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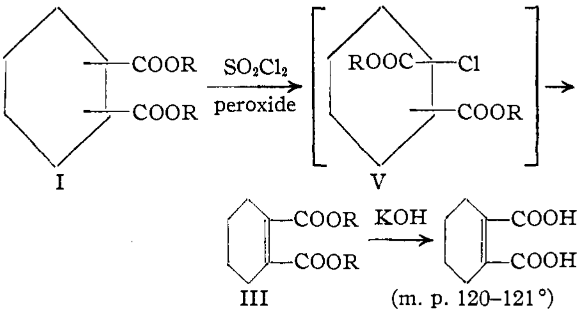
The Chlorination of *cis*- and *trans*-Diethyl Hexahydrophthalates[1]

BY CHARLES C. PRICE AND MORTON SCHWARCZ

The halogenation of *cis*- and *trans*-diethylhexahydrophthalates has been investigated with the object of determining whether, in these two diastereoisomers, replacement of an α-hydrogen atom by a halogen atom through an atomic mechanism proceeds with retention of configuration, racemization or inversion.[2]

The *cis*- and *trans*-diethyl hexahydrophthalates were selected for this study since the pure isomeric forms were readily obtainable and since chlorination was found to give clear-cut results. No appreciable bromination occurred even after several days of exposure to ultraviolet light, but chlorination through an atomic mechanism was accomplished by a method recently described by Kharasch and Brown[3] using sulfuryl chloride with benzoyl peroxide catalysis. In boiling chloroform or carbon tetrachloride, the *cis*- and *trans*-diethyl hexahydrophthalates (I and II) reacted smoothly, but the chloroesters decomposed and could not be isolated.[4] However, since Δ^1-diethyltetrahydrophthalate (III) and the Δ^2-ester (IV), respectively, were obtained as the sole product of reaction, the structures of the intermediate chloroesters (V and VI) may be deduced from the readily identified unsaturated ester each yielded on dehydrohalogenation.

Many investigators[5] have demonstrated that elimination of elements from the *trans*-position proceeds more readily than from the *cis*. Furthermore, in those cases in which it should be expected, *trans*-elimination from stereoisomers has been demonstrated to lead to isomeric unsaturated compounds. For instance, *meso*- and *dl*-2,3-dibromobutane eliminate bromine on treatment with iodide ion to form *trans*- and *cis*-2-butene, respectively,[6a] and *cis*- and *trans*-2-phenylcyclohexanol are dehydrated to 1- and 3-phenylcyclohexene, respectively.[6b]



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(1) Presented in part before the Division of Organic Chemistry at the Cincinnati meeting of the American Chemical Society, April 9, 1940.

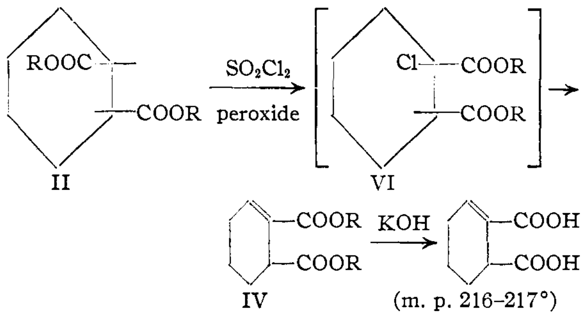
(2) An ionic mechanism involving primary enolization would obviously result in racemization.[7c] Vocke (*Ann.*, **497**, 271 (1932)), has reported that both *cis*- and *trans*-hexahydrophthalic acids yield the same bromoacid by the Hell-Volhard-Zelinsky procedure, in conformance with predictions of the enolization mechanism which has been suggested for halogenation by this procedure.[7]

(3) (a) Kharasch and Brown, THIS JOURNAL, **61**, 2142 (1939); (b) **62**, 925 (1940).

(4) Attempts to prepare solid chloro derivatives, which might be purified by recrystallization rather than distillation, were unsuccessful. Chlorination of the two acids or of the anhydrides failed, even on long refluxing with sulfuryl chloride and benzoyl peroxide. The acid chlorides could not be prepared in the pure isomeric forms. An attempt to prepare the amides by treatment of the esters with ammonia in alcohol failed; the esters were recovered unchanged.

(5) Michael, *Ber.*, **34**, 4215 (1901); Pfeiffer, *Z. physik. Chem.*, **48**, 40 (1904); Chavanne, *Bull. soc. chim. Belg.*, **28**, 240 (1914); van der Walle, *ibid.*, **28**, 369 (1914); Hückel and Neunhoeffer, *Ann.*, **477**, 135 (1930); Vavon and Barbier, *Bull. soc. chim.*, [4] **49**, 567 (1931).

(6) (a) Winstein, Pressman and Young, THIS JOURNAL, **61**, 1645 (1939); (b) Price and Karabinos, *ibid.*, **62**, 1159 (1940).



In view of this well-established rule, the formation of the two isomeric unsaturated esters from the *cis*- and *trans*-diethyl hexahydrophthalates can be interpreted on the basis of *trans*-elimination of hydrogen chloride from the intermediate chloroesters. Accordingly, chlorination of the *cis*- and *trans*-esters (I and II) yielded, respectively, the *trans*- and *cis*-chloroesters (V and VI), the formation of which could have occurred only with inversion during the replacement of the hydrogen by the chlorine atom.

Our results would substantiate a mechanism for the chlorination involving chlorine atoms as suggested by Kharasch and Brown,[3] at least in so far as the reaction could not have occurred by an ionic mechanism involving enolization of the α-hydrogen atom with attendant loss of asymmetry of the carbon atom involved.[7]

$$\begin{array}{rl} (RCO_2)_2 \longrightarrow & R\cdot \\ R\cdot + SO_2Cl_2 \longrightarrow & RCl + SO_2Cl\cdot \\ & \qquad\qquad \downarrow \\ & \qquad SO_2 + Cl\cdot \end{array}$$

The atomic chlorination in the case of the hexahydrophthalates, however, differed in one respect from simple aliphatic acids, since it was the α-hydrogen atom which was attacked almost exclusively. This is in contrast to butyric acid, for instance, which formed 10% α-, 45% β- and 45% γ-chlorobutyric acids.[3b] Similarly, ethyl butyrate has been found to yield the monochloro derivatives in about the same ratio.

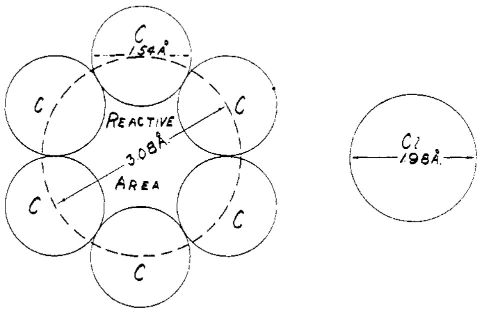


Fig. 1.

At least some degree of this difference may be attributed to the presence of the ring, since hexahydrobenzoyl chloride yielded a much higher proportion of α-chloro derivative than did the simple aliphatic acids. The chlorination of this compound with sulfuryl chloride and benzoyl peroxide gave a 65% yield of monochloro derivatives, more than half of which was α-chlorohexahydrobenzoyl chloride. A prediction on the basis of direct random attack at any hydrogen atom would have favored an even lower proportion of α-chlorination than for butyric acid, rather than such a marked increase.

If the chlorination had proceeded by direct attack on the hydrogen atoms, there should be no appreciable difference between the reactions of the paraffinic and cycloparaffinic acids. On the basis of a bimolecular inversion mechanism,[7d] however, involving approach to the face of the carbon atom opposite the hydrogen to be replaced, there could be a marked difference. It is obvious that, since a large portion of the solid angle ordinarily available for approach by an attacking atom at such a face is occupied by the ring, the attack is limited to approach in a direction more or less perpendicular to the ring. The reactive area for this type of reaction in a cyclic compound is thus narrowly limited. In the case of a six-membered ring this area would have a radius of only about twice the radius of a single carbon atom. This is illustrated schematically in Fig. 1 together with a chlorine atom for comparison.

If there are then any factors which might favor α-substitution,[8] they would have the opportunity to come into full play. In the case of an open chain compound, on the other hand, random attack from any direction may strike a reactive face before any forces which might favor α-substitution could become operative.

Further substantiation for a bimolecular in-

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[7] See, *e. g.*, (a) Ward, *J. Chem. Soc.*, **121**, 116 (1922); (b) Watson, *Chem. Rev.*, **7**, 78 (1930); (c) Bartlett and Stauffer, THIS JOURNAL, **57**, 2580 (1935).

[7d] As a general term for substitution reactions at a saturated carbon atom initiated by attack at the face of the carbon atom opposite the group to be replaced, we suggest the term "bimolecular inversion" rather than an extension of the term Walden inversion to such cases. Walden inversion refers to the change of configuration of an asymmetric carbon atom whereas the type of reaction referred to above may occur at any saturated carbon atom, asymmetric or not. Furthermore, some true Walden inversion reactions may proceed by a different mechanism.

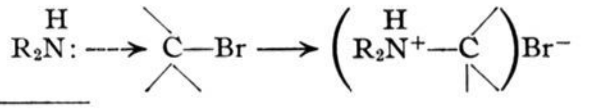
[8] The dipole of the carboxyl group, with its positive end toward the ring, would attract a chlorine atom which was in the reactive area, since, at close range, the predominant field of the neutral atom will be negative due to its outer shell of electrons.

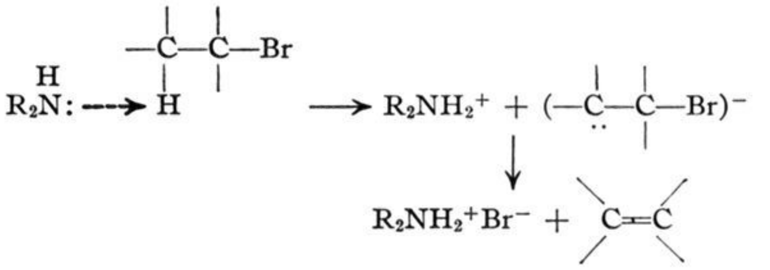
version mechanism for the atomic chlorination of the diethyl hexahydrophthalates (illustrated diagrammatically in Fig. 2 for the *cis*-ester) may be derived from the relative ease of reaction for the two esters with sulfuryl chloride. Using equivalent amounts of these reagents in refluxing carbon tetrachloride for six hours, 50% of the *trans*-diethyl hexahydrophthalate was converted to the corresponding unsaturated ester, while only 15% of the *cis*-ester had reacted. In each case, the remainder of the starting material was recovered unchanged. This three- or fourfold difference in rate of reaction can be accounted for as a steric effect, since, in the *cis*-ester, rearward approach to each α-carbon atom at the face opposite the α-hydrogen atom to be replaced is hindered by the adjacent carbethoxyl group, while in the *trans*-ester this factor is not present. If reaction had occurred by direct attack on the hydrogen atoms,[3] the steric effect of the adjacent carbethoxyl group would be just the reverse.

There are many other instances in which a significant difference between the reactions of cycloparaffin derivatives and the corresponding paraffin derivatives has been observed.[9] For example, Conant and Hussey found cyclohexyl chloride to be remarkably inert toward halogen interchange with potassium iodide, while Semb and McElvain made a similar observation for the reaction of cyclohexyl bromide with piperidine.

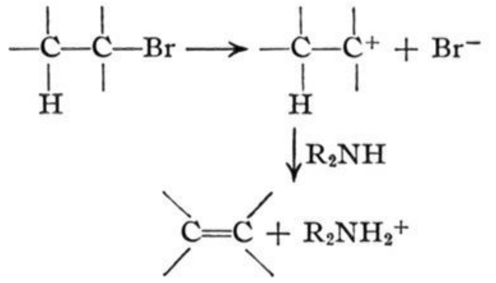
In the first case, it has been conclusively demonstrated that halogen interchange of this type proceeds by means of bimolecular inversion.[10]

In the second case, the reaction was not only slow as compared to the alkyl bromides, but it took a different course to a large degree, yielding a considerable proportion of olefin, as well as tertiary amine, the normal reaction product for secondary bromides. The reaction which was markedly slower, the formation of the tertiary amine, is the one which would be expected to proceed by a bimolecular inversion mechanism. Olefin formation, on the other hand, may involve either primary removal of a proton by the basic reagent[11]





or the primary ionization of the carbon–bromine bond, the latter a course of reaction which certainly exists for the tertiary halides.[11b]



Of these three reaction schemes, only tertiary amine formation proceeds by bimolecular inversion and is, therefore, the only one subject to hindrance by the ring.

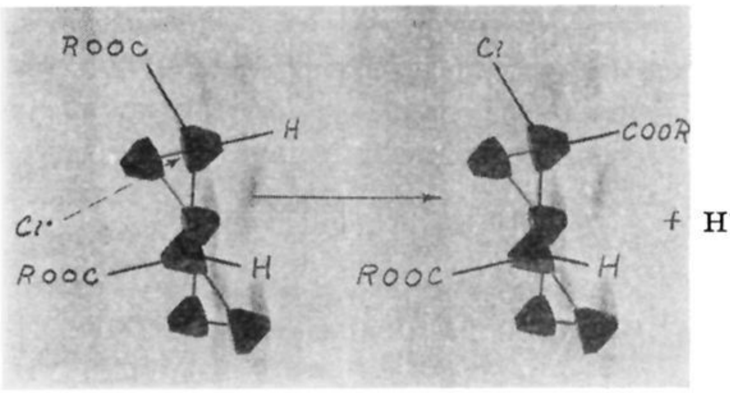


Fig. 2.

That the halogen interchange and tertiary amine formation above actually are subject to steric hindrance is indicated strongly by the fact that both reactions proceed much more rapidly for primary halides than for secondary, and more rapidly for secondary than for tertiary.

These observations all support the view that rearward approach to a carbon atom in a ring is considerably hindered, although not impossible. Therefore, those reactions at a carbon atom in a ring which proceed by a bimolecular inversion type of mechanism will be considerably modified in comparison with those of the corresponding chain compound. Reactions *not* involving bimolecular inversion (*e. g.*, the Friedel–Crafts reaction, formation of a Grignard reagent, and many reactions of a tertiary halogen atom) should and do proceed as readily at a carbon atom in a ring as at a corresponding carbon atom in a chain.

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(9) (a) Conant and Hussey, THIS JOURNAL, **47**, 479 (1925); (b) Semb and McElvain, *ibid.*, **53**, 690 (1931).

(10) Hughes, Juliusburger, Masterman, Topley, Weiss and Scott, *J. Chem. Soc.*, 1525 (1935); 1173 (1936).

(11) (a) Foreman and McElvain, THIS JOURNAL, **62**, 1435 (1940); (b) Hughes, Ingold and Scott, *J. Chem. Soc.*, 1271 (1937).

This pronounced effect of a ring should be a useful criterion for reactions proceeding by means of bimolecular inversion.

Experimental[12]

Diethyl phthalate (200 g.) was hydrogenated at 175° and 100 atmospheres with 5 g. of Raney nickel for six hours,[13] the catalyst was removed and the product fractionally distilled, yielding, as the main fraction (180 g., b. p. 122–124° (6 mm.), $n^{16.8}_{\mathrm{D}}$ 1.4530), a mixture of the *cis*- ($n^{16.8}_{\mathrm{D}}$ 1.4545)[14] and *trans*-diethyl hexahydrophthalates ($n^{14.7}_{\mathrm{D}}$ 1.4523).[14] Saponification yielded a mixture of acids (m. p. 180–181°), which, as is clearly shown by the melting point diagram (Fig. 3), consisted of 75% of the *cis*- (m. p. 190–191°) and 25% of the *trans*-acid (m. p. 219–220°) and which corresponds to the product obtained by Baeyer[15] by reduction of Δ^1-tetrahydrophthalic acid with sodium amalgam.

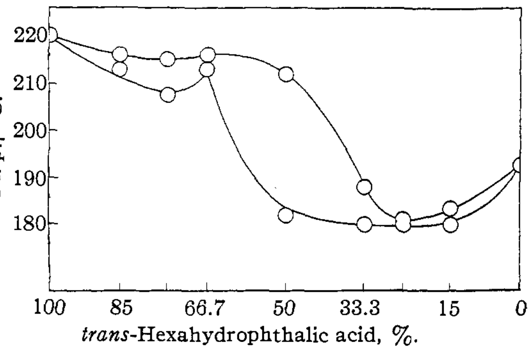

Fig. 3.—Melting point diagram for mixtures of *cis*- and *trans*-hexahydrophthalic acids.*

* These determinations were carried out by M. Ingleman.

***cis*-Diethyl Hexahydrophthalate** (I).—The mixture of acids obtained above (150 g.) was warmed on a steam-bath with 100 cc. of acetyl chloride for an hour and the product was distilled, yielding 100 g. (75%) of *cis*-hexahydrophthalic anhydride, b. p. 128–130° (5 mm.), m. p. 31–32°.[15] This anhydride was boiled six hours with 100 cc. of absolute ethanol and 5 cc. of sulfuric acid. The product, after treating with water and washing with sodium bicarbonate, consisted of 102 g. (70%) of the *cis*-ester, b. p. 130–132° (9 mm.), $n^{16.8}_{\mathrm{D}}$ 1.4543.[14]

***trans*-Diethyl Hexahydrophthalate** (II).—Conversion of the *cis*-hexahydrophthalate to the *trans* was accomplished by refluxing the ester with alcoholic alkali[16] rather than heating the acid with hydrochloric acid.[15] Ten grams of the product of the hydrogenation of diethyl phthalate was boiled one hour with 50 cc. of 1% alcoholic potassium hydroxide, water was added, and the ester was extracted with ether and distilled, yield, 9.5 g., b. p. 133–135° (10 mm.), $n^{14.7}_{\mathrm{D}}$ 1.4520,[14] n^{20}_{D} 1.4498.

***trans*-Hexahydrophthalic Acid.**—After a 10% alkaline alcoholic solution (50 cc.) of the mixed esters (10 g.) had been refluxed one hour, water was added slowly while alcohol was removed by distillation. The aqueous solution was boiled until saponification was complete. Acidification gave a precipitate which was recrystallized from acetone, yield, 7.0 g. (92%), m. p. 219–220°. Both the *trans*-acid and *trans*-ester prepared by alcoholic alkaline isomerization seem to be purer than any samples previously reported.[14,15]

Chlorination of *cis*-Diethyl Hexahydrophthalate (I).—Twenty grams of I (0.088 mole), 12 g. of sulfuryl chloride (0.088 mole), 30 cc. of purified carbon tetrachloride,[17] and 0.02 g. of benzoyl peroxide were boiled six hours in glass-stoppered apparatus. The solvent and sulfuryl chloride were then removed by warming at 50° under diminished pressure and the residue fractionally distilled in a modified Claisen flask. A typical fractionation gave (1) 13.2 g., b. p. 125° (7 mm.); (2) 2 g., b. p. 125–130° (7 mm.); (3) 3 g., b. p. 142–145° (8 mm.). The low-boiling material was I. The high-boiling fraction was identified as Δ^1-diethyltetrahydrophthalate (III) after redistillation; n^{20}_{D} 1.4745, d^{20}_{4} 1.0780. These values have been checked with samples from several different experiments. Kon and Nandi[18] reported n^{20}_{D} 1.4743 and d^{20}_{4} 1.0782 for this ester. In several experiments the reaction mixture was washed with water and dried before distillation, but with no effect on the results.

Saponification of 2 g. of the Δ^1-unsaturated ester (III) by heating with 10 cc. of 40% potassium hydroxide and a small amount of sodium lauryl sulfate ("Dreft") for fifteen minutes gave a mixture of Δ^1- and Δ^2-tetrahydrophthalic acids.[19] The pure Δ^1-acid, isolated through its cadmium salt,[18] melted at 120–121°.[15]

When two equivalents of sulfuryl chloride were used in the chlorination and the refluxing continued for eighteen hours, a 40% yield of diethyl Δ^1-tetrahydrophthalate was obtained.

Chlorination of *trans*-Diethyl Hexahydrophthalate (II).—Using the procedure described above for the *cis*-ester, the *trans* (II) yielded 8 g. of II, b. p. 132–133° (10 mm.) and 9.5 g. of diethyl Δ^2-tetrahydrophthalate (IV), b. p. 148–150° (10 mm.), n^{20}_{D} 1.4700, d^{20}_{4} 1.0761. These results have been checked repeatedly; the physical properties agree with the values of n^{20}_{D} 1.4700 and d^{20}_{4} 1.0760 reported by Kon and Nandi.[18] Saponification gave pure Δ^2-tetrahydrophthalic acid, m. p. 214–215°.[15]

When the benzoyl peroxide was omitted, the reaction mixture turned bright yellow (chlorine) and 18 g. (90%) of the starting material was recovered unchanged, b. p. 124–126° (7 mm.); n^{20}_{D} 1.4510, a few drops distilled at 126–128° (7 mm.). No unsaturated ester was detected.

Chlorination of Ethyl Butyrate.—The ester (104 g.) and sulfuryl chloride (75 cc.) were dissolved in 175 cc. of carbon tetrachloride. Benzoyl peroxide (1.5 g.) was added and the mixture warmed. After the vigorous initial reaction had subsided, the colorless mixture was refluxed for twenty

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(12) Analyses by L. G. Fauble.

(13) Wojcik and Covert, THIS JOURNAL, **55**, 1669 (1933).

(14) Von Auwers and Ottens, *Ber.*, **57**, 437 (1924).

(15) Baeyer, *Ann.*, **258**, 145–219 (1890). Baeyer reported a melting point of 215–221° for the *trans*-acid; we obtained a sample melting at 219–220°.

(16) See, *e. g.*, Diels and Alder, *ibid.*, **486**, 191 (1931); Bickel, THIS JOURNAL, **60**, 927 (1938).

(17) Price, *ibid.*, **58**, 1834 (1936).

(18) Kon and Nandi, *J. Chem. Soc.*, 1623 (1933).

(19) Baeyer[15] has reported that heating the Δ^1-acid for thirty minutes with alkali isomerized it to the Δ^2-acid. The reverse isomerization does not take place.[18]

hours. When the solvent and reagents were removed by distillation and the chloroesters by vacuum distillation, a heavy dark brown residue of 25 g. remained. The results of the fractionation of the crude distillate through a 75-cm. glass helix-filled column are summarized in Fig. 4.

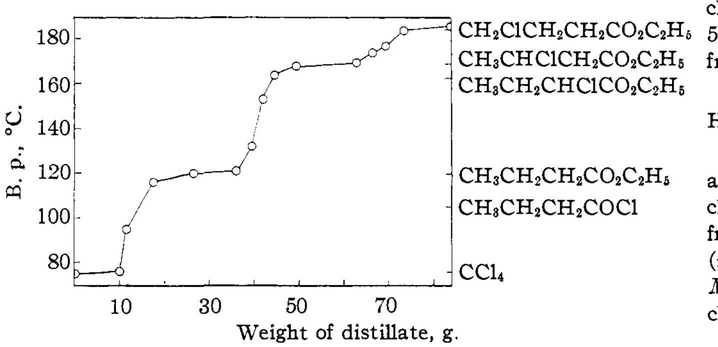

Fig. 4.—Fractionation of the chlorination mixture from ethyl butyrate.

The ethyl β-chlorobutyrate boiled at 168–169°, $n^{20}{}_D$ 1.4253 and the ethyl γ-chlorobutyrate at 184–186°, $n^{20}{}_D$ 1.4325. On the basis of this fractionation, the chloroester obtained consisted of not more than 10% α-, about 50% β- and 40% γ-chloro derivative.

Chlorination of Diethyl Succinate.—A similar procedure using 18.4 g. of diethyl succinate gave 6 g. of diethyl chlorosuccinate, b. p. 121–122° (15 mm.).[20] $n^{20}{}_D$ 1.4334, $d^{20}{}_4$ 1.148,[20] $M^{20}{}_D$ (calcd.) 47.32; $M^{20}{}_D$ (found) 47.27; 8 g. of starting material was recovered and a residue of 5 g. remained undistilled.

Chlorination of Hexahydrobenzoyl Chloride.—This acid chloride (137 g., b. p. 74–75° (18 mm.), $n^{20}{}_D$ 1.4711), 50 cc. of carbon tetrachloride, 81 cc. (135 g.) of sulfuryl chloride and 1.5 g. of benzoyl peroxide were heated ten hours on a steam plate and then distilled. The yield of α-chlorohexahydrobenzoyl chloride was 48.5 g. (34% conversion), b. p. 95–96° (18 mm.),[21] $n^{20}{}_D$ 1.4866, $d^{20}{}_4$ 1.2280, $M^{20}{}_D$ (calcd.) 42.07, $M^{20}{}_D$ (found) 42.36. When 5 g. of this material was poured dropwise into concentrated ammonium hydroxide, a quantitative yield (4.45 g.) of the white crystalline amide, m. p. 115–116°, separated. On recrystallization from aqueous methanol with minimum heating, it formed glistening needles, m. p. 117–118°.

Anal. Calcd. for $C_7H_{12}NOCl$: C, 51.98; H, 7.48; N, 8.66. Found: C, 52.32, 52.18; H, 7.72, 7.00; N, 8.82.

A sample of α-chlorohexahydrobenzamide which was prepared by passing chlorine through hexahydrobenzoyl chloride in the presence of iodine at 90–100° for four hours followed by fractional distillation and treatment with ammonium hydroxide, gave the same melting point and no depression in melting point when mixed with the sample above; von Braun, Jostes and Munch[21] have reported the melting point of this amide as 110°. The low melting point of their sample may have been due to loss of hydrogen chloride on recrystallization, a difficulty we encountered with the chloroamides unless heating was held to a strict minimum.

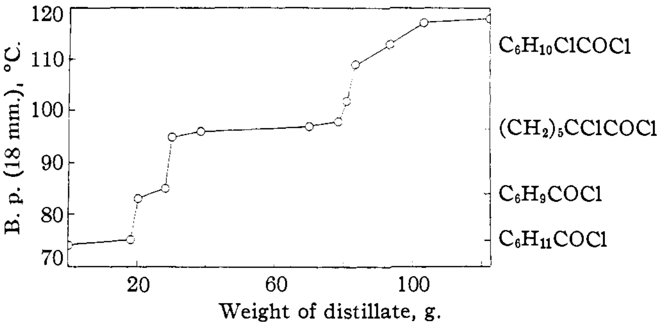

Fig. 5.—Fractionation of the chlorination mixture from hexahydrobenzoyl chloride.

When the chloroacid chloride was poured dropwise into aqueous ethylamine, glistening needles of N-ethyl-α-chlorohexahydrobenzamide separated, m. p. 55–55.5° (53°).[21] This compound recrystallized from aqueous methanol as long blades.

Anal. Calcd. for $C_9H_{16}ONCl$: C, 56.96; H, 8.48. Found: C, 56.83; H, 8.34.

The fractions boiling from 109–118° (15 mm.) apparently consisted of mixtures of isomeric chlorohexahydrobenzoyl chlorides. A sample from the fraction boiling at 113–117° (18 mm.) ($n^{20}{}_D$ 1.4953, $d^{20}{}_4$ 1.2455, $M^{20}{}_D$ (calcd.) 42.07, $M^{20}{}_D$ (found) 42.40), had the composition of a chlorohexahydrobenzoyl chloride.

Anal. Calcd. for $C_7H_{10}OCl_2$: C, 46.41; H, 5.57. Found: C, 46.70; H, 5.68.

The amide obtained by pouring this acid chloride into ammonium hydroxide, however, melted over a wide range (145–185°). Similarly, the amide from the fraction boiling at 109–113° ($n^{20}{}_D$ 1.4938) melted from 125–145°, and that from the fraction boiling at 117–118° ($n^{20}{}_D$ 1.4975, $d^{20}{}_4$ 1.2584, $M^{20}{}_D$ (calcd.) 42.07, $M^{20}{}_D$ (found) 42.00) from 115–175°. After repeated recrystallization from aqueous methanol or benzene and chloroform small amounts of an amide were obtained as rosets, m. p. 210–212°.

Anal. Calcd. for $C_7H_{12}NOCl$: C, 51.98; H, 7.48. Found: C, 52.54; H, 7.63.

Summary

The chlorination of *cis*- and *trans*-diethyl hexahydrophthalates by means of sulfuryl chloride with benzoyl peroxide catalysis gave diethyl Δ^1- and Δ^2-tetrahydrophthalates, respectively.

Similar chlorination of hexahydrobenzoyl chloride gave chiefly the α-chloro derivative, while diethyl succinate was converted to diethyl chlorosuccinate in 50% yield.

These results are interpreted as evidence that

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[20] Emery, *Ber.*, **23**, 3757 (1890); Holmberg, *ibid.*, **61**, 1905 (1928).

[21] Von Braun, Jostes and Munch, *Ann.*, **453**, 128 (1927), reported the boiling point to be 83–85° (13 mm.).

chlorination through chlorine atoms involves inversion of the configuration of the carbon atom involved.

It is suggested that certain differences in reactivity between paraffin and cycloparaffin derivatives may be ascribed to differing steric factors for a carbon atom in a chain as compared with one in a ring in reactions proceeding by a bimolecular inversion mechanism.

URBANA, ILLINOIS RECEIVED FEBRUARY 28, 1940

[CONTRIBUTION FROM THE DEPARTMENT OF PHARMACEUTICAL CHEMISTRY, NATIONAL MEDICAL COLLEGE OF SHANGHAI, AND THE DEPARTMENT OF CHEMISTRY, GREAT CHINA UNIVERSITY]

The Alkaloids of *Fritilaria Roylei*. II. Isolation of Peiminine[1]

BY YUOH-FONG CHI, YEE-SHENG KAO AND KOU-JEN CHANG[2]

In the previous communication (I)[3] on this subject we showed that the formula for peimine is $C_{26}H_{43}O_3N$ rather than $C_{19}H_{30}O_2N$ which was assigned to it by Chou and Chen.[4] A sample of peimine which Dr. Chou has now kindly sent to us, mixed with some of our material, melts at 221–223°, which does not differ significantly from the melting point (224°) of our peimine, indicating that the two samples are identical.

Chou and Chen's[4] opinion regarding the second crystalline alkaloid (peiminine) isolated from *Fritilaria* also was not in agreement with that of Fukuda[5] and others. Through Dr. Chou's kindness we have received a sample of *peiminine*, for which we determined again its true melting point. Fukuda's *Verticillin* sintered at 130°, melted at 148–50°, solidified again at 157–159°, and finally decomposed at 212–213°. The behavior of our preparation agrees better with that of Fukuda's observation, sintering at 140°, melting at 147–148°, resolidifying at 157°, and finally melting at 212–123° to a brown oil. After drying in a vacuum at 110°, our preparation melted sharply at 212–213°. The analytical data applying to this crystalline base, its methiodide, and its salts proved it to be represented by formula $C_{26}H_{43}NO_3$, instead of formula $C_{18}H_{28}NO_2$ assigned to peiminine by Chou.

Furthermore, the formula of the first crystalline alkaloid, *peimine*, was further substantiated by the results of analysis of its hydriodide, its nitrate and the methyl chloride addition compound of peimine and the platinic chloride salt.

Experimental Part

Peiminine hydrochloride was separated from peimine hydrochloride by fractional crystallization in an alcohol-ether mixture, as described in our previous communication, peiminine hydrochloride being the more soluble. The peiminine was then liberated from its hydrochloride by means of sodium carbonate and separated in colorless needles from a mixture of alcohol and petroleum ether. These needles sintered at 140°, melted at 147–148°, resolidified at 157° and finally melted at 212–213° to a brown oil. A specific rotation determination gave the value $[\alpha]^{13}\text{D}$ $-65.8°$.

Peimine Hydriodide.—One hundred milligrams of peimine was neutralized with a dilute hydriodic acid. On concentration in a vacuum desiccator, the hydriodide separated in long needles. It was recrystallized from a mixture of alcohol and ether, and melted at 282–283°. It was dried for analysis over phosphorus pentoxide at 80° in a vacuum.

Anal. Calcd. for $C_{26}H_{43}NO_3 \cdot HI$: C, 57.22; H, 8.13. Found: C, 57.72, 57.49; H, 81.4, 7.95.

Peimine Nitrate.—One hundred milligrams of peimine was neutralized with dilute nitric acid. This was concentrated in a vacuum desiccator, whereupon the nitrate separated in long needles, m. p. 265–267°. It was recrystallized from a mixture of alcohol and ether and melted at 268–269°. It was dried for analysis over phosphorus pentoxide at 80° in a vacuum.

Anal. Calcd. for $C_{26}H_{43}NO_3 \cdot HNO_3$: C, 64.95; H, 9.19, N, 5.83. Found: C, 65.08; H, 8.95; N, 5.66.

Peimine Methiodide.—Two-tenths gram of peimine, dissolved in a small volume of acetone, was treated with 0.3 cc. of methyl iodide. The mixture was then allowed to stand for twenty-four hours. The acetone solution was evaporated to dryness on a water-bath, leaving behind a yellow residue which solidified on cooling. This residue was

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