used. A sample of I (52 g.), which had remained at laboratory temperatures for two months, was stirred with 50 ml. of ice water and filtered to yield 2.1 g. (4%) of colorless needles. After recrystallization from water IV melted from 260–262° with decomposition.

Anal. Calcd. for $C_{12}H_{24}N_4O_2$: C, 56.2; H, 9.4; N, 21.9; neut. equiv., 128; mol. wt., 256. Found: C, 56.6; H, 9.2; N, 21.8; neut. equiv., 129; mol. wt., 234 (Rast), 284 (Barger).

A nitroso derivative of IV was prepared by treating an aqueous solution of the hydrochloride with sodium nitrite. After recrystallization from dimethylformamide the nitroso derivative of IV melted from 255–263° with decomposition.

Anal. Calcd. for $C_{12}H_{22}N_6O_4$: N, 26.7. Found: N, 26.9.

A benzoyl derivative of IV was prepared by the usual procedure and was recrystallized from acetic acid, m.p. 296–298° with decomposition.

Anal. Calcd. for $C_{26}H_{32}N_4O_4$: N, 12.1. Found: N, 11.9.

2-(2-Aminoethylamino)propanenitrile (V). Acrylonitrile (10.6 g., 0.20 mole) was added dropwise with stirring, over a period of 90 min., to 36.0 g. (0.60 mole) of ethylenediamine. The mixture was allowed to stand at room temperature overnight and was then distilled under reduced pressure to yield 13.4 g. (59%) of V, b.p. 124–127° at 10 mm. (reported[4] 101° at 1.5 mm.).

Anal. Calcd. for $C_5H_{11}N_3$: neut. equiv., 56.6. Found: neut. equiv., 57.9.

The dihydrochloride of V was prepared in ethanol by the addition of ethanolic hydrogen chloride. After recrystallization from ethanol the salt was isolated as colorless, hygroscopic needles of m.p. 129–131° (reported[4] only that this substance is a very hygroscopic solid).

Anal. Calcd. for $C_5H_{13}Cl_2N_3$: Cl, 38.1; N, 22.6. Found: C, 38.2; N, 22.9.

The benzoyl derivative of V was prepared in the usual manner and was obtained initially as an oil. A benzene solution of the oil was concentrated and the derivative crystallized by the addition of ligroin. After several recrystallizations from benzene, *N,N'-dibenzoyl-3-(2-aminoethylamino) propanenitrile* was isolated as a colorless solid of m.p. 96–98° (a monobenzoyl derivative has been reported[4]).

Anal. Calcd. for $C_{19}H_{19}N_3O_2$: N, 13.1. Found: N, 13.0.

Ethyl 3-(2-aminoethylamino) propanoate dihydrochloride (VI). The amino nitrile V (1.00 g.) was added dropwise to 10 ml. of absolute ethanol saturated with dry hydrogen chloride. After the addition of 0.2 ml. of water the mixture was tightly stoppered and left at room temperature overnight. After heating under reflux for 5 hr. the mixture was filtered hot and on cooling the filtrate deposited 0.79 g. (38%) of VI as very hygroscopic, colorless plates of m.p. 152–154° with previous softening.

Anal. Calcd. for $C_7H_{18}Cl_2N_2O_2$: N, 12.0. Found: N, 12.2.

3-(2-Aminoethylamino)propanoic acid dihydrochloride (VII). The ester dihydrochloride VI (1.000 g.) was dissolved in 10 ml. of dilute hydrochloric acid and the solution was refluxed for 90 min. Evaporation under reduced pressure gave a solid which was recrystallized from ethanol to yield 0.668 g. (76%) of VII as tiny, colorless plates, m.p. 153–155° with previous softening.

Anal. Calcd. for $C_5H_{14}Cl_2N_2O_2$: Cl, 34.6; N, 13.7. Found: Cl, 34.4; N, 13.8.

A sample of VII was converted to the dibenzoyl derivative in the usual manner. After recrystallization from a mixture of benzene and ethanol, *N,N'-dibenzoyl-3-(2-aminoethylamino)propanoic acid* was obtained as clusters of thin, colorless needles of m.p. 149–151° with previous softening at 145°.

Anal. Calcd. for $C_{19}H_{20}N_2O_4$: N, 8.2. Found: N, 8.1.

NEW YORK 53, N. Y.

[CONTRIBUTION NO. 443 FROM THE RESEARCH LABORATORIES OF HOFFMANN-LA ROCHE, INC.]

Pyridindene Derivatives. III. Synthesis from Arecoline

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Two racemic forms of 1-methyl-3-carbomethoxy-4-phenylpiperidine have been obtained from the reaction of phenylmagnesium bromide with arecoline. The two racemic acids were cyclized to the same 2-methyl-2,3,4,4a,9,9a-hexahydro-9-keto-1-pyridindene (VIII).

Treatment with lithium phenyl gave the 9-hydroxy-9-phenyl compound (IX), which was converted into the 9-chloro derivative. The latter was dehydrohalogenated to 2-methyl-9-phenyl-2,3,4,9-tetrahydro-1-pyridindene (XII).

Our earlier work on derivatives of pyridindene has been extended with the objective of devising a synthesis independent of the earlier route.[2] We hoped that this synthesis would allow us to prepare a larger number of derivatives and at the same time serve as an independent confirmation of the structure.

Accordingly, the preparation of 1-methyl-3-carboxy-4-phenyl-piperidine (IV) was investigated as a starting material for the compound XII. Koelsch[3] obtained compound IV by a series of reactions involving a Michael condensation of ethyl cyanoacetate and ethyl cinnamate, reduction over Raney nickel to give the piperidone I, reduction of the carbonyl group with sodium and butanol, and finally N-methylation with formaldehyde. Although the process is feasible, considerable technical difficulty is involved, especially in the reduction with sodium. Other methods of reduction were tried and some limited success was obtained with the copper chromite catalyst.[4] This catalyst in the presence of methanol not only reduced the carbonyl group but simultaneously led to the methylation of the nitrogen, resulting in the ester III (R = ethyl). Hydrolysis of this ester yielded a free acid, which proved to be identical with the acid obtained by the

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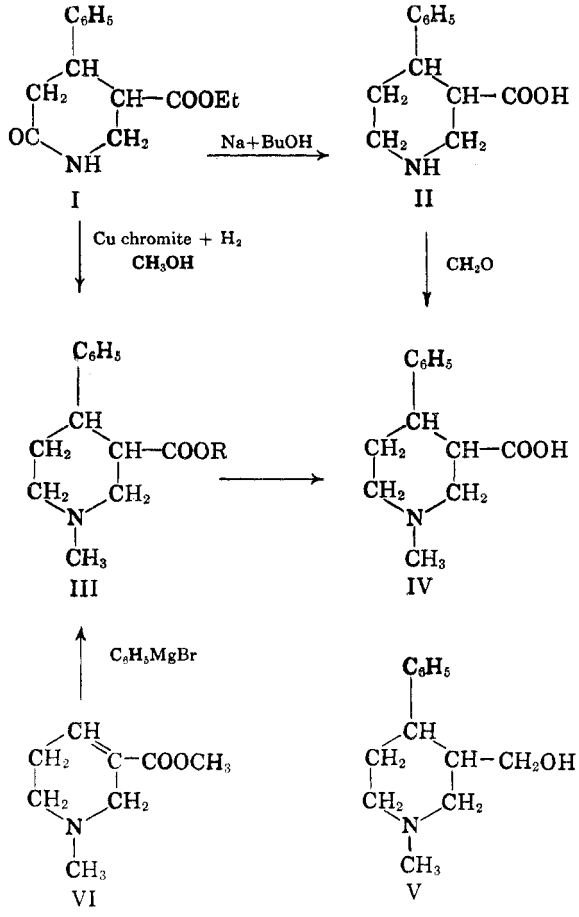
(2) J. T. Plati and W. Wenner, *J. Org. Chem.*, **20**, 1412 (1955).

(3) C. F. Koelsch, *J. Am. Chem. Soc.*, **65**, 2459 (1943).

(4) H. B. Adkins, *Reactions of Hydrogen*, The University of Wisconsin Press, Madison, Wis., 1944, p. 13.

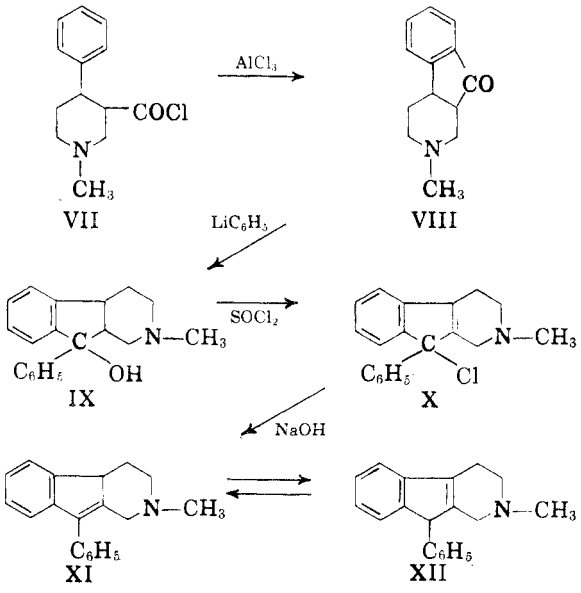
Koelsch procedure. However, the yield in the copper chromite reduction was low. This low yield was due in part to further reduction of the ester group with formation of the carbinol V.



I II III IV V VI

Our attention was then directed to an investigation of the reaction of arecoline (VI) with phenylmagnesium bromide. Two racemic methyl esters of structure III (R = CH_3) were obtained as a result of 1,4-addition. These were arbitrarily designated as belonging to an α- and to a β-series corresponding to the two theoretically possible racemic forms. Hydrolysis of the esters gave the corresponding acids (IV). The acid belonging to the α-series was identical with that obtained by the copper chromite reduction as well as by the Koelsch process. The acid from the β-series was obtained in considerably greater yield.

Both of the stereoisomeric acids (IV) were converted by means of thionyl chloride into their respective acid chlorides (VII), which were not isolated but were cyclized by means of aluminum chloride to the same azafluorenone (VIII). Treatment of this latter compound with lithium phenyl gave the expected product, the tertiary alcohol (IX). Further reaction with thionyl chloride gave a product, presumably the chloro derivative (X) which gave the desired 2-methyl-9-phenyl-2,3,4,9-tetrahydro-1-pyridindene (XII) after stirring with alkali. Its identity was established beyond doubt not only by its physical properties but also by the preparation of a thiocyanate and by its characteristic isomerization to 2-methyl-9-phenyl-2,3,4,4a-tetrahydro-1-pyridindene (XI), isolated as a nitrate.[2]



VII VIII IX X XI XII

Thus, it is evident that the above process lends itself to the preparation of a large variety of pyridindenes since three different reagents can be varied, namely, the unsaturated piperidine, the Grignard reagent, and the organolithium compound.

EXPERIMENTAL

All melting points are uncorrected.

Reduction of 5-carbethoxy-4-phenyl-2-piperidone (I) *with copper chromite catalyst in methanol. 1-Methyl-3-hydroxymethyl-4-phenylpiperidine* (V). A mixture of 30 g. of 5-carbethoxy-4-phenyl-2-piperidone (I),[3] 176 cc. of methanol, and 12 g. of copper chromite catalyst[4] was hydrogenated for 3.5 hr. at 3000 lb. at 160–200°. The mixture was filtered and the solvent removed at diminished pressure. The residue was then fractionally distilled and separated into two fractions, one fraction weighing 2.8 g. and boiling at 76–90° at 0.6 mm. and a second fraction weighing 32.7 g. and boiling at 125–127° at 0.6 mm.

The second fraction was dissolved in 100 cc. of petroleum ether (b.p. 30–75°) and permitted to crystallize. The crystals were filtered and dried in a dry air stream at 50°. The yield was 12.6 g. of material melting at 104–106°. After recrystallization from ethyl acetate the compound melted at 107–109°.

Anal. Calcd. for $C_{13}H_{19}NO$: C, 76.05; H, 9.33; N, 6.82; neut. equiv., 205. Found: C, 75.96; H, 9.60; N, 6.72; neut. equiv., 204.

1-Methyl-3-carbethoxy-4-phenylpiperidine (III, R = Et) (*α-series*). The petroleum ether filtrate from above was distilled to dryness and the residue was dissolved in ether. The ether solution was treated with dry hydrogen bromide gas to give 23.0 g. of the crude hydrobromide. After two crystallizations from alcohol and drying in a vacuum desiccator over potassium hydroxide, a melting point of 206–207.5° was obtained for the pure hydrobromide.

Anal. Calcd. for $C_{15}H_{21}NO_2 \cdot HBr$: C, 54.88; H, 6.76; Br, 24.35. Found: C, 54.43; H, 6.58; Br, 24.41.

The free base was obtained from the aqueous solution of the hydrobromide by adding 50% potassium carbonate

below 15° and extracting with ether. The ether was distilled off on the steam bath, and the residual oil was then distilled. On distillation, a material boiling at 125–126°/0.15 mm., $n_D^{19.5}$ 1.5159, was obtained.

1-Methyl-3-carboxy-4-phenylpiperidine hydrochloride (IV) (*α-series*). A mixture of 10 g. of 1-methyl-3-carbethoxy-4-phenyl piperidine base and 50 cc. of constant boiling hydrochloric acid was distilled through a packed column of approximately 12 theoretical plates until the distillation temperature rose to 110°. After distilling at 110° for about 30 to 40 min. the mixture was distilled to dryness *in vacuo* and the residue dried overnight in a vacuum desiccator with potassium hydroxide. An amorphous white powder weighing 10.3 g. was thus obtained. When one gram of this amorphous powder was dissolved in 3 cc. of alcohol, 0.85 g. of pure product, m.p. 219–221° was obtained. This melting point agrees with that of the compound described by Koelsch.[3]

Reaction of arecoline (VI) *with phenylmagnesium bromide.* To a mixture of 38 g. of arecoline (VI) hydrobromide (0.16 mole) and 30 cc. of water was added 25 cc. of 50% potassium carbonate (by weight) with cooling. The mixture was extracted with 100 cc. of benzene five times. At the end of the second and third extractions, an additional charge of potassium carbonate solution was added. Thus, a total of 75 cc. of potassium carbonate solution and 500 cc. of benzene was used. The combined benzene extracts were dried with sodium sulfate, and the benzene removed *in vacuo.* The residue weighed 25 g. and represented the arecoline base.

Into a 500-cc. three-necked flask were placed 7.94 g. (0.33 gram atom) of magnesium turnings and about 100 cc. of dry ether. A solution of 50.5 g. (0.32 mole) of bromobenzene in 100 cc. of ethereal solution was added in the course of an hour to maintain gentle reflux. After stirring for 30 min. the mixture was cooled to −10°, and 65 cc. of an ether solution of the arecoline base was added during the course of one hr. The mixture was stirred for 20 min. longer at the same temperature, poured into cracked ice, and then treated slowly with 160 cc. of ice cold 6*N* hydrochloric acid The aqueous layer was separated, extracted with 200 cc. of ether, and then treated with cooling in an ice bath with 200 cc. of 50% potassium carbonate (by weight). The mixture was extracted with 400 cc. of ether, and the ethereal layer was separated by centrifuging. The aqueous layer containing insoluble magnesium hydroxide was extracted with 350 and 250 cc. of ether. The combined ether extracts were dried with sodium sulfate, and after removing the ether, the residue was distilled. In this manner, 27.7 g (73%) of oil boiling mostly at 124–128° at 0.5 mm. was obtained. This oil represented a mixture of the two stereoisomeric forms of 1-methyl-3-carbomethoxy-4-phenyl piperidine. These isomers may be conveniently designated as belonging to an α- and a β- series.

Anal. Calcd. for $C_{14}H_{19}NO_2$: Neut. equiv., 233. Found: Neut. equiv., 232.

1-Methyl-3-carbomethoxy-4-phenylpiperidine (III, R = Me) *hydrobromide* (*α- series*). The ester mixture from above was dissolved in about 1 liter of ether, and hydrogen bromide gas was introduced. The precipitate was crystallized from 150 cc. of methanol to give 8.15 g. of crystals, m.p. 204–207°. The melting point was raised to 214–217° by recrystallization from ethyl alcohol. This compound represents the pure hydrobromide of one of the stereoisomeric forms of 1-methyl-3-carbomethoxy-4-phenyl piperidine (III, R = Me) which will be referred to as belonging to the α- series.

Anal. Calcd. for $C_{14}H_{19}NO_2 \cdot HBr$: C, 53.51; H, 6.42. Found: C, 53.63; H, 6.36.

1-Methyl-3-carbomethoxy-4-phenylpiperidine (III, R = Me) (*α- series*). To a mixture of 8.09 g. of the above hydrobromide and 50 cc. of water was added with cooling 8 cc. of 50% potassium carbonate (by weight). The mixture was extracted twice with 25 cc. of ether, and the ether solution was dried with sodium sulfate. Distillation gave 5.44 g. of free α- ester, b.p. 100° at 0.2 mm., $n_D^{24.5}$ 1.5188.

Hydrolysis to 1-methyl-3-carboxy-4-phenylpiperidine (IV) *hydrochloride* (*α-series*). To this base were added 11 cc. of water and 15 cc. of concentrated hydrochloric acid, and the mixture was distilled slowly during 25 min. until no more methanol distilled over. After distilling off the solvent *in vacuo* in a bath which was gradually brought to 85°, the residue was crystallized from 15 cc. of ethanol. In this manner, 4.57 g. of 1-methyl-3-carboxy-4-phenyl-piperidine (IV) hydrochloride, m.p. 214–216°, was obtained. This material crystallized in prisms and was identical in appearance with the material obtained through the copper chromite reduction. It showed no depression in melting point when mixed with this substance.

1-Methyl-3-carbomethoxy-4-phenylpiperidine (III, R = Me) *oxalate* (*β-series*). The methanol filtrate from the crystallization of the crude hydrobromide mixture was distilled to dryness *in vacuo.* The residue weighed 19.8 g. and melted at 166–168°. This material plus an additional amount from another experiment, making a total of 23.4 g., was treated with cooling with 90 cc. of 10% sodium carbonate and extracted with 150, 100, and 100 cc. portions of ether. The ether extracts were treated with a saturated solution of oxalic acid in ether until no further precipitation occurred, and the crude precipitate was crystallized from 150 cc. ethyl alcohol. In this manner, 18.2 g. of the oxalate of the β-ester, m.p. 157–158° was obtained.

Anal. Calcd. for $C_{14}H_{19}NO_2 \cdot C_2H_2O_4$: C, 59.43; H, 6.55. Found: C, 59.23; H, 6.26.

1-Methyl-3-carbomethoxy-4-phenylpiperidine (III, R = Me) (*β-series*). To a solution of 18.3 g. of the oxalate, m.p. 157–158°, in 150 cc. of water was added 50 cc. of 50% potassium carbonate. A solid base was precipitated. This was extracted with 100 cc. of ether, and the ether solution was dried with sodium sulfate and distilled at 100–110° and 0.25 mm. A yield of 12.0 g. of distillate was obtained which later solidified in the receiver. The 1-methyl-3-carbomethoxy-4-phenyl-piperidine of the β- series, thus obtained, melted at 55–58°.

1-Methyl-3-carboxy-4-phenylpiperidine (IV) *hydrochloride* (*β-series*). A mixture of 12.0 g. of the above β-ester, 33 cc. of water and 44 cc. of concentrated hydrochloric acid was distilled through a 12-plate column over a period of about 30 min. until methanol no longer came over. The mixture was distilled to dryness *in vacuo* in a bath, which was gradually brought to 80°. The residue was crystallized from 40 cc. of hot ethyl alcohol to give 14.3 g. of platelike crystals, melting at 212–213°. The yield and the analysis indicate that the substance contains a molecule of alcohol of crystallization. The substance gives a distinct depression in melting point when mixed with the corresponding substance from the α-series. The hygroscopic nature of the compound as well as the alcohol of crystallization presented some difficulty in the analysis. The compound was dried *in vacuo* at room temperature first over potassium hydroxide for about 20 hr. and then over P_2O_5 for several hours. The following data were obtained.

Anal. Calcd. for $C_{13}H_{17}NO_2 \cdot HCl \cdot C_2H_5OH$: C, 59.69; H, 8.02; C_2H_5O, 14.93. Found: C, 59.85; H, 8.15; C_2H_5O, 14.31.

An ethoxyl value of 1.71% was found even after drying *in vacuo* at 100° over P_2O_5.

2-METHYL-2,3,4,4a,9,9a-HEXAHYDRO-9-KETO-1-PYRIDINDENE (VIII)

From the α-series. To 7.25 g. of 1-methyl-3-carboxy-4-phenyl-piperidine (IV) hydrochloride (α-series) was added 50 cc. of thionyl chloride. Complete solution occurred. After standing at room temperature for 2 hr., the thionyl chloride was distilled off at diminished pressure below 50°. To the yellow residue was added 100 cc. of anhydrous tetrachloroethane. After stirring for a short time the yellow

residue went into solution and the resulting solution was again subjected to distillation at diminished pressure until 50 cc. of distillate was obtained. To the residual solution was added 50 cc. more of tetrachloroethane. The solution was warmed to 40° with stirring and 4 g. of anhydrous aluminum chloride added. No hydrogen chloride was liberated. Five more grams of anhydrous aluminum chloride was then added. A vigorous evolution of hydrogen chloride commenced. After complete addition of the second batch of anhydrous aluminum chloride, the reaction mixture was permitted to stir for one more hour at 40°. The reaction mixture was poured into 300 g. of ice and 25 cc. of concentrated hydrochloric acid. After standing overnight the organic and aqueous layers were separated. The tetrachloroethane layer was extracted once more with 20 cc. of water and then discarded. The combined aqueous liquors were extracted once with ether, cooled to 15°, and made strongly alkaline with 50% sodium hydroxide. The resulting mixture was then extracted once with 150 cc. of ether and then three times more with 25 cc. of ether. The combined ether extracts were dried over sodium sulfate and concentrated on the steam bath. The residue was then distilled at diminished pressure to give 5.1 g. of material boiling at 120° at 0.15 mm. This corresponds to 88% of the theoretical yield. The distillate after standing a short time crystallized and melted at 64.5–65.5°. One gram of the above distillate was dissolved in 50 cc. of dry ether, and dry hydrogen bromide gas was introduced. The precipitate was filtered and crystallized from 7 cc. of ethanol. The crystals of 2-methyl-2,3,4,4a,9,9a-hexahydro-9-keto-1-pyridindene (VIII) hydrobromide weighed 1.2 g. and melted at 208–210°. It was crystallized once more and analyzed.

Anal. Calcd. for $C_{13}H_{15}NO \cdot HBr$: C, 55.33; H, 5.71. Found: C, 55.27; H, 5.40.

From the β-series. To 40 g. (0.13 mole) of 1-methyl-3-carboxy-4-phenyl piperidine (IV) hydrochloride containing alcohol of crystallization (β-series) was added, with cooling and stirring, 160 cc. of thionyl chloride. After standing at room temperature for 3.5 hr., the thionyl chloride was removed at reduced pressure in a bath which was gradually heated to 60°. To the residue, 250 cc. of tetrachloroethane was added, and 50 cc. was distilled at reduced pressure in order to remove traces of thionyl chloride. During 45 min., 50 g. (0.37 mole) of aluminum chloride was added at 40° in a bath maintained at about 38°. The mixture was stirred for an additional 30 min. and poured into 400 g. of ice and 50 cc. of concentrated hydrochloric acid. The aqueous layer was separated, extracted with 100 cc. of ether, and with cooling below 15°, treated with 300 cc. of 30% sodium hydroxide. The organic base was extracted with 200- and 100-cc. portions of ether. After drying with sodium sulfate, the ether was removed and the residue distilled. At about 127° and 0.3 mm., 19.8 g. (74%) of 2-methyl-2,3,4,4a,9,9a-hexahydro-9-keto-1-pyridindene (VIII) was obtained. The material solidifies in the receiver. It turns brown on standing.

The hydrobromide was prepared by passing hydrogen bromide gas into a solution of one gram of the ketone in 50 cc. of ether. The precipitate was digested with 20 cc. of hot acetone, cooled, and filtered. In this manner, 1.12 g. of the almost pure hydrobromide, m.p. 204–207° was obtained. Further crystallization from ethyl alcohol raised the melting point to 208–211°. A mixed melting point with the product from the α- series (part IIIA), gave no depression.

Anal. Calcd. for $C_{13}H_{15}NO \cdot HBr$: C, 55.32; H, 5.72. Found: C, 55.09; H, 5.48.

A sample of the hydrobromide was dissolved in a little water, and dilute sodium hydroxide was added. The *free base* thus precipitated melted at 64–65°. In a mixed melting point determination with the base prepared in a similar manner from the α- series, no depression was noted.

2-Methyl-2,3,4,4a,9,9a-hexahydro-9-hydroxy-9-phenyl-1-pyridindene (IX). In a 1-l. 3-necked flask provided with stirrer and condenser was placed about 200 cc. of dry ether and 1.17 g. (0.170 g.-atom) of lithium wire cut in small pieces. During a period of 1 hr., 60 cc. of an ether solution containing 13.1 g. (0.083 mole) of bromobenzene was added to maintain gentle reflux. After stirring for 2 hr. more to complete the formation of the lithium phenyl, the mixture was cooled in an ice bath to 3° and a solution of 16.7 g. of 2-methyl-2,3,4,4a,9,9a-hexahydro-9-keto-1-pyridindene (VIII) in about 65 cc. of dry ether was added in 40 min. at 3–5°. The mixture was stirred for an additional 22 min. in the ice bath, and then the ice bath was removed, and stirring continued for 1.5 hr. A white solid was gradually precipitated.

The mixture was again cooled in the ice bath, and 53.4 cc. of 3.18*N* sulfuric acid in 150 cc. of water was added slowly. In order to neutralize the excess acid, 33.7 cc. of 2.48*N* sodium hydroxide was added, and the ether layer was separated. To insure complete separation of the base, the aqueous layer was reated with 40 cc. of 50% potassium carbonate and extracted with 100 cc. of ether. The combined ether solutions were dried with sodium sulfate and treated with a saturated ethereal solution of oxalic acid. The precipitate was crystallized from 100 cc. of methanol to give 10.6 g. of crystals, melting at 208–210° with effervescence. For analysis, a sample was crystallized but the melting point remained unchanged. This substance represents the *oxalate* of 2-methyl-2,3,4,4a,9,9a-hexahydro-9-hydroxy-9-phenyl-1-pyridindene. An additional 2.13 g. of oxalate was obtained from the mother liquor.

Anal. Calcd. for $C_{19}H_{21}NO \cdot C_2H_2O_4$: C, 68.28; H, 6.28; neut. equiv., 369. Found: C, 68.13; H, 6.39; neut. equiv., 371.

Free base. A hot solution of 8.2 g. of the oxalate in 200 cc. of water was cooled to room temperature and 30 cc. of 10% sodium hydroxide was added. The gummy precipitate, first obtained, gradually hardened and it was crushed and filtered. It weighed 6.07 g. on drying and melted at 90–92°. A sample was crystallized from dilute alcohol. It melted at 91–93°.

Anal. Calcd. for $C_{19}H_{21}NO$: C, 81.68; H, 7.57. Found: C, 81.44; H, 7.34.

Dehydration of 2-methyl-2,3,4,4a,9,9a-hexahydro-9-hydroxy-9-phenyl-1-pyridindene (IX). *2-Methyl-9-phenyl-2,3,4,9-tetrahydro-1-pyridindene* (XI). To 1 g. of the hydroxy compound (IX) was added with cooling about 10 cc. of thionyl chloride, and the mixture was allowed to stand for 1.5 hr. The thionyl chloride was removed at reduced pressure below 50°, and to the residue was added 10 cc. of 10% sodium hydroxide. After shaking for a few minutes, 5 cc. of ethyl alcohol and 5 cc. of concentrated ammonium hydroxide were added. The mixture was seeded and allowed to stand overnight. The solid which was obtained was crystallized from dilute acetone to give 0.25 g. of crystals melting at 82–84°. Another crystallization gave 0.15 g. of crystals melting at 89–90°, which had the same ultraviolet absorption spectrum as an authentic sample of 2-methyl-9-phenyl-2,3,4,9-tetrahydro-1-pyridindene[2] and showed no depression in a mixed melting point determination.

2-Methyl-9-phenyl-2,3,4,9-tetrahydro-1-pyridindene thiocyanate salt. To 1 g. of the hydroxy compound (IX) was added with cooling 10 cc. of thionyl chloride. After standing overnight at room temperature, 10 cc. of 10% sodium hydroxide was added. After a few minutes shaking during which heat was evolved, 5 cc. of ethyl alcohol was added. After standing for 2 hr. at room temperature, 5 cc. of concentrated ammonium hydroxide was added, and the mixture was agitated mechanically for 3 hr. On standing overnight, the precipitate was filtered, washed with water, and dissolved in a small excess of dilute hydrochloric acid. Dilute sodium hydroxide was added to bring the *p*H to about 6–7. At this point this solution was diluted to 20 cc. and divided into two 10-cc. portions. To one of these 10-cc. portions was added a solution of 3 g. of potassium thiocyanate in 3 cc. of water. After standing for 30 min. the oily precipitate was crystallized in an atmosphere of nitrogen from about 5 cc. of ethanol. In this manner, 0.30 g. of a thiocyanate, m.p.

191–192°, was obtained. The crystalline appearance and the melting point are substantially those of 2-methyl-9-phenyl-2,3,4,9-tetrahydro-1-pyridindene thiocyanate.[2]

Nitrate of 2-methyl-9-phenyl-2,3,4,4a-tetrahydro-1-pyridindene (XI). To the other 10-cc. portion mentioned above was added a supercooled solution of 3 g. of potassium nitrate in 5 cc. of water. After 30 min., the supernatant liquor was decanted from the oily precipitate which was digested for a few minutes with about 5 cc. of hot acetone. After standing for about 3 hr. at room temperature, the mixture was filtered. In this manner, 0.30 g. of solid, m.p. 173–175°, was obtained. After crystallization from ethanol, 0.185 g. of crystals melting at 176–179°, were obtained. The compound was further identified by its absorption spectrum as the nitrate of 2-methyl-9-phenyl-2,3,4,4a-tetrahydro-1-pyridindene (XI).[2]

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NUTLEY, N. J.

[CONTRIBUTION FROM THE W. A. NOYES LABORATORY OF CHEMISTRY, UNIVERSITY OF ILLINOIS]

Nitrogen Compounds of the Phosphoric and Phosphonic Acids. III. Preparation and Properties of Amides of Phenylphosphonic and Phenylphosphonothioic Acids[1]

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Phenylphosphonic diamide, $C_6H_5PO(NH_2)_2$ (I), and the thioic diamide, $C_6H_5PS(NH_2)_2$ (II), can be prepared readily by interaction of the respective chlorides with liquid ammonia. Partial alcoholysis of (I) leads to formation of the alkyl P-phenylphosphonamidates, $C_6H_5PO(NH_2)(OR)$, where R = C_2H_5, *n*-C_3H_7, *n*-C_4H_9, and *n*-C_5H_{11}. Partial hydrazinolysis of (I) gives the phenylphosphonamidic hydrazide, $C_6H_5PO(NH_2)(N_2H_3)$, which reacts with *p*-methoxybenzaldehyde and with acetone to form the respective N^2-arylidene(alkylidene)phenylphosphonamidic hydrazides.

Only a limited number of unsubstituted amides of P-alkyl or -arylphosphonic acids have been described in the literature[4,5] and only one of the corresponding thioic compounds has been reported.[6] A convenient method for preparing phenylphosphonic diamide (I), and the previously unknown phenylphosphonothioic diamide (II) is given in the present paper. A new type of reaction by which alkyl P-phenylphosphonamidates, $C_6H_5PO(NH_2)OR$, are obtained by the alcoholysis of (I) is also described. The preparation of phenylphosphonamidic hydrazide by the hydrazinolysis of (I) is also discussed.

Both phenylphosphonic diamide (I) and phenylphosphonothioic diamide (II) were prepared in excellent yields by interaction of the corresponding dichlorides with liquid ammonia. It was found that (II) is much less stable toward hydrolysis than the oxo-analog.

The partial alcoholysis of (I) with ethyl, *n*-propyl, *n*-butyl, and *n*-amyl alcohols resulted in the formation of a new class of compounds that may be designated as alkyl P-phenylphosphonamidates, $RPO(NH_2)(OR)$ (III to VI, respectively). The compounds are solids that can be purified readily by recrystallization. There was no marked tendency for further alcoholysis to the ester to take place. The time required for reaction decreased with increasing molecular weight of the alcohol employed, presumably due in large measure to the progressively higher reaction temperature attained.

Hydrazinolysis of (I) gave phenylphosphonamidic hydrazide (VII), $C_6H_5PO(NH_2)N_2H_3$, in moderate yield. No phenylphosphonic dihydrazide was obtained in the reaction. The identity of (VII) was confirmed (*a*) by cryoscopic studies in water, (*b*) by the determination of the percentage of nitrogen present as hydrazine nitrogen, and (*c*) by conversion into aldehyde and ketone derivatives.

EXPERIMENTAL[7,8]

Phenylphosphonic diamide (I), $C_6H_5PO(NH_2)_2$. Attempts to prepare (I) by the method of Michaelis,[9] based upon the reaction of the acid chloride with concentrated aqueous

(1) For the second article of this series see Smith, Gher, and Audrieth, *J. Org. Chem.*, **21**, 113 (1956).

(2) Abstracted from doctoral dissertation submitted to the Graduate College of the University of Illinois by W. C. Smith (1954).

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(4) Kosolapoff, *Organophosphorus Compounds*, John Wiley and Sons, Inc., New York, N. Y., 1950.

(5) Rätz, *J. Am. Chem. Soc.*, **77**, 4170 (1955).

(6) Michaelis, *Ann.*, **315**, 43 (1901).

(7) The analytical values for the percentage of carbon were outside experimental error in several instances, even though the other analytical values were quite satisfactory. Despite repeated efforts by Mr. J. Nemith, to whom the authors are grateful for carrying out microanalyses of compounds described in this and previous articles of this series, no method for attaining more acceptable values could be developed.

(8) Melting points are uncorrected.

(9) Michaelis, *Ann.*, **293**, 193 (1896).