Phenylcyclobutane Amino Alcohols and Amino Ketones

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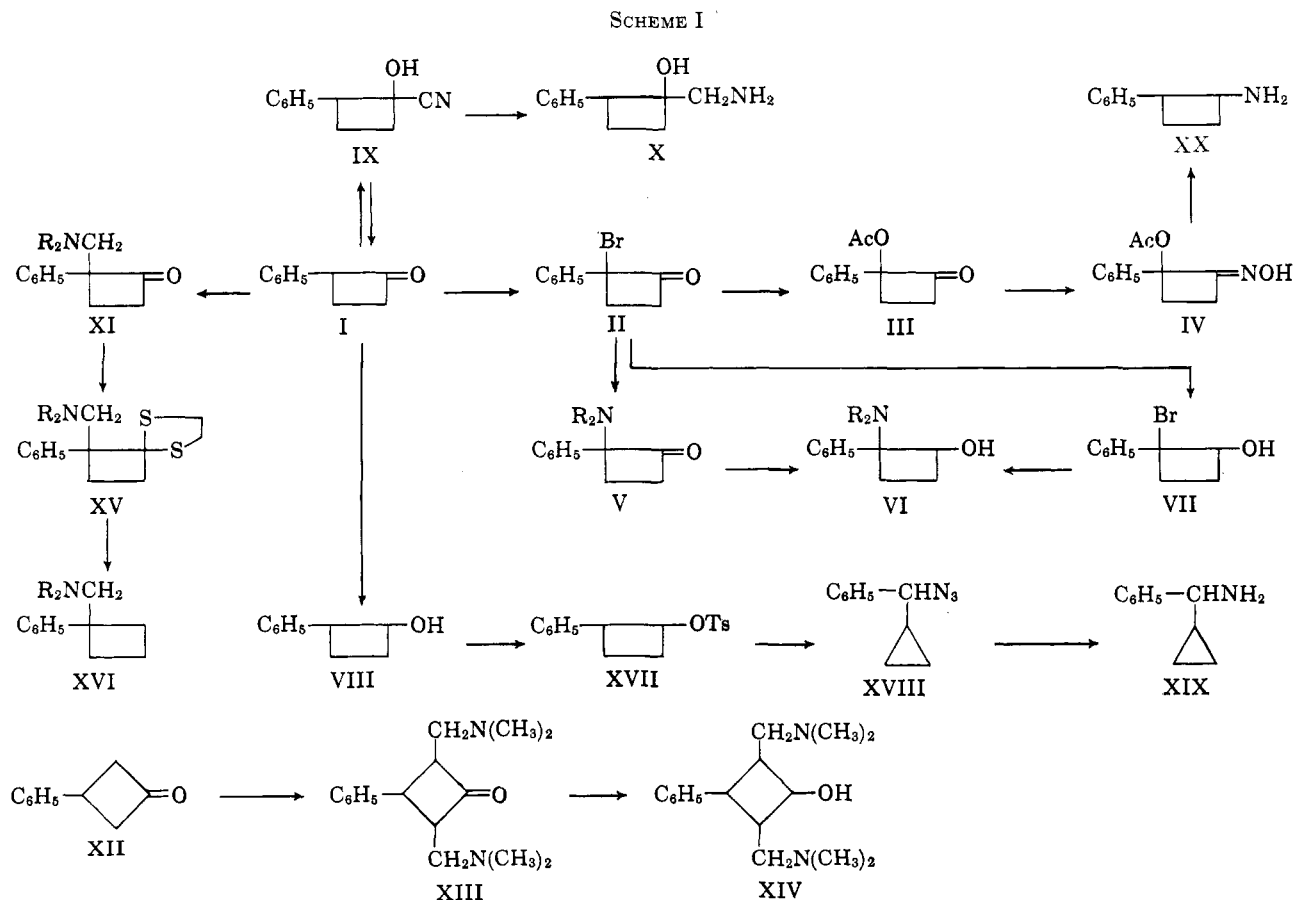
2-Bromo-2-phenylcyclobutanone reacted with amines to give amino ketones and with silver acetate to furnish an acetoxy ketone. The amino ketones were reduced to amino alcohols; the oxime of the acetoxy ketone suffered hydrogenolysis and gave 2-phenylcyclobutylamine. Mannich monoamino ketones could be prepared normally from 2-phenylcyclobutanone, but only diamino ketones were obtained from 3-phenylcyclobutanone by an analogous procedure. 2-Phenylcyclobutanone added HCN, and the cyanohydrin was reduced to an amino alcohol. 2-Phenylcyclobutanol tosylate, on treatment with sodium azide, suffered ring contraction. The resulting azide was reduced to α-cyclopropylbenzylamine. · The structures of these and additional compounds in these series were supported by spectroscopic evidence.

When 2-phenylcyclobutanone (I)[1] was brominated in carbon tetrachloride solution in a manner patterned upon the bromination of 2-phenylcyclohexanone,[2] monobromination could be controlled well by adjustment of the rate of addition of bromine and of the temperature. Other brominating agents, such as N-bromosuccinimide, pyridine hydrobromide perbromide, and dioxane–bromine complex, produced erratic results and lower yields.

obtained, as shown from its spectrum (1790 and 1740 cm.$^{-1}$) and the formation of carbonyl derivatives. Reduction of its oxime (IV) furnished a mixture from which 2-phenylcyclobutylamine (XX) could be fractionated as the principal constituent; obviously, hydrogenolysis had removed the ester group (see Scheme I).

In nonpolar solvents also, 2-bromo-2-phenylcyclobutanone exchanged the bromine atom with amino groups of secondary amines in good yields. From a

Scheme I

2-Bromo-2-phenylcyclobutanone (II) reacted rapidly with silver nitrate and sodium iodide. However, treatment with sodium acetate in absolute ethanol led to an ester which no longer exhibited cyclobutanone absorption (1790 cm.$^{-1}$) in the infrared. When silver acetate and benzene were substituted for these conditions, the expected 2-acetoxy-2-phenylcyclobutanone (III) was

comparison of the ratios of metathesis to dehydrohalogenation of alicyclic halides in the presence of a variety of organic bases,[3] a greater trend to undergo elimination reactions could have been expected for our tertiary halo ketone. However, the strained four-membered ring counteracted this tendency. Tertiary amines (pyridine and collidine) converted the bromo ketone to unstable quaternary salts which decomposed on

(1) C. Beard and A. Burger, *J. Org. Chem.*, **26**, 2335 (1961).
(2) W. E. Bachmann and L. B. Wick, *J. Am. Chem. Soc.*, **72**, 3388 (1950).
(3) J. Semb and S. M. McElvain, *ibid.*, **53**, 690 (1931).

Table I
Derivatives of Phenylcyclobutane

No.	R	R	Yield, %	M.p., °C. (cor.) or b.p., °C. (mm.)	Solvent of crystallization	Composition	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
1	$N(CH_3)_2 \cdot HBr$	=O		147–149	EtOH–Me$_2$CO–Et$_2$O	$C_{12}H_{16}BrNO$	53.32	53.27	6.00	6.19
2	$N(CH_3)_2$	OH	74	117.5–119	Et$_2$O	$C_{12}H_{17}NO^a$	75.33	75.10	8.95	9.11
3	$N(C_2H_5)_2$	=O	82							
4	$N(C_2H_5)_2 \cdot HBr$	=O		143–144	EtOH–Et$_2$O	$C_{14}H_{20}BrNO$	56.32	56.33	6.76	7.10
5	$N(C_2H_5)_2$	OH	69	140–141 (1.5 mm.)						
6	$N(C_2H_5)_2 \cdot HBr$	OH		159–161 dec.	EtOH–Et$_2$O	$C_{14}H_{22}BrNO$	56.01	55.74	7.39	7.78
7	$NC_5H_{10} \cdot HBr$	=O	75	177–179 dec.	MeOH–Me$_2$CO–Et$_2$O	$C_{15}H_{20}BrNO$	58.07	57.76	4.49	4.77
8	$NC_5H_{10} \cdot HBr$	OH		206–207 dec.	EtOH–Et$_2$O	$C_{15}H_{22}BrNO$	57.72	57.74	7.07	7.28
9	$CH_2N(CH_3)_2$	=O	78	110–113 (0.8 mm.)						
10	$CH_2N(CH_3)_2 \cdot HBr$	=O		169–170	MeOH–EtOAc–Et$_2$O	$C_{13}H_{18}BrNO$	54.93	54.59	6.83	6.13
11	$CH_2N(CH_3)_2$	OH		86–87.5	Et$_2$O	$C_{13}H_{19}NO$	76.05	76.31	9.33	9.43
12	$CH_2N(CH_3)_2 \cdot HBr$	(dithiolane)		206–208 dec.	EtOH–Et$_2$O	$C_{15}H_{22}BrNS_2{}^b$	49.98	49.96	6.15	6.32
13	$CH_2N(CH_3)_2 \cdot HBr$	H	31	182–183.5	EtOH–Et$_2$O	$C_{13}H_{20}BrN^c$	57.78	57.50	7.46	7.90
14	AcO	=O	30	133–135 (0.8 mm.)		d				
15	AcO	=NNH–CONH$_2$		196–197.5	EtOH	$C_{13}H_{15}N_3O_3$	59.75	60.24	5.78	6.21
16	$CH_2N(CH_3)_2$	NH$_2$		110–113 (1 mm.)						
17	$CH_2N(CH_3)_2 \cdot HBr$	NH$_2$		202–203	EtOH–EtOAc	$C_{13}H_{21}BrN_2{}^e$	54.84	54.43	7.40	7.04

^{a} Infrared band (weak) at 3450 cm.$^{-1}$ did not change upon dilution. ^{b} Fluffy colorless crystals. ^{c} Glistening hygroscopic plates. ^{d} Infrared: 1790 cm.$^{-1}$ (C=O in four-membered ring), 1740 cm.$^{-1}$ (ester). ^{e} Shiny platelets.

heating. Only diethylaniline was found to eliminate hydrogen bromide quantitatively from the bromo ketone at 100°, in 12 hr. Even though the reaction was conducted under a nitrogen atmosphere, the crude α,β-unsaturated ketone (infrared bands, 1725 and 1790 cm.$^{-1}$), polymerized in a matter of seconds and could not be manipulated. Apparently, the formation of a four-membered ring with an endocyclic double bond in addition to an exocyclic carbonyl function is highly unfavored thermodynamically; this has been observed also for other cyclobutenones with reactive hydrogen atoms.[4]

The 2-dialkylamino-2-phenylcyclobutanones (V) were reduced smoothly by lithium aluminum hydride. In a typical example, only one stereoisomer of 2-dimethylamino-2-phenylcyclobutanol (VI, R = CH$_3$; Table I, 2) could be elaborated from the reduction of the 2-dimethylamino ketone. The product exhibited a smeared and wide band at 3400 cm.$^{-1}$, much weaker than would be expected for a nonbonded hydroxyl. The intensity and shape of the band did not change upon dilution, implicating intramolecular bonding; this is, however, in contrast to the postulate that intramolecular hydrogen bonding generally requires the formation of a six-membered ring.[5]

With aluminum isopropoxide, 2-bromo-2-phenylcyclobutanone was reduced to a mixture of cis- and trans-bromohydrins (VII). Prolonged treatment of this mixture with dimethylamine yielded a small amount of 2α-dimethylamino-2β-phenyl-1α-cyclobutanol (Table I, 2), identical in every respect with the amino alcohol from the reduction of 2-dimethylamino-2-phenylcyclobutanone.

The strain of the 2-phenylcyclobutanone system manifested itself also in its tendency to undergo addition reactions. The ketone was reduced readily with lithium aluminum hydride to 2-phenylcyclobutanol

(VIII).[6] The cyanohydrin derivative (1-cyano-2-phenylcyclobutanol, IX) was also prepared in nearly quantitative yield via the bisulfite adduct. The crude cyanohydrin, although fairly stable in the presence of a trace of acid, lost hydrogen cyanide quickly under the catalytic influence of a base; indeed, it reverted to 2-phenylcyclobutanone completely on standing in a glass container for 3 days.[7] However, it could be reduced readily with an excess of lithium aluminum hydride. Attempts to synthesize the resulting 1-aminomethyl-2-phenylcyclobutanol (X) by an alternate pathway, i.e., condensation of 2-phenylcyclobutanone with nitromethane followed by reduction of the nitro group, proved inoperable. The doubly activated α-hydrogen of 2-phenylcyclobutanone apparently competed with those of nitromethane for the catalyzing base, and, as a result, polymers of the ketone were formed instead of a nitromethyl alcohol.

A similar activation of the α-hydrogen atom appeared to play a role in the outcome of a Mannich reaction with dimethylammonium chloride, formaldehyde, and 2-phenylcyclobutanone. The dimethylamino ketone (XI, R = CH$_3$; Table I, 9) obtained in good yield, lacked a triplet at δ 4.3 in its n.m.r. spectrum. This triplet, found in the spectrum of 2-phenylcyclobutanone, corresponds in position, intensity, and shape to the expected absorption of the C-2 proton. Furthermore, 3-phenylcyclobutanone (XII), which lacks the double activation of the benzyl hydrogen, reacted with dimethylammonium chloride and formaldehyde three times more slowly than the 2-phenyl isomer. An unambiguous chemical assignment of the structure of bis(dimethylaminomethyl)-3-phenylcyclobutanone (XIII) was not undertaken. The compound was reduced uneventfully to the corresponding amino alcohol XIV.

The dithioethylene ketal of 2-dimethylaminomethyl-2-phenylcyclobutanone (XV, Table I, 12) could be

(4) E. Vogel and K. Hasse, Ann. Chem., 615, 22 (1958).
(5) G. W. Wheland, "Advanced Organic Chemistry," 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1954, p. 52.
(6) Cf. ref. 1 describing another route to this alcohol.
(7) C. D. Gutsche and T. D. Smith, J. Am. Chem. Soc., 82, 4067 (1960).

desulfurized readily to 1-dimethylaminomethyl-1-phenylcyclobutane (XVI, Table I, 13). The ketone itself could not be reduced by a modified Wolff–Kishner reaction.

2-Dimethylaminomethyl-2-phenylcyclobutanone oxime was reduced to 2-dimethylaminomethyl-2-phenyl-cyclobutylamine (Table I, 16) without complications.

In an attempt to gain easier access to 2-phenylcyclo-butylamine for further studies, we tried to apply the successful sequence of reactions leading from cis-3-phenylcyclobutanol to trans-3-phenylcyclobutylamine[8] to the 2-phenylcyclobutanol series. The formation of the tosylate XVII of this alcohol, and conversion to an azide were confirmed by infrared spectroscopy. However, the amine from the reduction of the azide was neither cis- nor trans-2-phenylcyclobutylamine, but an isomer of these compounds. The infrared spectrum of the hydrochloride revealed little additional information other than the presence of an aromatic ring and a primary amino group. The clue to its structure was contained in its n.m.r. spectrum (see Experimental). This indicated that the compound was α-cyclopropylbenzylamine (XIX) hydrochloride, previously prepared by another route.[9]

A direct comparison with an authentic sample[9] confirmed the identity of the two salts. Ring contraction must have occurred during the displacement of the tosylate by the azide ion; this was the only step which involved the breaking of the C–O bond and was therefore capable of carbonium ion formation, an intermediate also present in Demjanov and similar rearrangements. The azide, therefore, was α-cyclo-propylbenzyl azide (XVIII).

Experimental[10]

1-Aminomethyl-2-phenylcyclobutanol (X).—A mixture of 1 g. (7 mmoles) of 2-phenylcyclobutanone, 1.5 g. (14 mmoles) of sodium bisulfite, and 5 ml. of water was stirred for 3 hr. The addition product separated as long, silky needles. The mixture was cooled to 10°, a solution of 3 g. (46 mmoles) of potassium cyanide in 1 ml. of water was added slowly, and stirring was continued for an additional 2 hr. at 5–10°. The separated oil was extracted with two 50-ml. portions of ether; the ether extract was washed with water, then 10% sodium bisulfite solution, and again water. After drying (Na₂SO₄) for 8 hr. the ether was evaporated. The infrared spectrum of the oil showed a strong band at 3550 cm.⁻¹ (OH) and a weak band at 2250 cm.⁻¹ (C≡N). The crude cyanohydrin lost HCN rapidly on standing in a glass container at 25° and was not purified further.

A solution of the cyanohydrin thus prepared in 20 ml. of ether was added to a slurry of 1.5 g. (8 mmoles) of lithium aluminum hydride in 40 ml. of dry ether at 0° over a period of 20 min. Refluxing set in spontaneously as a grayish precipitate separated. After being stirred at 25° for another 12 hr., the mixture was decomposed with 1.5 ml. of water, 1.5 ml. of 15% sodium hydroxide solution, and 4.5 ml. of water. The ether solution was filtered, the granular precipitate was extracted with two 50-ml. portions of hot benzene, and the combined washings were evaporated at 50° under reduced pressure. The residual solid (1.1 g., 90%) was recrystallized from benzene–petroleum ether (b.p. 30–60°), m.p. 120–122°.

Anal. Calcd. for C₁₁H₁₅NO: C, 74.55; H, 8.53. Found: C, 74.79; H, 8.83.

(8) C. Beard and A. Burger, J. Org. Chem., 27, 1647 (1962).

(9) W. J. Close, J. Am. Chem. Soc., 79, 1455 (1957).

(10) Melting points are corrected and were taken in a Hershberg-type bath. Infrared spectra were measured with a Perkin-Elmer Infracord and n.m.r. spectra with a Varian A-60 spectrometer, using tetramethylsilane as an external standard. Microanalyses were by Mrs. W. E. Coyne, Miss M. Siegfried, and H. H. Ong.

Infrared spectrum showed a strong band at 1600 cm.⁻¹ (NH₂) and a weak wide band at 3500 cm.⁻¹ (bonded OH). N.m.r. spectrum had bands at δ 2 to 3 (protons on four-membered ring). Other features could not be identified, especially OH protons, since in a bonded situation they are less readily recognizable.[11]

2-Bromo-2-phenylcyclobutanone (II).—A solution of 2.4 g. (15 mmoles) of bromine in 24 ml. of carbon tetrachloride was added slowly to a stirred solution of 2.1 g. (15 mmoles) of 2-phenylcyclobutanone in 10 ml. of carbon tetrachloride at −5° over a period of 50 min. A faint pink color persisted at the end of the addition. The solvent was removed under vacuum at 50° and the residual oil was distilled, b.p. 113–115° (1.2 mm.), yield 3.0 g. (80%). The compound was used for various reactions without further purification.

2-Bromo-2-phenylcyclobutanol (VII).—A solution of 2 g. (9 mmoles) of 2-bromo-2-phenylcyclobutanone and 8.2 g. (40 mmoles) of aluminum isopropoxide in 60 ml. of isopropyl alcohol was refluxed for 2 hr., the solvent was removed under reduced pressure, and the residue was cooled and acidified cautiously with dilute sulfuric acid. The oil which separated was taken up in ether and washed with 10-ml. portions of water. The ether solution was dried (Na₂SO₄) and fractionated. The main fraction (1.4 g., 70%) was almost colorless, b.p. 125–129° (1.8 mm.), strong infrared band at 3550 cm.⁻¹.

2-Dialkylamino-2-phenylcyclobutanone (V).—In general, 2 g. of 2-bromo-2-phenylcyclobutanone was mixed with a solution of a tenfold excess of the respective dialkylamine in 10–50 ml. of dry ether, and the mixture was allowed to stand for 2–4 hr. at 25° with occasional shaking. The separated dialkylammonium bromide was filtered off, the ether solution was washed with water, and the dried (Na₂SO₄) ether solution was evaporated under vacuum at 50°. The residual oil was converted to the hydrobromide salt in anhydrous ether and recrystallized (see Table I, 1, 3, 4, and 7).

2-Dialkylamino-2-phenylcyclobutanol (VI). A.—A solution of 1 g. of the 2-dialkylamino-2-phenylcyclobutanone in 15 ml. of anhydrous ether was added dropwise to a stirred slurry of 0.5 g. (13 mmoles) of lithium aluminum hydride. After the spontaneous refluxing had subsided, the mixture was stirred at 25° for another 2 hr. and decomposed as usual. The granular aluminum hydroxide was filtered off and washed with ether, and the ether solution was dried (Na₂SO₄) and evaporated. The residue, if oily, was distilled or, if solid, recrystallized (see Table I, 2, 5, 6, and 8).

B.—A mixture of 1 g. of 2-bromo-2-phenylcyclobutanol and 25 ml. of a 10% ethereal solution of dimethylamine was kept in a tightly stoppered vessel for 1 week. The solvent was removed under vacuum at 50° and the residue was treated with a few drops of ether. On chilling and standing overnight, 0.12 g. of a solid, m.p. 116–117°, separated. After recrystallization from ether it melted at 117–119°. A mixture melting point with 2-dimethyl-amino-2-phenylcyclobutanol, prepared by method A, showed no depression.

Other unidentified materials from the reaction with dimethyl-amine were not investigated further.

2-Dimethylaminomethyl-2-phenylcyclobutanone (9).—A mixture of 1.46 g. (10 mmoles) of 2-phenylcyclobutanone, 0.45 g. (15 mmoles) of paraformaldehyde, 1.23 g. (15 mmoles) of dimethylammonium chloride, and 3 ml. of absolute ethanol was acidified with 1 drop of concentrated hydrochloric acid and refluxed gently for 12 hr. The solvent was removed under reduced pressure at 70°. The residual colorless hygroscopic solid was treated with 5 ml. of water and extracted with 15 ml. of ether to remove unchanged ketone. The aqueous solution was cooled to 0° and carefully made alkaline with 10 g. of potassium carbonate. The oily amino ketone was extracted into ether, dried (Na₂SO₄), and fractionated. The hydrobromide was precipitated in ether (see Table I, 10).

In an attempt to prepare the semicarbazone with sodium acetate buffered semicarbazide in water solution at 90° for 30 min., the resulting solution was cooled and made slightly alkaline with 40% sodium hydroxide. The colorless fluffy crystals which appeared on standing melted at 164–165°. A mixture melting point with authentic 2-phenylcyclobutanone semicarbazone (lit.¹ m.p. 163–165°) showed no depression.

(11) W. J. Schneider, H. J. Bernstein, and J. A. Pople [Can. J. Chem., 35, 1487 (1957)] observed that hydrogen bonding can cause a large paramagnetic shift of the magnitude of 6–7 p.p.m.

2-Dimethylaminomethyl-2-phenylcyclobutanol (11).—The dimethylaminomethyl ketone (9) was reduced with lithium aluminum hydride in ether as described for the lower homolog (2).

2,4-Bis(dimethylaminomethyl)-3-phenylcyclobutanone (XIII).—A mixture of 0.75 g. of 3-phenylcyclobutanone,[8] 0.3 g. of paraformaldehyde, 1.0 g. of dimethylammonium chloride, and 3 ml. of absolute ethanol was acidified with 1 drop of concentrated hydrochloric acid, refluxed for 24 hr., and worked up as described for the Mannich reaction of the 2-phenyl ketone (9) above. The crude oily amino ketone could not be fractionated. It was converted to the dihydrobromide which, after three recrystallizations from ethanol–ether, melted at 192–193° after sintering and darkening.

Anal. Calcd. for $C_{16}H_{26}Br_2N_2O$: C, 45.51; H, 6.25. Found: C, 45.42; H, 6.62.

2,4-Bis(dimethylaminomethyl)-3-phenylcyclobutanol (XIV).—Reduction of the amino ketone just described with lithium aluminum hydride in ether for 2 hr. and work-up in the usual manner gave a yellow oily amino alcohol in 79% yield, b.p. 138° (0.3 mm.).

Anal. Calcd. for $C_{16}H_{20}N_2O$: C, 73.23; H, 9.98. Found: C, 72.85; H, 9.76.

2-Dimethylaminomethyl-2-phenylcyclobutanone Dithioethylene Ketal (XV).—A solution of 1.5 g. (26 mmoles) of 2-dimethylaminomethyl-2-phenylcyclobutanone in 10 ml. of glacial acetic acid was mixed cautiously with 3 ml. of ethanedithiol and 3 ml. of boron trifluoride etherate. The temperature rose to 45°. After standing at 26° for 18 hr., volatile constituents were distilled off under vacuum at 80°, and the yellowish viscous residue was washed with two 20-ml. portions of warm water and made strongly alkaline with 40% sodium hydroxide solution. The separated oil was taken up in ether, washed, dried (Na_2SO_4), and converted to the hydrobromide (see Table I, 12).

1-Dimethylaminomethyl-1-phenylcyclobutane (13).—A solution of 1.5 g. (5.4 mmoles) of 2-dimethylaminomethyl-2-phenylcyclobutanone dithioethylene ketal in 150 ml. of methanol was refluxed gently with 15 g. of freshly prepared W-4 Raney nickel for 18 hr. The liquid was decanted from the cooled mixture and the catalyst was washed repeatedly with 50-ml. portions of methanol until the washings were neutral to litmus. The solutions were cleared by filtration through Celite and concentrated under vacuum. The colorless oily amine was converted to the hydrobromide (see Table I).

2-Acetoxy-2-phenylcyclobutanone (14).—A mixture of 2.2 g. (0.01 mole) of 2-bromo-2-phenylcyclobutanone, 3 g. of silver acetate, and 50 ml. of dry benzene was refluxed for 18 hr. The white solid gradually turned grayish silver. The mixture was filtered and the filtrate was concentrated under vacuum. The yellowish residue was fractionated with some decomposition and yielded 0.6 g. (30%) of a colorless oil. The infrared spectrum (see Table I) was practically identical with that of the undistilled material.

The semicarbazone (Table I, 15), prepared by refluxing the acetoxy ketone with semicarbazide hydrochloride and pyridine in ethanol, also appeared sensitive to heat and was converted to a different solid, m.p. 205–206°, on prolonged heating in ethanol. This material was not studied further.

Reduction of 2-Acetoxy-2-phenylcyclobutanone Oxime (IV) to 2-Phenylcyclobutylamine (XX).—A mixture of 2 g. (0.01 mole) of the acetoxy ketone (14), 10 ml. of dry pyridine, 2 g. of hydroxylamine hydrochloride, and 10 ml. of absolute ethanol was allowed to stand at 26° for 48 hr. Excess solvent was distilled off at 60° under reduced pressure, the residue was extracted with three 50-ml. portions of ether and dried (Na_2SO_4), and the ether was removed. The viscous oily oxime (1.9 g., 86%) did not crystallize. Infrared spectrum showed a strong band at 3450 cm.⁻¹ (OH) and 1740 cm.⁻¹ (ester).

A solution of 4 g. (19 mmoles) of this oxime in 40 ml. of anhydrous ether was dropped slowly into a slurry of 2 g. of lithium aluminum hydride in 150 ml. of ether. After spontaneous refluxing had subsided, the mixture was stirred and boiled for another 24 hr. and decomposed as usual (H_2O, 2 ml.; 15% NaOH, 2 ml.; H_2O, 6 ml.). The filtered and dried (Na_2SO_4) ether solution was fractionated. A bitter oil (1.8 g.), b.p. 90–95° (1.2 mm.), constituted the main fraction. Its picrate, prepared in ether and recrystallized as fine needles from ethanol, had m.p. 145–145.5°.

Anal. Calcd. for $C_{16}H_{16}N_4O_8$: C, 51.06; H, 4.26. Found: C, 51.29; H, 4.56.

A comparison with stereochemically uniform 2-phenylcyclobutylamine[1] could not be made by conversion of the picrate to the hydrochloride, or *vice versa*, because of lack of material.

2-Dimethylaminomethyl-2-phenylcyclobutylamine (16).—A mixture of 1.9 g. (0.01 mole) of 2-dimethylaminomethyl-2-phenylcyclobutanone, 2 g. of hydroxylamine hydrochloride, 10 ml. of pyridine, and 10 ml. of absolute ethanol was allowed to stand at 25° for 48 hr. The solvent was removed at 60° under reduced pressure and the residue was mixed with 15 ml. of ice–water and extracted with three 50-ml. portions of ether. Evaporation of the dried (Na_2SO_4) ether solution yielded 1.4 g. (67%) of a thick oil (infrared band at 1450 cm.⁻¹). A solution of 1 g. (5 mmoles) of the oily oxime in 20 ml. of anhydrous ether was added dropwise to a stirred slurry of 1 g. of lithium aluminum hydride in 30 ml. of ether, refluxed for 12 hr., and worked up as usual. Fractionation of the oily amine afforded 0.53 g. of material; for the hydrobromide, see Table I, 17.

2-Phenylcyclobutanol (VIII).[6]—A solution of 1.5 g. (0.01 mole) of 2-phenylcyclobutanone in 20 ml. of anhydrous ether was dropped slowly into a stirred slurry of 1.0 g. (0.026 mole) of lithium aluminum hydride. After spontaneous refluxing had subsided, the mixture was stirred and boiled for 2 hr., cooled, and decomposed in the usual manner with water (1 ml.), 15% sodium hydroxide (1 ml.), and water (3 ml.). After drying, the ether layer was fractionated. The colorless oily distillate weighed 1.2 g. (80% yield), b.p. 102–103° (1 mm.) and 77–78° (0.25 mm.), $n^{20}D$ 1.5461. The infrared showed a strong band at 3500 cm.⁻¹ and a medium strong band at 1100 cm.⁻¹ (secondary alcohol).

Anal. Calcd. for $C_{10}H_{12}O$: C, 81.04; H, 8.16. Found: C, 81.34; H, 8.37.

The phenylurethane melted at 125.5–126.5°.

Anal. Calcd. for $C_{17}H_{17}NO_2$: C, 76.38; H, 6.41. Found: C, 76.17; H, 6.60.

A mixture melting point with a sample prepared previously[1] (m.p. 118–120°) was 124–126°. The infrared spectra of the two samples were superimposable. Since the earlier sample[1] had been prepared *via* hydroboration of 1-phenylcyclobutene, it must have been *trans*, and this must also be the configuration of our present 2-phenylcyclobutanol.

Conversion of 2-Phenylcyclobutanol to α-Cyclopropylbenzylamine (XIX).—A solution of 1.5 g. (0.01 mole) of 2-phenylcyclobutanol in 5 ml. of pyridine was cooled to 0°, and 2.1 g. (0.011 mole) of p-toluenesulfonyl chloride was added slowly while the temperature was kept below 10°. The mixture was shaken vigorously for 5 min., allowed to stand at 25° for 24 hr., then acidified with ether, washed twice with cold water, and dried (Na_2SO_4); the ether was evaporated at 40°. The residual brownish viscous oily tosylate (XVII) (1.7 g., 85%) showed a strong infrared band at 1350 cm.⁻¹ (tosyl ester); the OH band (3500 cm.⁻¹) of the starting compound had disappeared.

A solution of 1.3 g. (2 mmoles) of sodium azide in 10 ml. of 50% ethanol was added to the tosylate and the mixture was refluxed gently for 12 hr. A deep red color developed. The cooled solution was treated with water, the separated oil taken up in ether and dried, and the ether was evaporated. The fragrant azide (XVIII) had a strong infrared band at 2125 cm.⁻¹ (N≡N). One gram of this azide was dissolved in 10 ml. of anhydrous ether and dropped into a stirred slurry of 1 g. of lithium aluminum hydride in 30 ml. of ether. Gas evolution started immediately. The mixture was stirred for an additional 2 hr., decomposed, and worked up as usual. The colorless oily amine (0.45 g., 52%) had b.p. 82° (1 mm.). The hydrochloride, prepared in ether, crystallized from ethanol–ether as fluffy crystals, m.p. 232–234°.

Anal. Calcd. for $C_{10}H_{14}ClN$: C, 65.48; H, 7.68. Found: C, 65.04; H, 7.91.

A mixture melting point with a sample of authentic hydrochloride of α-cyclopropylbenzylamine (XIX, m.p. 234–236°), kindly furnished by Dr. W. J. Close of Abbott Laboratories, showed no depression, and the respective infrared and n.m.r. spectra were superimposable. The n.m.r. spectrum, measured at 40 Mc. in deuterium oxide, contained six absorption bands in an intensity ratio of 4:1:0.5:0.5:3:5. As the salt contains only 14 protons, two peaks at δ 3.6 (relative intensity 0.5) are a pair of doublets arising from spin–spin splitting. The first broad band at δ 0.7 corresponds to four CH_2 protons in a cyclopropane ring surrounded by nearly identical chemical environments. The

second peak, equivalent in intensity to one proton and differing only little in position from the first four protons, could be a CH proton in the cyclopropane ring. A wide choice of structural features could be held responsible for the doublets at δ 3.6, most

likely, an alkyl group adjacent to a quaternary nitrogen. Of the remaining eight protons, the sharp lines at δ 4.7 and 7.3, respectively, are considered to be due to ammonium hydrogen and phenyl protons.

The Reactions of Sulfonamides with Oxalyl Chloride

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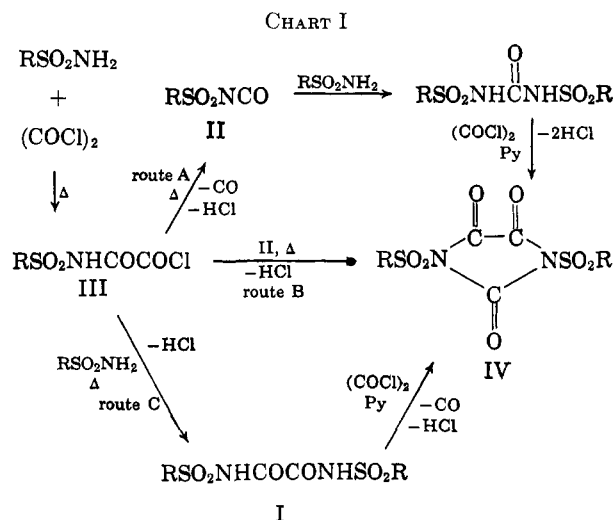*Research Department, Organic Chemicals Division, Monsanto Company, St. Louis 77, Missouri*

The reactions of aryl and alkyl sulfonamides with oxalyl chloride have been investigated. The uncatalyzed reaction produced sulfonyloxamides or sulfonyloxamoyl chlorides depending on the mole ratio of reactants. In the presence of a tertiary amine catalyst, however, the major products were sulfonylparabanates or mixtures of sulfonyl isocyanate and sulfonyl chloride. Probable mechanisms of these transformations are discussed. Several reactions of the new intermediate oxamoyl chlorides and parabanates are described. The pyrolyses of the latter products represent novel syntheses of sulfonyl isocyanates.

The reaction of oxalyl chloride with 2 moles of benzenesulfonamide has afforded N,N'-bis(benzenesulfonyl)oxamide (Ia)[1-3] in high yield. More complex acylation products such as parabanic acid derivatives[4] were absent. That the reaction may take a more complex course has been shown by investigations in this laboratory. Thus, while Ia was the major product (60%) in the reaction of 1 mole of oxalyl chloride with 1 mole of benzenesulfonamide, benzenesulfonyl isocyanate (IIa) and the oxamoyl chloride (IIIa) were also obtained. Addition of a catalytic amount of pyridine to this reaction mixture, followed by additional heating, gave a 60% yield of N,N'-bis-(benzenesulfonyl)parabanate (IVa) and a substantial amount of benzenesulfonyl isocyanate. No bis(benzenesulfonyl)oxamide was recoverable. The same overall result was obtained when pyridine was incorporated in the original reaction mixture.

The oxamoyl chloride (IIIa) was formed in 95% yield by heating benzenesulfonamide with a 4 molar excess of oxalyl chloride. This product was a hygroscopic white solid which formed IVa at the melting point. When heated in o-dichlorobenzene, however, IIIa decomposed smoothly to IIa in 81% yield.[5] IIIa exhibited the expected reactivity with water, methanol, and ammonia giving the acid, methyl ester, and amide, respectively.
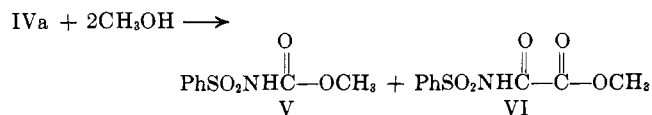
These results are readily explained on the basis of the following competitive reactions in which the oxamoyl chloride III is a key intermediate (Chart I). In route A the independent conversion of III to II in high yield was just described. The formation of the sulfonyl urea from the isocyanate and benzenesulfonamide is a known reaction.[6] Finally, the conversion of N,N'-bisbenzenesulfonylurea to IV by heating with oxaloyl chloride in the presence of pyridine was shown to proceed in 91% yield. The formation of IV at the melting point of III is represented by route B and undoubtedly involves the interaction of III and the inter-

CHART I

RSO₂NH₂ + (COCl)₂ →

RSO₂NCO (II) →(RSO₂NH₂)→ RSO₂NHCNHSO₂R

route A: Δ, $-CO$, $-HCl$

RSO₂NHCOCOCl (III) →(II, Δ; $-HCl$; route B)→ IV

RSO₂NH₂, Δ, route C; $-HCl$ →

RSO₂NHCOCONHSO₂R (I)

IV →(COCl)₂, Py; $-CO$, $-HCl$→

a, R = C₆H₅;   b, R = p-CH₃C₆H₄;   c, R = CH₃;   d, R = n-C₈H₁₇

mediate II. The preparation of both III and I in high yields according to route C has been independently accomplished in the absence of a basic catalyst (see Experimental). As mentioned earlier, I is converted to IV by heating with oxaloyl chloride in the presence of pyridine. Although the latter reaction may involve the formation of tetraketopiperazines,[4,7] intermediates of this type were not isolated. It may be concluded, therefore, that each of the reaction steps shown in Chart I has been substantiated and routes A, B, and C probably compete in the formation of IV.

The parabanate IVa was readily solvolyzed by warm methanol to give V and VI.

$$\text{IVa} + 2\text{CH}_3\text{OH} \longrightarrow$$

$$\text{PhSO}_2\text{NHC}-\text{OCH}_3 + \text{PhSO}_2\text{NHC}-\text{C}-\text{OCH}_3$$
$$\text{V} \qquad\qquad \text{VI}$$

Both products were identified by isolation and comparison with authentic materials. That V and VI were obtained in essentially equivalent amounts was shown by a comparison of the melting points (91–101°) and infrared spectra of the crude reaction products with an equimolar mixture of pure V and VI. Hot water converted IVa to benzenesulfonamide and oxalic acid. Pyrolysis of the parabanate yielded

(1) J. M. V. Charante, *Rec. trav. chim.*, **32**, 90 (1913).

(2) R. Adams and W. Reifschneider, *J. Am. Chem. Soc.*, **78**, 3825 (1956).

(3) S. I. Burmistrov, *Ukr. Khim. Zh.*, **24**, 764 (1958).

(4) J. T. Bornwater, *Rec. trav. chim.*, **31**, 105 (1912).

(5) A. J. Speziale and L. R. Smith [*J. Org. Chem.*, **28**, 1805 (1963)] have postulated an acyloxamic acid chloride as a possible intermediate in their preparation of acyl isocyanates. Whereas they were unable to isolate such an intermediate (RCONHCOCOCl), the corresponding sulfonyl compounds are isolable.

(6) O. C. Billeter, *Ber.*, **37**, 690 (1904).

(7) A. T. DeMouilpied and A. Rule, *J. Chem. Soc.*, **91**, 177 (1907).