0.01 mole) and sulfur (0.64 g., 0.02 mole) was heated at 160° for one hour. The contents of the flask was boiled with benzene (50 cc.) and the solid was removed by filtration. The product weighed 1.80 g. (72% yield) and was quite pure as indicated by almost quantitative recovery on sublimation.

Summary

A detailed reaction mechanism has been suggested for the conversion, in the Willgerodt reaction, of a primary thiol to a carboxylic acid derivative. Experimental data have been presented in support of the mechanism and various interrelationships between the reaction intermediates have been demonstrated.

RENSSELAER, NEW YORK RECEIVED MAY 5, 1948

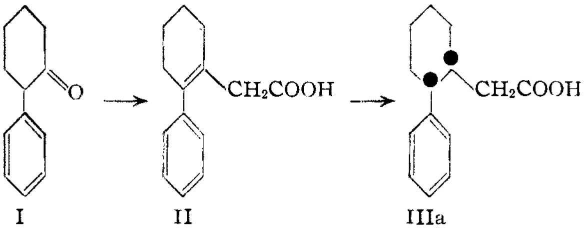
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, WASHINGTON UNIVERSITY]

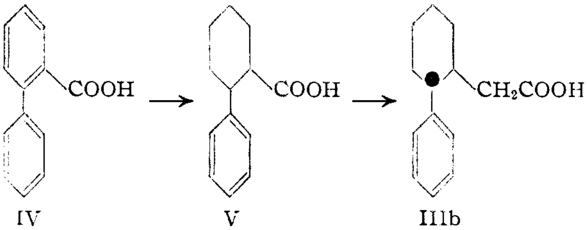
The Stereochemistry of the 2-Phenylcyclohexanecarboxylic Acids and the β-(2-Phenylcyclohexane)-propionic Acids

BY C. DAVID GUTSCHE

The preparation of the *cis* and *trans* isomers of 2-phenylcyclohexanecarboxylic acid, 2-phenylcyclohexaneacetic acid and β-(2-phenylcyclohexane)-propionic acid was undertaken because of the relation of these acids to our studies of various tricyclic ketones. The *cis* and *trans* 2-phenylcyclohexaneacetic acids have been previously prepared and their configurations unequivocally established. Cook and his co-workers[1] who first synthesized the isomers postulated the configurations from physical data.[2] Their assignment of configuration was later substantiated by the very elegant work of Linstead and his co-workers[3,4] in which the proof depended upon conclusive chemical relationships. It is this pair of acids, IIIa and IIIb,[5] that has served as a reference point in the present investigation, for through the application of known methods of chain elongation and degradation, the 2-phenylcyclohexanecarboxylic acids, Va and Vb, and the β-(2-phenylcyclohexane)-propionic acids, VIa and VIb, have been related to IIIa and IIIb and their stereochemical configurations have thereby been established.

The *cis*- and *trans*-2-phenylcyclohexaneacetic acids, the reference compounds, were synthesized by methods already described in the literature. 2-Phenyl-Δ^1-cyclohexeneacetic acid, II, prepared from 2-phenylcyclohexanone, I, according to a somewhat modified method of Cook and co-workers,[1] was catalytically hydrogenated to *cis*-2-phenylcyclohexaneacetic acid, IIIa, in 52.5% over-all yield from I. 2-Phenylcyclohexanecarboxylic acid, V, prepared by the sodium and amyl alcohol reduction of 2-phenylbenzoic acid, IV, was converted by a modification of a previously described method[6] to *trans*-2-phenylcyclohexaneacetic acid, IIIb, in 70% yield from II.





The 2-Phenylcyclohexanecarboxylic Acids (V).—One of the isomers of this pair has been synthesized previously by a number of methods. Kipping and Perkin[7] first prepared 2-phenylcyclohexanecarboxylic acid, V, by the sodium ethoxide catalyzed condensation of diethyl malonate with 1-phenyl-1,5-dibromopentane followed by hydrolysis and decarboxylation. Several workers[6,8,9,10] have obtained V by the sodium and amyl alcohol reduction of 2-phenylbenzoic acid, IV. Cook and Hewett[10] and Blumenfeld[11] have employed Diels–Alder reactions between phenylbutadiene and acrolein or ethyl acrylate in the synthesis of V. All of these methods yielded the same acid melting at 107–108°,[12] and the conversion of V to IIIb suggested a *trans* configuration for this isomer. The possibility of an inversion during the chain elongation, however, could not be overlooked, for Wallis

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[1] Cook, Hewett and Lawrence, *J. Chem. Soc.*, 71 (1936).

[2] Cook, Hewett and Robinson, *ibid.*, 168 (1939).

[3] Linstead, Whetstone and Levine, THIS JOURNAL, **64**, 2014 (1942).

[4] Linstead, Davis and Whetstone, *ibid.*, **64**, 2009 (1942).

[5] The representation of configuration is that employed by Linstead [*Chemistry & Industry*, **56**, 510 (1937)] in which the positions of the hydrogen atoms are shown in the formulas by black dots, a dot indicating that the hydrogen is above the plane of the molecule.

[6] Gutsche and Johnson, THIS JOURNAL, **68**, 2239 (1946).

[7] Kipping and Perkin, *J. Chem. Soc.*, 304 (1890).

[8] Ranedo and León, *Añal. soc. españ. fis. quím.*, **23**, 113 (1925) [*Chem. Zentr.*, **96**, I, 2557 (1925)].

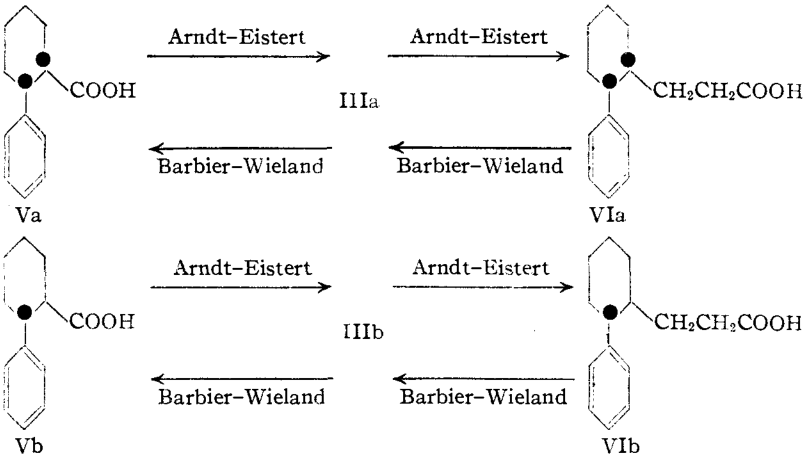
[9] Fujise, *Ber.*, **71B**, 2461 (1938).

[10] Cook and Hewitt, *J. Chem. Soc.*, 62 (1936).

[11] Blumenfeld, *Ber.*, **74B**, 524 (1941).

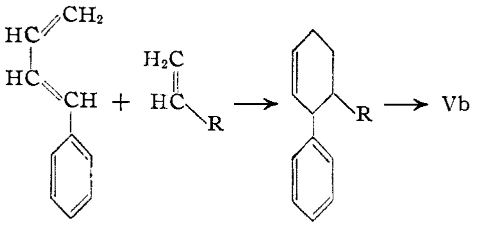
[12] This is the melting point of the purest sample obtained in this Laboratory and is slightly different from those previously recorded: 103–105°,[8] 104–105°,[7] 105–106°,[9] 105–107°,[10] 110°.[11]

and co-workers[13] have shown that optically active compounds of the type $R_1R_2CHCOOH$ undergo racemization when subjected to the Arndt–Eistert reaction. This has been provisionally attributed by Wallis to enolization involving the α-hydrogen, for compounds of the type $R_1R_2R_3CCOOH$ are not racemized under similar conditions.[14] A somewhat similar situation obtains in the present case where an α-hydrogen might be involved during the Wolff rearrangement and lead to inversion of configuration. That such inversion did not occur was demonstrated by the same method that was used by Lane and Wallis.[14] Thus acid IIIb when subjected to the Barbier–Wieland degradation yielded the starting acid Vb and not an isomer thereof. This cycle of reactions proves that the Arndt–Eistert reaction proceeds in the present case without inversion of configuration and thereby establishes the 2-phenylcyclohexanecarboxylic acid, Vb, melting at 108° as the *trans* isomer.



The hitherto unknown *cis*-2-phenylcyclohexanecarboxylic acid, Va, was prepared by a Barbier–Wieland degradation of IIIa and obtained as a crystalline solid melting at 76–77°. The completion of the proof of configuration by reconversion of Va to IIIa caused some difficulty for when Va was subjected to the conditions of the Arndt–Eistert reaction as employed in the *trans* series, IIIb was obtained, an inversion to the *trans* form having taken place at some point in the chain lengthening process. That the inversion occurred not during the Wolff rearrangement but in the formation of the acid chloride was indicated by ammonolysis of the acid chloride of Va to an amide identical with that from Vb. It was found, however, that inversion could be prevented by carrying out the reaction of Va and thionyl chloride at room temperature instead of at reflux temperature.[15] Thus when the Arndt–Eistert reaction was carried out on the acid chloride from Va prepared at room temperature, IIIa was obtained in fair yield. In this series, too, therefore, the Wolff rearrangement proceeds without inversion of configuration, and the 77° acid is established as the *cis* isomer. Further characterization of the *cis* and *trans* acids was carried out by the preparation of the S-benzylthiouronium salts which were obtained as two different, sharply melting compounds.

As mentioned previously, a Diels–Alder condensation between VII and acrolein to form VIIIa or ethyl acrylate to form VIIIb has been employed in the preparation of Vb. The formation of Vb instead of Va is somewhat unexpected, for Meek and Ragsdale[16] have shown that the reaction between piperylene and acrylonitrile or methyl acrylate yields the *cis* isomers almost exclusively. The formation of Vb may be attributed either to inversion of configuration during the conversion of VIIIa or VIIIb to Vb or to the formation of the *trans* structure in the Diels–Alder reaction. The now established configurations of Va and Vb should facilitate the clarification of this point, and experiments to this end are being pursued elsewhere.[17]



VII

VIIIa (R=CHO)
VIIIb (R=$COOC_2H_5$)

The β-(2-Phenylcyclohexane)-propionic Acids (VI).—The *cis*- and *trans*-β-(2-phenylcyclohexane)-propionic acids, both hitherto unknown, were obtained by an Arndt–Eistert chain lengthening of the corresponding 2-phenylcyclohexaneacetic acid, III. The possibility of an inversion during the homologation in this case seemed entirely excluded, and the degradation of VIa to IIIa and VIb to IIIb was not anticipated as necessary. The Arndt–Eistert reaction, however, yielded what appeared to be a mixture of acids from which a relatively poor yield of crystalline material could be obtained. It was deemed ad-

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(13) Lane, Willenz, Weissberger and Wallis, *J. Org. Chem.*, **5**, 276 (1940); Lane and Wallis, *ibid.*, **6**, 443 (1941).

(14) Lane and Wallis, THIS JOURNAL, **63**, 1674 (1941).

(15) Rearrangements of another type due to the presence of thionyl chloride have been encountered by Ställberg-Stenhagen [*ibid.*, **69**, 2568 (1947)] and by Cason [*ibid.*, **69**, 1548 (1947)] and have been found to be avoided by carrying out the reaction at room temperature.

(16) Meek and Ragsdale, *ibid.*, **70**, 2502 (1948).

(17) (a) Dr. J. S. Meek, private communication; (b) Ropp and Coyner, Abstracts of Papers, 114th Meeting of the American Chemical Society, St. Louis, Mo., 1948.

TABLE I

MELTING POINTS OF ACIDS

	2-Phenylcyclohexanecarboxylic Acid (V)		2-Phenylcyclohexaneacetic Acid (III)		2-Phenylcyclohexanepropionic Acid (VI)	
	cis	*trans*	*cis*	*trans*	*cis*	*trans*
Acid, °C.	76–77	107–108	169–170	114–114.5	93.5–94.5	83.5–84.5
Amide, °C.	80–80.5	135–136	141.5–142	127–128	88–89	134–135

visable, therefore, to complete the cycle as described for the previous cases. The crystalline fraction from the Arndt–Eistert homologation of IIIa or IIIb when subjected to the Barbier–Wieland degradation yielded IIIa or IIIb, respectively, thus establishing the structure as well as the configuration of VIa and VIb. The identity of the other acids accompanying VIa and VIb has not been ascertained.

The melting points of these acids are rather interesting in that the characteristic periodicity is exhibited in both the *cis* and the *trans* series but with a curious reversal of higher melting isomer between V and III. It would be interesting to extend this series to discover if and at what point another reversal occurs. The melting points of the acids and their amides are given in Table I.

Acknowledgment.—We gratefully acknowledge a generous Research Corporation grant which has made possible the purchase of several pieces of equipment helpful in the pursuance of research in this field. We are also indebted to Alice Gutsche for aid in the preparation of some of the starting materials and to Dorothy Kuenne for performing most of the micro-analyses.

Experimental[18]

2-Phenyl-Δ^1-cyclohexeneacetic Acid (II).—A 50.0-g. sample of 2-phenylcyclohexanone, prepared according to the method of Newman and Farbman,[19] was converted to 2-phenyl-Δ^1-cyclohexeneacetic acid by a method which differed from that described by Cook and co-workers[1] in that zinc activated by the method of Fieser and Johnson[20] was used, decomposition of the Reformatsky complex was carried out with ethanol, and the intermediate hydroxy ester and unsaturated ester were not isolated and purified. The modified procedure yielded 50.2 g. (81%) of the unsaturated acid, II, as a pale yellow, viscous oil; b. p. 155–160° (0.2 mm.), which slowly solidified upon standing to an almost colorless material, m. p. 65–72°. The pure compound is reported[1,3] to melt at 92–93°. Attempts to effect the dehydration by refluxing the crude hydroxy ester for one hour with 90% formic acid resulted in only partial removal of water. Dehydration with phosphorus pentoxide as described by Linstead[3] gave somewhat lower yields of the unsaturated acid. An experiment in which an excess of ethyl α-bromoacetate and zinc was used,[21] the excess added in several portions during the course of the reaction, yielded the unsaturated acid, II, in only 64% yield.

cis-**2-Phenylcyclohexaneacetic acid** (IIIa) was prepared from II as previously described.[1,3] Reduction of 50.2 g. of 2-phenyl-Δ^1-cyclohexeneacetic acid (m. p. 65–72°) with hydrogen and palladium chloride on charcoal[22] yielded, after recrystallization from acetic acid and benzene, 33.0 g. (65%) of colorless plates, m. p. 168.5–170° (slight previous softening). The reported m. p. is 168–170°.[1,3]

cis-**2-Phenylcyclohexaneacetamide** was prepared by ammonolysis of the acid chloride formed by refluxing IIIa for one and one-half hours with purified[23] thionyl chloride. Several recrystallizations of the crude product from benzene–petroleum ether (b. p. 30–60°) produced colorless, very short needles, m. p. 141.5–142°.

Anal. Calcd. for $C_{14}H_{19}NO$: C, 77.37; H, 8.81. Found: C, 77.22; H, 8.54.

trans-**2-Phenylcyclohexaneacetic Acid** (IIIb).—*trans*-ω-Diazo-2-phenylhexahydroacetophenone, prepared as described previously,[6] was rearranged to the ester of IIIb by a method similar to one described by Bachmann and co-workers[21] and the ester then converted to IIIb by saponification with potassium hydroxide. From 1.00 g. of the diazo ketone (m. p. 100–102°) there was obtained 0.80 g. (84%) of the crude acid, IIIb, m. p. 106–111°. Recrystallization from hexane gave 0.67 g. (70%) of light tan plates, m. p. 112–114° (slight previous softening). Concentration of the mother liquors produced a second crop of only 0.02 g., m. p. 109–112°. The m. p. of the pure material[3,6,11] is 114–114.5°. Rearrangement of 6.4 g. of diazo ketone by this same procedure yielded 4.1 g. (67%) of recrystallized acid.

Barbier–Wieland Degradation of IIIb to *trans*-**2-Phenylcyclohexanecarboxylic Acid** (Vb).—The degradation was carried out according to the directions of Lane and Wallis.[14] From 2.15 g. of *trans*-2-phenylcyclohexaneacetic acid (m. p. 106–111°) there was obtained 0.74 g. (37%) of a pale yellow oil which solidified upon standing. Recrystallization from a mixture of low boiling (b. p. 40–60°) and high boiling (b. p. 60–68°) petroleum ether gave 0.51 g. (25%) of almost colorless crystals, m. p. 104–106° (slight previous softening). Several recrystallizations from petroleum ether (b. p. 60–68°) produced colorless, glistening prisms, m. p. 107–108°. A mixed m. p. with *trans*-2-phenylcyclohexanecarboxylic acid obtained from 2-phenylbenzoic acid by sodium and amyl alcohol reduction[6,8,9,10] was 105.5–107°.

S-Benzylthiouronium Salt of *trans*-**2-Phenylcyclohexanecarboxylic Acid.**—The directions of Cheronis and Entrikin[24] were followed in the preparation of this derivative. From 0.200 g. of *trans*-2-phenylcyclohexanecarboxylic acid (m. p. 105–107°) treated with 0.250 g. of S-benzylthiouronium chloride there was obtained a sticky white precipitate. This was washed several times by decantation with water, dried in vacuum, and triturated with ether. The product consisted of 0.300 g. (83%) of a fine white powder; m. p. 126.5–127°.

Anal. Calcd. for $C_{21}H_{26}N_2O_2S$: C, 68.07; H, 7.04. Found: C, 68.17; H, 6.88.

The salt could be recrystallized from ethyl acetate but with some difficulty and the product obtained melted at 122–123°.

Barbier–Wieland Degradation of IIIa to *cis*-**2-Phenylcyclohexanecarboxylic Acid** (Va).—A 25.0-g. sample of *cis*-2-phenylcyclohexaneacetic acid (m. p. 168–170°) was degraded by the method of Lane and Wallis[14] with only a few minor changes. The period of refluxing with the phenylmagnesium bromide after removal of the ether and benzene was extended to three hours and the period of

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(18) The melting points were taken on an electrically heated microscope stage calibrated against the conventional capillary tube melting point apparatus.

(19) Newman and Farbman, THIS JOURNAL, **66**, 1550 (1944).

(20) Fieser and Johnson, *ibid.*, **62**, 575 (1940).

(21) Bachmann, Cole and Wilds, *ibid.*, **62**, 824 (1940).

(22) Mozingo, "Organic Syntheses," **26**, 78 (1946).

(23) Fieser, "Experiments in Organic Chemistry," 2nd ed., D. C. Heath and Co., Boston, Mass., 1941, p. 381.

(24) Cheronis and Entrikin, "Semimicro Qualitative Organic Analysis," T. Y. Crowell Co., New York, N. Y., 1947, p. 324.

refluxing with acetic anhydride was extended to one and one-half hours. Also the saponification to remove unreacted ester after the Grignard reaction and the steam distillation of the Grignard product to remove biphenyl were omitted. From the degradation there was obtained 11.40 g. (49%) of a viscous, red-brown oil which failed at first to solidify. When seeded with crystals obtained by crystallization of an evaporative distillate of the crude oil from water a dark brown solid was obtained, m. p. 60–72°. Recrystallization of the crude product from petroleum ether (b. p. 30–60°) gave 5.5 g. (24%) of slightly yellow crystals, m. p. 73.5–75°. Evaporative distillation followed by two recrystallizations from petroleum ether (b. p. 30–60°) produced colorless, transparent, diamond-shaped plates, m. p. 76–77°.

Anal. Calcd. for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.68; H, 7.94.

cis-**2-Phenylcyclohexanecarboxamide.**—A 0.400-g. sample of *cis*-2-phenylcyclohexanecarboxylic acid was dissolved in 3.5 cc. of benzene and 1.0 cc. of purified[23] thionyl chloride and the solution allowed to stand at room temperature for twenty-two hours. The benzene and excess thionyl chloride were removed under vacuum at 30–40°. The liquid residue was treated with ammonium hydroxide and the amide isolated in the usual manner as an almost colorless solid; m. p. 68–72° (previous softening). Two recrystallizations from hexane produced colorless, broad blades, m. p. 80–80.5°.

Anal. Calcd. for $C_{13}H_{17}NO$: C, 76.81; H, 8.43. Found: C, 77.11; H, 8.23.

The S-benzylthiouronium salt of *cis*-**2-phenylcyclohexanecarboxylic acid** was prepared as described above for the *trans* acid and was obtained as a colorless powder, m. p. 152–153°.

Anal. Calcd. for $C_{21}H_{26}N_2O_2S$: C, 68.07; H, 7.04. Found: C, 67.97; H, 6.89.

cis-ω-**Diazo-2-phenylhexahydroacetophenone.**—A 1.5-g. sample of *cis*-2-phenylcyclohexanecarboxylic acid was converted to the acid chloride with 3 cc. of purified[23] thionyl chloride in 6 cc. of benzene at room temperature and then treated with diazomethane (from 5 g. of nitrosomethylurea) to yield 1.65 g. (98%) of the crude diazo ketone as yellow needles, m. p. 53–57° (slight previous softening). Purification by two recrystallizations from dry ether cooled in a Dry Ice–acetone bath yielded the analytical sample as pale yellow needles, m. p. 59–60° (dec.).

Anal. Calcd. for $C_{14}H_{16}N_2O$: C, 73.65; H, 7.01. Found: C, 73.97; H, 6.87.

Rearrangement of *cis*-ω-**Diazo-2-phenylhexahydroacetophenone to IIIb.**—A 0.70-g. sample of the crude diazo ketone (m. p. 53–57°) prepared as described above was rearranged in methanol and the ester saponified as described for the *trans* series to yield 0.60 g. (90%) of IIIb as a yellow solid; m. p. 150–165°. Recrystallization from benzene–hexane gave 0.30 g. (45%) of glistening plates, m. p. 168–169°, showing no depression in m. p. upon admixture with an authentic sample of *cis*-2-phenylcyclohexaneacetic acid. A rearrangement of the diazo ketone from 1.00 g. of Va to IIIa directly[6] yielded only 0.09 g. of acidic material, m. p. 149–167°.

Reactions Involving Inversion of *cis*-**2-Phenylcyclohexanecarboxylic Acid (Va).** (a) **Formation of** *trans*-**2-Phenylcyclohexanecarboxamide from Va.**—A 0.45-g. sample of *cis*-2-phenylcyclohexanecarboxylic acid was refluxed for one and three-fourths hours with 3 cc. of purified[23] thionyl chloride, the thionyl chloride was removed in the usual manner, and the acid chloride then treated with ammonium hydroxide. The crude amide so obtained melted at 116–122° and after two recrystallizations from hexane–benzene yielded colorless needles, m. p. 135–136°, showing no depression in m. p. when admixed with a sample of the amide prepared from Vb. Ranedo and León[25] found the m. p. of the amide of Vb to be 137°.

(b) **Formation of** *trans*-**2-Phenylcyclohexaneacetic Acid from Va.**—A 0.300-g. sample of *cis*-2-phenylcyclohexanecarboxylic acid was converted to the acid chloride with refluxing thionyl chloride, this treated with diazomethane to produce the diazo ketone, and the diazo ketone rearranged as described above to yield an orange semi-solid. Recrystallization from petroleum ether (b. p. 30–60°) gave 0.050 g. of glistening plates, m. p. 105–109°. Upon admixture with an authentic sample of *trans*-2-phenylcyclohexaneacetic acid (m. p. 114–114.5°) the m. p. was 107–113°.

(c) **Formation of** *trans*-**2-Phenylcyclohexanecarboxylic Acid from Va.**—Hydrolysis of the acid chloride formed from 0.100 g. of Va and refluxing thionyl chloride yielded a semi-solid. Recrystallization from hexane produced 0.010 g. of colorless prisms, m. p. 102–105°. A mixed m. p. with *trans*-2-phenylcyclohexanecarboxylic acid (m. p. 107–108°) was 104–107°.

cis-β-**(2-Phenylcyclohexane)-propionic Acid (VIa).**—The diazo ketone from 4.00 g. of *cis*-2-phenylcyclohexaneacetic acid (m. p. 168–170°) was obtained in the usual manner as a somewhat viscous, orange oil, and no attempt was made to purify it further. The crude diazo ketone was rearranged as described previously to yield 3.77 g. (89%) of a pale orange solid, m. p. 78–82° (previous softening). Recrystallization from petroleum ether (b. p. 30–60°) produced 1.55 g. (36.5%) of almost colorless crystals, m. p. 81–91°. An analytical sample, procured by evaporative distillation at 140° (0.05 mm.) followed by two recrystallizations of the distillate from hexane, existed as colorless, glistening plates, m. p. 93.5–94.5°.

Anal. Calcd. for $C_{15}H_{20}O_2$: C, 77.52; H, 8.68. Found: C, 77.21; H, 8.58.

cis-β-**(2-Phenylcyclohexane)-propionamide** was prepared from VIa in the usual manner. The crude product was recrystallized six times from benzene–petroleum ether (b. p. 30–60°) to give colorless, very small blades, m. p. 88–89°. In spite of strenuous purification and prolonged drying the analyses persistently showed low carbon and hydrogen values.

Anal. Calcd. for $C_{15}H_{21}NO$: C, 77.87; H, 9.15. Found: C, 77.31; H, 8.73.

trans-β-**(2-Phenylcyclohexane)-propionic Acid (VIb).**—A 4.00-g. sample of *trans*-2-phenylcyclohexaneacetic acid (m. p. 112–114°) was subjected to the Arndt–Eistert reaction under the conditions described for the corresponding *cis* isomer to yield 3.60 g. (84.5%) of a viscous, orange oil. Crystallization from petroleum ether (b. p. 30–60°) cooled in an ice-bath produced 1.40 g. (33%) of almost colorless crystals, m. p. 78–82°. Two recrystallizations from petroleum ether (b. p. 30–60°) gave colorless blades, m. p. 83.5–84.5°.

Anal. Calcd. for $C_{15}H_{20}O_2$: C, 77.52: H, 8.68. Found: C, 77.73; H, 8.51.

A chromatographic separation on alumina (acid washed) was made on 1.60 g. of the residual oil from which the crystalline material had been separated. The middle four fractions (0.52 g.) solidified but did not melt sharply (48–56°, 50–58°, 56–68°, 64–70°) and failed to yield to purification by recrystallization.

trans-β-**(2-Phenylcyclohexane)-propionamide** was prepared in the usual manner to yield, after several recrystallizations from benzene–petroleum ether (b. p. 30–60°), a colorless powder, m. p. 134–135°.

Anal. Calcd. for $C_{15}H_{21}NO$: C, 77.87; H, 9.15. Found: C, 77.55; H, 8.98.

Barbier–Wieland Degradation of VIa to *cis*-**2-Phenylcyclohexaneacetic Acid (IIIa).**—From 0.500 g. of *cis*-β-(2-phenylcyclohexane)-propionic acid (m. p. 89–91°) there was obtained, following the previously described method, 0.150 g. (32%) of IIIa as a colorless powder, m. p. 160–168°. Recrystallization from benzene yielded colorless plates, m. p. 169–170°, which showed no depression in m. p. when admixed with an authentic sample of *cis*-2-phenylcyclohexaneacetic acid.

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(25) Ranedo and León, *Añal. soc. españ. fís. quím.*, **24**, 552 (1926) [*Chem. Zentr.*, **98**, I, 1267 (1927)].

Barbier-Wieland Degradation of VIb to *trans*-2-Phenylcyclohexaneacetic Acid (IIIb).—A 0.500-g. sample of *trans*-β-(2-phenylcyclohexane)-propionic acid (m. p. 78–82°) was subjected to the Barbier–Wieland degradation under previously described[14] conditions except that the time of refluxing with acetic anhydride was increased to two and one-half hours. The crude product (IIIb) consisted of 0.110 g. (23%) of a white powder, m. p. 110–114° (previous softening). Recrystallization from hexane gave colorless plates, m. p. 113.5–114.5°, showing no depression in m. p. when admixed with an authentic sample of *trans*-2-phenylcyclohexaneacetic acid.

Summary

The configurations of the *cis*- and *trans*-2-phenylcyclohexanecarboxylic acids and the *cis*- and *trans*-β-(2-phenylcyclohexane)-propionic acids have been proved by relating these acids, *via* the Arndt–Eistert homologation and the Barbier–Wieland degradation, to the configurationally established *cis*- and *trans*-2-phenylcyclohexaneacetic acids.

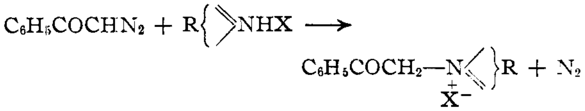
ST. LOUIS, MISSOURI RECEIVED JUNE 10, 1948

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

The Reaction of Diazoketones with Heterocyclic Amine Salts

BY L. CARROLL KING AND F. M. MILLER

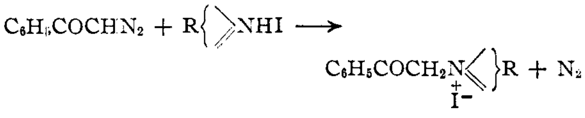
It has been found that diazoketones react with salts of certain heterocyclic amines to yield the corresponding quaternary salts.[1] Using diazoacetophenone, the reaction may be formulated as



$$C_6H_5COCHN_2 + R\{\ \}NHX \longrightarrow C_6H_5COCH_2{-}\underset{X^-}{\overset{+}{N}}\langle\ \}R + N_2$$

where N⟨ ⟩R represents any of the heterocyclic bases listed in Table I, and X⁻ may be the anion of hydrochloric, hydrobromic, hydriodic, phosphoric, sulfuric, perchloric or *p*-toluenesulfonic acid.

TABLE I



$$C_6H_5COCHN_2 + R\{\ \}NHI \longrightarrow C_6H_5COCH_2\underset{I^-}{\overset{+}{N}}\langle\ \}R + N_2$$

Compound		Yield,[a] %	M. p., °C.[b] Found	M. p., °C.[b] Reported
1-Phenacyl-2-picolinium	iodide	27	203–205	200–202[c]
	perchlorate[e]		183–188	185–189[c]
1-Phenacylquinolinium	iodide	21	185–188	187–192[c]
	perchlorate[e]		191–193	193–195[c]
2-Phenacylisoquinolinium	iodide	68	176–177	178–180[c]
	perchlorate[e]		189–192	194–197[c]
2-Phenacyl-3-methylisoquinolinium	iodide	60	196–198	199–199.7[d]
	perchlorate[e]		191–193	193–195

[a] Based on the diazoketone. These preparations were carried out by method (b) (see experimental part). [b] All melting points were observed on a Fisher–Johns melting point block. [c] These compounds were compared with authentic material previously prepared in this Laboratory, King and McWhirter, THIS JOURNAL, **68**, 717 (1946). [d] Hartwell and Kornberg, *ibid.*, **68**, 868 (1946). [e] Prepared by adding perchloric acid to the iodide in dilute alcohol solution.

The generality of this method was established by allowing diazoacetophenone to react with the hydriodide salts of a number of heterocyclic bases, Table I, and with a number of acid salts of pyridine, Table II. In all cases the expected quaternary salt was obtained and the yield of it compared favorably with the yield of the substance as prepared by other methods.[1] The yield obtained from the perchloric acid salt of pyridine was particularly good.

TABLE II[a]

$$C_6H_5COCH_2N + C_5H_5NHX \longrightarrow C_6H_5COCH_2\underset{X^-}{\overset{+}{N}}C_5H_5 + N_2$$

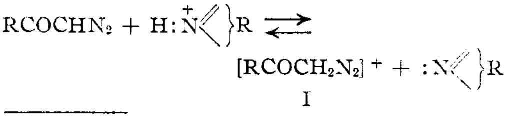
Yield, %,[b] of 1-phenacylpyridinium salt

X⁻	Method a[c]	Method b[c]	Method c[c]
Iodide	66[d]	70[d]	65[d]
Chloride	74[e]	84[e]	70[e]
Bromide	73[e]	86[e]	74[e]
Sulfate	14[e]	19[e]	15[e]
Phosphate	15[e]	22[e]	14[e]
Tosylate	60[e]	71[e]	63[e]
Perchlorate	..[f]	88[e]	93[e]

[a] Phenacylpyridinium iodide and perchlorate have been repeatedly prepared and characterized in this Laboratory, King, THIS JOURNAL, **66**, 894 (1944). The substances reported in this table were compared with authentic specimens. [b] Based on the diazoketone. [c] For a description of the method see the experimental part. [d] Isolated as the iodide. [e] Isolated as the perchlorate. [f] Decomposed violently on heating.

The reaction was carried out in three ways, (a) by warming an intimate mixture of the amine salt and the diazoketone on the steam-bath, (b) by warming an alcoholic solution of the reaction components and (c) by warming an alcoholic solution of the reactants in the presence of an excess of the base.

A plausible explanation for these results may involve reversible addition of a proton to form the ion, (I).[2] I could then react with the base as



$$RCOCHN_2 + H{:}\overset{+}{N}\langle\ \}R \rightleftarrows \underset{I}{[RCOCH_2N_2]^+} + {:}N\langle\ \}R \quad (1)$$

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(1) For previous papers in this series dealing with quaternary salt formation, see King and co-workers, THIS JOURNAL, **70**, 242 (1948), and references therein.

(2) This is analogous to the explanation proposed by Hammett for certain reactions of diazoacetic ester with hydronium ions. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Company, Inc., New York, N. Y., 1940, p. 288.