the product of each reaction.

In the reactions of the last three ketones in the table, appreciable amounts of the amide resulting from migration of the cyclopropyl group were indicated to have been formed, although it was possible to isolate this isomer only in the last case. In these cases, no evidence was found for the presence of ethylenic unsaturation or of heterocyclic nitrogen compounds. The migration of the cyclopropyl group without change was thus confirmed.

Cyclopropyl styryl ketone (V) gave a complex reaction with hydrazoic acid; cyclopropanecarboxylic acid, ammonium chloride, phenylacetalde-

(1) Abstracted from a part of the Doctoral Thesis of Stanley C. Bunce, Rensselaer Polytechnic Institute. Presented before the Division of Organic Chemistry at the 119th Meeting of the American Chemical Society at Boston, Mass., April, 1951.

(2) J. B. Cloke, THIS JOURNAL, **51**, 1174 (1929).

(3) E. C. Knowles and J. B. Cloke, *ibid.*, **54**, 2028 (1932).

(4) J. B. Cloke and T. S. Leary, *ibid.*, **67**, 1249 (1945).

(5) J. B. Cloke, L. H. Baer, J. M. Robbins and G. E. Smith, *ibid.*, **67**, 2155 (1945).

(6) N. Kishner, *J. Russ. Phys. Chem. Soc.*, **37**, 316 (1905); *Chem. Centr.*, **76**, I, 1703 (1905).

(7) N. J. Demjanow, *Ber.*, **40**, 4393 (1907).

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

(9) H. A. Saroff, Ph.D. Thesis, Rensselaer Polytechnic Institute, 1940, presented in part (H. A. Saroff and J. B. Cloke) before the Division of Organic Chemistry at the 111th Meeting of the American Chemical Society at Atlantic City, N. J., April, 1947.

(10) H. Wolff, "The Schmidt Reaction," in R. Adams, "Organic Reactions," Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1946, pp. 307-336.

(11) P. A. S. Smith, THIS JOURNAL, **70**, 320 (1948). See also M. S. Newman and H. Gildenhorn, *ibid.*, **70**, 317 (1948).

(12) C. Schuerch, Jr., and E. H. Huntress, *ibid.*, **71**, 2233, 2238 (1949).

(13) C. L. Arcus, J. Kenyon and S. Levin, *J. Chem. Soc.*, 407 (1951).

(14) J. D. Roberts and V. C. Chambers, THIS JOURNAL, **73**, 3176 (1951), have recently reported the preparation of cyclopropylamine by Beckmann rearrangement from cyclopropyl methyl ketone in 68% yield.

(15) M. J. Schlatter, *ibid.*, **63**, 1733 (1941).

TABLE I

REACTIONS OF CYCLOPROPYL KETONES WITH HYDRAZOIC ACID

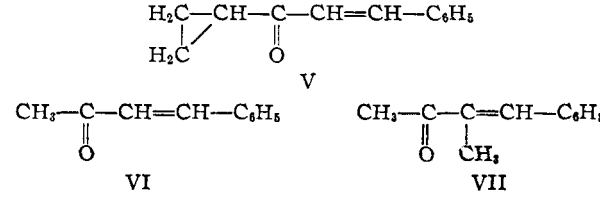
Ketone R—C(=O)—R′	Yield mixed amide, %	Amide isolated	Hydrolysis products isolated from mixed amide[a]	%	Migrations calculated R, %	Ratio R:R′
Cyclopropyl *p*-tolyl	61	Cyclopropanecarboxy-*p*-toluide	Cyclopropanecarboxylic acid	20	0	1:19
			p-Toluidine	20		
Cyclopropyl *o*-anisyl	85	Cyclopropanecarboxy-*o*-aniside	Cyclopropanecarboxylic acid	50	1	
			o-Anisidine	68		
			o-Methoxybenzoic acid	1		
Cyclopropyl phenyl	76	.....	Aniline	77	5	
			Benzoic acid	4		
Cyclopropyl styryl	35[b]	N-Styrylcyclopropane-carboxamide	Phenylacetaldehyde	38	9	1:10
			Benzyl cyanide	21		
			Phenylacetic acid[b]	32		
			Benzylamine	3		
			Cyclopropanecarboxylic acid[b]	18		
			Cinnamic acid[b]	9		
Cyclopropyl methyl	75	N-Methylcyclopropane-carboxamide	Cyclopropanecarboxylic acid	64.5	23 ± 2	1:3.3
			Methylamine	73.1		
			Acetic acid	20.9		
			Cyclopropylamine	21.1		
1-Phenylcyclopropyl phenyl	66	.....	Benzoic acid[b]	52	61	1:0.6
			1-Phenylcyclopropanecarboxylic acid[b]	28		
			Aniline[b]	39		
1-Phenylcyclopropyl methyl	81	N-1-Phenylcyclopropyl-acetamide	1-Phenylcyclopropylamine	57	77	1:0.3
			1-Phenylcyclopropanecarboxylic acid	17		

[a] Percentages are based on the weight of amide hydrolyzed. [b] Amounts estimated by indirect methods, such as titration of mixtures, described in the Experimental section.

hyde and benzyl cyanide were identified in the reaction products. The presence of the first three compounds was explained by a possible hydrolysis, during the Schmidt reaction, of the N-styrylcyclopropanecarboxamide formed by styryl group migration, to phenylacetaldehyde and cyclopropanecarboxylic acid; phenylacetaldehyde might give benzyl cyanide by reaction with hydrazoic acid. Subsequent quantitative hydrolytic investigations resulted in the isolation of benzylamine (formed by hydrolysis of the second possible product of the reaction of phenylacetaldehyde with hydrazoic acid, N-benzylformamide) and of cyclopropylamine (formed both by reaction of cyclopropanecarboxylic acid with hydrazoic acid and by hydrolysis of the second of the two possible primary reaction products, N-cyclopropylcinnamamide). Indirect evidence was obtained for the presence of cinnamic acid and of phenylacetic acid. The analogous reaction of the unsaturated ketone VII, subsequently reported, confirmed this interpretation of the results.[16]

The question of the relative amounts formed of the isomeric amides has been of interest in view of the work of Smith and Horwitz on the effect of structure on the course of the Schmidt reaction with unsymmetrical ketones. With few exceptions, unsymmetrical ketones give as the predominant product the amide formed by migration of the bulkier alkyl or aryl group.[17-19] These facts have supported the interpretation that the geometry of the intermediate II is relatively fixed, as is the case with an unsymmetrical ketoxime, and that the relative amounts of IIa and IIb formed are determined largely by the steric nature of the groups R and R′.[16]

The approximate migration ratios R:R′, listed in Table I form a series in which the groups opposed to the cyclopropyl groups which are progressively less bulky migrate to lesser extents. Although the precision of the determination of the migration ratio is not great in some of these cases, the series is consistent in indicating lesser migrations of the cyclopropyl and 1-phenylcyclopropyl groups than might be expected from steric considerations. The ratios found for the cyclopropyl aryl ketones are roughly equivalent to those reported for the methyl aryl ketones,[19] and indicate lesser migration of the cyclopropyl group than was found for the alkyl groups in ethyl phenyl ketone and isopropyl phenyl ketone.[16] The predominant migration of the styryl group found in the reaction of V may be compared with the results reported for the two unsaturated ketones VI and VII, in which the first gave exclusive migration of the methyl group and the second gave exclusive migration of the unsaturated group.[16] The 77 ± 2% methyl group mi-



V

VI VII

(16) P. A. S. Smith and J. P. Horwitz, THIS JOURNAL, **72**, 3718 (1950).

(17) (a) P. A. S. Smith and B. Ashby, *ibid.*, **72**, 2503 (1950); (b) H. Schechter and J. C. Kirk, *ibid.*, **73**, 3087 (1951); (c) F. R. Benson, L. W. Hartzel and W. L. Savell, *ibid.*, **71**, 1111 (1949).

(18) J. R. Dice and P. A. S. Smith, *J. Org. Chem.*, **14**, 179 (1949).

(19) H. H. Szmant and J. J. McIntosh, THIS JOURNAL, **72**, 4835 (1950).

gration found for cyclopropyl methyl ketone may be contrasted with the predominant migrations of the cyclopropyl group, 68%[14] and 88%[20] which have been observed in the Beckmann rearrangement of cyclopropyl methyl ketoxime. The isolation of appreciable amounts of the product resulting from migration of the methyl group, in the case of 1-phenylcyclopropyl methyl ketone, was somewhat surprising.

There have been noted several other cases in the Schmidt reaction[17a,18,21] which cannot readily be explained by the steric requirements. In the Beckmann rearrangement, which serves as a useful analog for the Schmidt reaction, there are some exceptions to the rule that the oxime configuration which might be expected to be sterically preferable is the most stable. Electronic effects must operate, at least in minor fashion, to determine the relative migrations of the groups under the conditions employed in these reactions, and the cyclopropyl group might be expected to contribute significantly in that respect.[22]

In some other similar rearrangement reactions, such as the reaction of hydrazoic acid with a tertiary alcohol,[23] steric effects may be absent or may be separated from electronic effects. Investigation of the relative migration of the cyclopropyl group in such reactions is in progress.

Experimental[24]

For reaction with hydrazoic acid, the ketones were dissolved in chloroform in a three-necked flask fitted with a toluene-sealed stirrer, dropping funnel, thermometer and reflux condenser. A portion of the sulfuric acid was added and an equivalent amount of a solution of hydrazoic acid in chloroform[25] was introduced at such a rate as to maintain a temperature of 25–35°. The volume of nitrogen was measured, and as the rate of nitrogen evolution lessened, heating to 35° and addition of more sulfuric acid ensured completion of the reaction. The mixtures were then cooled to 5°, diluted with ice, and the chloroform and water layers were separated. The water layer, made basic, was extracted with ether to recover small amounts of amines sometimes formed from hydrolysis of the amides during the reactions. Alkaline extraction of the chloroform layer was similarly employed to recover acids. The chloroform was then evaporated from the washed neutral material.

Cyclopropyl *p*-Tolyl Ketone.—A portion of 6.5 g. (0.04 mole) of cyclopropyl *p*-tolyl ketone, prepared by hydrolysis of cyclopropyl *p*-tolyl ketimine[5] was stirred in chloroform solution with 0.044 mole of hydrazoic acid and 6 g. of sulfuric acid for 7 hours at 25–35°. Recrystallization of the crude reaction product from alcohol gave 4.3 g. of amide, m.p. 146–152°. A 2.2-g. portion of the amide refluxed 8 hours with 10% sulfuric acid gave 0.2 g. of cyclopropanecarboxylic acid, b.p. 170–175° (lit., 182°), and 0.2 g. of *p*-toluidinium chloride, m.p. 232–235°. An attempted alkaline hydrolysis was unsatisfactory. Cyclopropanecarboxy-*p*-toluide, m.p. 164.3–165.8° (cor.), recrystallized twice from benzene, was soluble in alcohol, and slightly soluble in benzene, chloroform, and ether.

Anal. Calcd. for $C_{11}H_{13}ON$: N, 8.05. Found: N, 8.01.

Cyclopropyl *o*-Anisyl Ketone.—An ether solution containing 23.5 g. (0.35 mole) of cyclopropanecarbonitrile[26] was added slowly to the Grignard reagent prepared by refluxing 96 g. (0.515 mole) of *o*-bromoanisole, b.p. 119–121° at 25 mm., and 12 g. (0.5 mole) of magnesium in dry ether. After refluxing 6 hours the suspension was added to 400 ml. of liquid ammonia. Ammonia was removed by bubbling nitrogen through the filtrate, hydrogen chloride was introduced, and the precipitated ketimmonium chloride was washed by suspending it in chloroform and collecting on a filter. Cyclopropyl *o*-anisyl ketimmonium chloride, 16 g. (22%), melted at 194.5–195°.

Anal. Calcd. for $C_{11}H_{14}ONCl$: Cl, 16.79. Found: Cl, 16.98.

The ketimmonium salt dissolved in water to give a clear solution which slowly became cloudy due to hydrolysis to the ketone. Addition of alkali to a freshly prepared solution precipitated solid cyclopropyl *o*-anisyl ketimine which hydrolyzed slowly in water.

Cyclopropyl *o*-anisyl ketimmonium chloride gave 2-*o*-anisylpyrrolinium chloride by the thermal rearrangement typical of cyclopropyl ketimmonium chlorides.[5] A 2.0-g. sample was heated for 1 hour at 200° in an atmosphere of nitrogen. The crude solid pyrroline, 1.1 g., was precipitated by the addition of dilute sodium hydroxide to the solution obtained by extracting the cooled melt with boiling water, boiling with charcoal, and filtering. The light yellow 2-*o*-anisylpyrroline, m.p. 65.6–66.5° (cor.), was crystallized twice from heptane; the picrate, m.p. 178.1–179.3° dec. (cor.), was crystallized from acetic acid.

Anal. Calcd. for $C_{17}H_{16}O_8N_4$: N, 13.85. Found: N, 13.49, 14.26.

Cyclopropyl *o*-anisyl ketone was recovered by treating with dilute hydrochloric acid all of the residual solutions and solids from the foregoing preparation, then extracting with ether. The washed and dried ether solution gave 29 g., b.p. 123–125° at 7 mm. (47.5%). An analytical sample had b.p. 125° at 7 mm., $n^{20}D$ 1.5552, d^{20}_4 1.106, which correspond to a molecular refraction, MR_D, 51.17. The value calculated by adding the observed molar refractions of anisole and cyclopropyl phenyl ketone and subtracting that of benzene is 50.81. The exaltation of 0.36 is comparable with that found for *o*-methoxybenzaldehyde (P_i = 0.2).[27] It was colorless, darkened slowly on standing, and was soluble in 50% alcohol, heptane and carbon tetrachloride.[28] No crystalline semicarbazone was obtained. The 2,4-dinitrophenylhydrazone, recrystallized twice from alcohol, orange plates, melted at 128.4–129.2° (cor.).

Anal. Calcd. for $C_{17}H_{16}O_5N_4$: N, 15.73. Found: N, 15.78.

Cyclopropyl *o*-anisyl ketone, 9.0 g. (0.05 mole), treated with 0.05 mole of hydrazoic acid and 11 g. of sulfuric acid for 5 hours at 30–38°, gave 8.1 g. of crude product which crystallized in 2 weeks. Slow recrystallization from alcohol gave 5.2 g., m.p. 75–85°, of crude cyclopropanecarboxy-*o*-aniside. A 1.5-g. portion, hydrolyzed by refluxing with 20 ml. of 20% sulfuric acid for 20 hours, gave 0.35 g. of cyclopropanecarboxylic acid, b.p. 170–180°, and 0.55 g. of crude *o*-anisidine, b.p. 210–220° (lit. 225°). The pure *o*-aniside, m.p. 86.7–87.5° (cor.), crystallized from hexane, was soluble in alcohol, benzene, ether and carbon tetrachloride.

Anal. Calcd. for $C_{11}H_{15}O_2N$: N, 7.33. Found: N, 7.29.

The residues from the first alcohol recrystallization, similarly hydrolyzed, gave 0.2 g. of *o*-anisidine and an acid fraction from which 0.05 g. of crude *o*-methoxybenzoic acid, m.p. 89–94°, was obtained. After recrystallization from water, the sample, of m.p. 95–97°, did not depress the melting point of *o*-methoxybenzoic acid, m.p. 100–101.4°, prepared[29] from salicylic acid.

An additional 0.3 g. of *o*-anisidine was separated from the aqueous acid solution from the reaction.

(20) A. D. McLaren and R. E. Schachat, *J. Org. Chem.*, **14**, 254, (1949).

(21) G. M. Badger, R. T. Howard and A. Simons, *J. Chem. Soc.*, 2849 (1952).

(22) See, for example, P. A. S. Smith, THIS JOURNAL, **76**, 431 (1954).

(23) S. N. Ege and K. W. Sherk, *ibid.*, **75**, 354 (1953).

(24) Boiling points are uncorrected; melting points indicated as corrected were obtained by the capillary method with a thermometer *calibrated with a series of pure compounds of known melting point* [S. Bunce, *Anal. Chem.*, **25**, 825 (1953)].

(25) H. Wolff, ref. 10, p. 327. Two times the specified amount of sulfuric acid gave solutions of approximately 0.06 g. of hydrazoic acid per ml.

(26) J. B. Cloke, R. J. Anderson, J. Lachmann and G. E. Smith, THIS JOURNAL, **53**, 2791 (1931).

(27) C. Curran and F. Palermiti, *ibid.*, **73**, 3733 (1951).

(28) Infrared absorption studies of the liquid cyclopropyl ketones have been reported previously: S. E. Wiberley and S. C. Bunce, *Anal. Chem.*, **24**, 623 (1952).

(29) C. Graebe, *Ann.*, **340**, 210 (1905).

Cyclopropyl Phenyl Ketone.—A mixture of 1.40 g. (0.01 mole) of cyclopropyl phenyl ketone,[2] b.p. 115–118° at 12 mm., 0.01 mole of hydrazoic acid and 3 g. of sulfuric acid was stirred in chloroform for 2 hours at 28–36°. The 1.49 g. of crude amide obtained was refluxed for 30 hours with 10 ml. of 20% sulfuric acid. After separation of the acidic and basic hydrolysis products, 0.35 g. of neutral material remained.

Bromine vapor was aspirated through an aqueous sulfuric acid solution of the basic hydrolysis products and 1.80 g. of tribromoaniline, m.p. 115–117° (lit. 119°), precipitated.

The alkaline solution of the acidic hydrolysis products was concentrated to 5 ml., acidified to *p*H 10, and excess copper sulfate solution was added. The copper benzoate, separated by centrifuging, was treated with 2 ml. of 2.2 *N* hydrochloric acid, and the precipitated benzoic acid was washed with two 1-ml. portions of 2.2 *N* hydrochloric acid and dried. The weight (41 mg.) was equivalent to 0.34 millimole; its titer of 0.1 *N* alkali was 0.23 meq.

Cyclopropyl Styryl Ketone.—Cyclopropyl styryl ketone[30] was prepared by the condensation of equivalent amounts of cyclopropyl methyl ketone and benzaldehyde in the presence of 10% sodium hydroxide in 50% alcohol at 40° for 1 hour. The crude solid reaction product, recrystallized twice from dilute alcohol, gave a 70% yield of cyclopropyl styryl ketone of m.p. 52.8–53.2° (cor.).

In several reactions of cyclopropyl styryl ketone with hydrazoic acid, the optimum concentration of sulfuric acid for initiating reaction without polymerizing the ketone was found to be 80%. In a typical reaction, 0.2 mole of cyclopropyl styryl ketone was stirred with 0.2 mole of hydrazoic acid, 20 ml. of 80% sulfuric acid was added dropwise during 4 hours at 28–34°, then 20 ml. of concentrated sulfuric acid was added similarly during 4 hours and the mixture was stirred for 16 hours at 25–50°. It was not possible to crystallize the crude reaction product.

Cyclopropanecarboxylic acid, ammonium chloride and unreacted ketone were identified in the crude product from one reaction; in addition, benzyl cyanide and phenylacetaldehyde were isolated from two subsequent reactions.

A small amount of N-styrylcyclopropanecarboxamide was subsequently isolated from the crude product by distilling all compounds volatile at 5 μ at 70°, dissolving the residue in benzene, and passing it through a column packed with Norit A. Several adjacent cut sections of the adsorbent from the column gave crystalline residues when dried and extracted with alcohol; these were combined and crystallized from hexane and from dilute alcohol. N-Styrylcyclopropanecarboxamide, m.p. 117–117.5° (cor.), was hydrolyzed by boiling with 20% sulfuric acid to phenylacetaldehyde.

Anal. Calcd. for $C_{12}H_{13}ON$: N, 7.49. Found: N, 7.35.

The composition of the crude product from one reaction (0.1 mole) was determined by steam distillation and hydrolysis. After distillation of the chloroform, steam distillation in the presence of 5%, then 10% sulfuric acid gave first 1 liter of distillate A having a positive Schiff test, then 1 liter of distillate B containing ketone.

Each distillate was made basic and continuously extracted with ether. From the ether extract of A there was obtained 4 g. of phenylacetaldehyde 2,4-dinitrophenylhydrazone, m.p. 205–210°, and 0.8 g. of benzyl cyanide, b.p. 105–110° at 12 mm., which was hydrolyzed by 75% sulfuric acid at 150° for 2 hours to phenylacetic acid, m.p. 75–76.5°. Ether extraction of B gave 1.5 g. (9%) of unreacted cyclopropyl styryl ketone.

The aqueous solution of the amine salts was separated from the neutral residue from the steam distillation with sulfuric acid, and the latter was boiled with 10% sodium hydroxide. The volatile amines were collected in dilute hydrochloric acid; the non-volatile amines were separated from the ether solution of the residue by extraction with dilute hydrochloric acid. The neutral material remaining, 5.8 g., was a tar not hydrolyzed by boiling 50% sulfuric acid.

The solution of the sodium salts of the acids obtained by the hydrolysis with 10% sodium hydroxide was acidified and separated into a solid water-insoluble fraction of mixed acids and a water-soluble acid fraction. The latter, after combining with the aqueous solutions remaining from the extractions of the steam distillates A and B, was made strongly acid with sulfuric acid and continuously extracted with ether. The liquid fraction of the acids, 1.45 g., which was obtained by evaporation of the ether was assumed to be a mixture of cyclopropanecarboxylic acid and phenylacetic acid. It was estimated from the neutral equivalent, 113, to contain 35% cyclopropanecarboxylic acid and 65% phenylacetic acid. The solid acid fraction, 1.0 g., was estimated by permanganate titration to contain 42% cinnamic acid and 58% phenylacetic acid.

The amine salt solutions separated from the successive hydrolyses were combined, basified, and extracted with ether. The hydrochlorides precipitated by dry hydrogen chloride were separated by their differential solubility in chloroform into a 0.2-g. fraction of m.p. 75–82° and 0.2 g. of benzylammonium chloride, m.p. 202–222°. The latter sample, recrystallized, m.p. 241–246°, did not depress the melting point of authentic benzylammonium chloride. Most of the cyclopropylamine (hydrochloride m.p. 85–86°[15]) escaped isolation; since it was an eventual product to be expected from the migration of either group in the reaction of cyclopropyl styryl ketone with hydrazoic acid its isolation was not essential for calculation of the relative migrations.

There were obtained, in all, 32% of products resulting from styryl group migration, 3% (estimated) from cyclopropyl group migration, 9% unreacted material and 31% tar.

Cyclopropyl Methyl Ketone.—In a typical reaction, 33.6 g. (0.4 mole) of cyclopropyl methyl ketone, b.p. 110.5–112°, was stirred with 0.4 mole of hydrazoic acid and 49 g. of sulfuric acid for 12 hours at 25–38° until nitrogen evolution ceased. The dried chloroform solution afforded 23 g. of amide, b.p. 127.5–130.5° at 24 mm.; continuous ether extraction of the water layer and washes gave 7 g. of similar boiling point. No separation of the amides could be observed in these distillations.

A 15.5-g. portion of the mixed amide distillate was boiled with 150 ml. of 10% sodium hydroxide; the theoretical amount of amine had been distilled into a trap containing standard acid in 9 hr. The crude acids obtained by acidification and continuous ether extraction gave fractions, of total weight 5.9 g., boiling from 60 to 170°, and 6.7 g. of cyclopropanecarboxylic acid, b.p. 170–178°. The presence of acetic acid in a fraction b.p. 108–120° was demonstrated by the preparation from it of 2-methylbenzimidazole,[31] m.p. 173–174.2° (cor.) (177–177.5°[31b]), which did not depress the melting point of an authentic sample. 2-Cyclopropylbenzimidazole, prepared from the fraction b.p. 170–178°, melted 229–230° (cor.), after crystallization from benzene, 10% alcohol and benzene–hexane. Its yellow picrate, recrystallized three times from dilute alcohol, melted 212.4–213.6° (cor.).

Anal. Calcd. for $C_{16}H_{12}O_7N_6$: N, 18.15. Found: N, 17.57, 17.94.

Determination of the relative amounts of acetic acid and cyclopropanecarboxylic acid in the samples obtained by hydrolysis of larger amounts of the mixed amides proved difficult. Selective precipitation of lead or mercuric salts was unsuccessful, and the two acids could not be differentiated by their Duclaux values. Titration to determine the average neutral equivalent indicated a composition of 100% cyclopropanecarboxylic acid; this procedure might be expected to give a low value for the amount of acetic acid. The acid sample from hydrolysis of 0.04 mole of the mixed amide was then distilled azeotropically with benzene, according to the analytical method of Schicktanz.[32] An aqueous solution, neutralized with sodium hydroxide (39.3 meq.), was dried azeotropically with benzene, a 15% excess of anhydrous *p*-toluenesulfonic acid in 400 ml. of benzene was introduced, and the mixture was distilled through an efficient column at a reflux ratio of 30–1, until the distillate fractions contained insignificant amounts of acid; 8.4 milli-

(30) W. A. West, Ph.D. Thesis, Rensselaer Polytechnic Institute, 1950. An independent report of the preparation of cyclopropyl styryl ketone by this method [L. I. Smith and E. R. Rogier, THIS JOURNAL, **73**, 3831 (1951)] appeared after this work was completed.

(31) (a) The general procedure of E. L. Brown and N. Campbell, *J. Chem. Soc.*, 1699 (1937), was used. (b) The procedure of W. O. Pool, H. J. Harwood and A. W. Ralston, THIS JOURNAL, **59**, 178 (1937), gave less satisfactory yields of the cyclopropyl derivative.

(32) S. T. Schicktanz, W. I. Steele and A. C. Blaisdell, *Ind. Eng. Chem., Anal. Ed.*, **12**, 320 (1940).

equivalents of acetic acid was so distilled with 320 ml. of benzene. In preliminary tests, it was found that further distillation with xylene at atmospheric pressure caused decomposition. The cyclopropanecarboxylic acid remaining in the sample was therefore co-distilled with kerosene, b.p. 190–210° at 30 mm.; 25.8 meq. was obtained.

The amine hydrochloride sample from hydrolysis of the mixed amides was dried by azeotropic distillation with benzene, and the crystalline material obtained was titrated potentiometrically with 0.1 *N* alcoholic potassium hydroxide (inflection points, *p*H 10.5–11.0). The average equivalent weight indicated a composition of 58% methylammonium chloride, 42% cyclopropylammonium chloride. This procedure might be expected to give low values for the amount of methylamine. A 0.32-mole sample of the mixed amine hydrochlorides was then separated by extracting with successive 1.5-liter portions of boiling chloroform. Each of the six chloroform solutions so obtained was concentrated, cooled, and the cyclopropylammonium chloride which crystallized was separated. The successive samples, 6.0 g. combined weight, all melted in the range 78–93°; 15.3 grams of methylammonium chloride, m.p. 195–205°, remained.

In one reaction in which much of the product was lost during its isolation, the amide, obtained in 30% yield, appeared from hydrolysis studies to be nearly pure N-methylcyclopropanecarboxamide. Recrystallization of this hygroscopic product from hexane gave pure N-methylcyclopropanecarboxamide, m.p. 60.4–61.4° (cor.), which did not depress the m.p. of a sample prepared from cyclopropanecarboxylic acid by reaction with thionyl chloride in benzene followed by addition of dry methylamine. Melting points were determined on samples dried in large capillary tubes at 1 mm. over phosphorus pentoxide, and sealed in the tubes.

1-Phenylcyclopropyl Phenyl Ketone.—1-Phenylcyclopropyl phenyl ketone[3] was prepared in 54% yield by the reaction of phenylmagnesium bromide with 1-phenylcyclopropanecarbonitrile,[3] b.p. 123–127° at 14 mm. The reaction required 72 hours refluxing in ether, and decomposition of the addition compound required warming with dilute hydrochloric acid. The distillate from the dried ether solution, b.p. 125–137° at 1 mm., crystallized from dilute alcohol with m.p. 73.6–73.9° (cor.). The yellow 2,4-dinitrophenylhydrazone, recrystallized from benzene–alcohol and alcohol, melted 184.8–185.3° (cor.).

Anal. Calcd. for $C_{22}H_{18}O_4N_4$: N, 13.93. Found: N, 13.66.

Addition of sulfuric acid to chloroform solutions of 1-phenylcyclopropyl phenyl ketone caused rapid darkening, so all of the hydrazoic acid (0.019 mole) was mixed with 3.0 g. (0.014 mole) of the ketone in a typical reaction, and 6 g. of sulfuric acid was added during 5 hours at 27–32°. The crude amide, 3.25 g., was dark colored and difficult to hydrolyze. Refluxing successively with 20% sulfuric acid, 10% sodium hydroxide, and 50% sulfuric acid left a residue of 48% neutral material. Hydrolysis with 100% orthophosphoric acid at 150° for 7 hours left 45% of neutral material in one case, 34% in another.

The carboxylic acids were obtained from the phosphoric acid hydrolysis mixture by extraction of its benzene solution with 10% sodium hydroxide and acidification. The dried sample of mixed acids (0.5 g., 80% based on weight of the amide hydrolyzed) was indicated, by determination of the neutral equivalent (136), to contain 65% benzoic acid, 35% 1-phenylcyclopropanecarboxylic acid. Little crystalline amine hydrochloride was obtained by treating with hydrogen chloride the dried ether solution of the amines extracted from the phosphoric acid hydrolysis mixtures. The combined solutions of the salts of the amines from the sulfuric acid–sodium hydroxide hydrolyses were made alkaline and extracted with ether; hydrogen chloride precipitated 0.35 g. of amine hydrochloride from the dried solution. Titration curves of mixed samples of pure anilinium chloride and 1-phenylcyclopropylammonium chloride with alcoholic potassium hydroxide showed inflections at *p*H 5.4 and 10.5 from which the respective amounts of anilinium chloride and 1-phenylcyclopropylammonium chloride could be calculated. The curve obtained by titration of a portion of the 0.35-g. sample showed only one inflection point at *p*H 8–8.5, and the calculated equivalent weight (137) was near that of anilinium chloride.

1-Phenylcyclopropyl Methyl Ketone.—1-Phenylcyclopropyl methyl ketone was prepared in 67% yield in a manner similar to that used for the phenyl analog and boiled at 120–127° at 25 mm. A pure sample, b.p. 122° at 25 mm., $n^{20}D$ 1.5280, d^{20}_4 1.024, MR_D 48.14 (calcd. MR_D 47.21; the exaltation of 0.9 is comparable with that (0.7)[33] usually associated with the cyclopropyl group), was soluble in carbon tetrachloride and in hexane. The 2,4-dinitrophenylhydrazone recrystallized from alcohol melted 129.2–130.2° (cor.). The semicarbazone, recrystallized twice from 50% alcohol, melted 172.0–172.5° (cor.).

Anal. Calcd. for $C_{12}H_{15}ON_3$: N, 19.34. Found: N, 19.46.

Reaction of 12.0 g. (0.075 mole) of 1-phenylcyclopropyl methyl ketone, 0.075 mole of hydrazoic acid and 12 g. of sulfuric acid for 8 hours at 26–32° gave 10.5 g. of crude crystalline amide.

A 5.0-g. portion was refluxed for 20 hours with 20% sulfuric acid. After separation of the organic acids and amines, 0.9 g. of neutral material remained; this when boiled with 15 ml. of 10% sodium hydroxide gave 0.14 g. of unhydrolyzed material. The amine from the first hydrolysis was recovered by extraction from the basified sulfuric acid solution and precipitation of the hydrochloride. The 2.4 g., m.p. 178–183°, afforded, on crystallization from dry alcohol by dilution with dry ether, 1.45 g. of pure 1-phenylcyclopropylammonium chloride, m.p. 194.7–194.9° (cor.). which did not depress the melting point of an authentic sample.[34] The portion of the amine from the second hydrolysis which was not water-soluble was 0.07 g. of crude 1-phenylcyclopropylamine; the water-soluble and volatile portions from both amine separations contained methylamine and ammonia. Acidification of the alkaline hydrolysis solution precipitated 0.57 g. of 1-phenylcyclopropanecarboxylic acid. After recrystallization from water, the sample, m.p. 84.8–86.1° (cor.), did not depress the melting point of an authentic sample. The water solution of the acids from the sulfuric acid hydrolysis was concentrated with loss of acetic acid, and an additional 0.2 g. of 1-phenylcyclopropanecarboxylic acid precipitated on cooling.

An additional 0.6 g. of impure 1-phenylcyclopropylamine was recovered from the acid washes of the crude reaction product.

A 5.5-g. portion of the crude amide was recrystallized from benzene and from hexane. N-1-Phenylcyclopropylacetamide, 2 g., m.p. 96.6–96.8° (cor.), soluble in carbon tetrachloride and insoluble in water, was obtained.

Anal. Calcd. for $C_{11}H_{13}ON$: N, 8.00. Found: N, 7.91.

TROY, NEW YORK

(33) G. J. Östling, *J. Chem. Soc.*, **101**, 457 (1912).

(34) G. W. Kidder, Ph.D. Thesis, Rensselaer Polytechnic Institute, 1935, prepared 1-phenylcyclopropylamine by the Hofmann reaction of 1-phenylcyclopropanecarboxamide, and reported: b.p. 71–75° at 4–6 mm., $n^{20}D$ 1.5531, d^{20}_4 1.02; hydrochloride, m.p. 193–194°; picrate, m.p. 194–195°; chloroplatinate, m.p. 177–182°.