has the molecular formula $C_{23}H_{20}O_7$ and is an unsaturated ketone containing two methoxyl groups.

Ichthynone kills goldfish at a concentration of, approximately, one part in a million.

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# The Nitrogen Compounds in Petroleum Distillates. XXV. Isolation and Identification of 3- and 4-Cyclopentylpyridines from California Petroleum

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In a recent communication from this Laboratory[4] the chloroform extraction method of Bailey and co-workers[5] was extended to the hydrochlorides of petroleum bases boiling below the quinolines in the hope that, just as in the higher boiling range where the quinolines are found in the water layer and those of the substituted pyridines in the chloroform layer, so in the lower range the water layer might selectively dissolve the hydrochlorides of pyridines carrying cyclic substituents while the chloroform layer might hold the alkyl substituted pyridines. The chloroform layer was indeed found to contain alkyl substituted pyridines of which *dl*-2-(*s*-butyl)-4,5-dimethylpyridine was identified and several others isolated and analyzed.[4]

The water layer from the chloroform extraction of hydrochlorides of bases boiling at 210–213° reported in the previous communication[4] has been studied to determine what type of bases predominate.

Using a combination of fractionation by distillation and by fractional neutralization two isomeric cyclopentylpyridines were isolated. Since 2-cyclopentylpyridine is easily prepared by the interesting reaction of Emmert,[6] this compound was synthesized but it was found that neither of the petroleum compounds was identical with it.

Since one of the petroleum pyridines must then be the 3- and the other the 4-cyclopentylpyridine and since there was not enough pure base available to warrant a study of conditions required to obtain nicotinic or isonicotinic acids by oxidation, the synthesis of 3- and 4-substituted pyridines was studied. The new method of Crouch and Lochte[7] was finally used to prepare both 3- and 4-cyclopentylpyridines and thus show that the base yielding a picrate melting at 117.5° is 3-cyclopentylpyridine and the other one is the 4-cyclopentyl isomer.

## Experimental

### Fractional Distillation of Bases from Water Layer of Chloroform Extraction of 210–213° California Petroleum

**Bases.**—Approximately three liters of bases were obtained from the water layer of the extraction reported in the previous paper.[4] These bases were distilled through a 12-foot Berl saddle-packed steel column at 20 mm. pressure using a 10:1 reflux ratio to yield 13 fractions of 240 cc. boiling at 207–219° with 9 fractions boiling between 212.5 and 214.0°. The index of refraction ranged from 1.502 to 1.516, that of the 9 fractions lay between 1.510 and 1.511, thus indicating that unsaturated or cyclic substituents might be expected.

**Fractional Acid Extraction.**—Fraction 6 (b. p. 213°; $n^{20}\text{D}$ 1.5102) was dissolved in 500 cc. of petroleum ether and extracted in the counter-current apparatus described in the previous paper,[4] Fig. 1, to yield 21 fractions with an average volume of 8 cc. and index of refraction, $n^{20}\text{D}$, ranging from 1.505 to 1.515.

**Isolation of 3-Cyclopentylpyridine.**—Since the index of refraction of the acid extraction fractions indicated that the alkyl substituted pyridines preceded those with cyclic side chain, fraction 19, with a volume of 25 cc. and $n^{20}\text{D}$ 1.5152, was selected to determine what type of substituents are present in the fractions with the high index of refraction. The base was dissolved in sulfurous acid and treated with picric acid. A crystalline picrate formed on standing in the ice-box. It melted at 117.5° after repeated recrystallizations from dilute ethanol and from 50% acetic acid. Additional amounts of the same picrate were obtained from fractions 17 and 18 of the same series.

*Anal.* Calcd. for $C_{16}H_{16}O_7N_4$: C, 51.06; H, 4.26; N, 14.89. Found: C, 50.97; H, 4.16; N, 15.03.

One gram of the picrate was heated with concentrated ammonium hydroxide to liberate the base which was extracted in benzene, dried and distilled in a semi-micro distillation apparatus. A middle fraction gave the following constants: b. p. 215.5° (747 mm.); $n^{20}\text{D}$ 1.5173.

*Anal.* Calcd. for $C_{10}H_{13}N$: N, 9.52. Found: N, 9.55.

**Isolation of 4-Cyclopentylpyridine.**—Fraction 21, volume 30 cc., $n^{20}\text{D}$ 1.5116, yielded a new crystalline picrate which after repeated recrystallizations from dilute ethanol and from 50% acetic acid melted at 145–146° but only a few grams of the pure crystalline picrate were obtained. Since this new base was isolated from the higher boiling fraction of fraction 6 of the distillation series it seemed probable that greater amounts could be isolated from a higher boiling fraction and fraction 11 was fractionally neutralized in the counter current column to yield 21 neutralization fractions. Fractions 10 through 12 yielded only oily picrates but 13 through 21 yielded larger amounts of a picrate melting at 145–146° and showing no depression when mixed with the previous picrate.

*Anal.* Calcd. for $C_{16}H_{16}O_7N_4$: C, 51.06; H, 4.26; N, 14.89. Found: C, 51.20; H, 4.45; N, 14.96.

One gram of the picrate was decomposed as before and fractionated, b. p. 218° (744 mm.); $n^{20}\text{D}$ 1.5167. Both of the cyclopentylpyridines were difficult to analyze, probably because of their tendency to take up moisture.

*Anal.* Calcd. for $C_{10}H_{13}N$: N, 9.52. Found: N, 9.30.

The chloroplatinate of this base crystallizes readily, forming orange needles decomposing at 225–227°.

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(1) A part of this material was presented in partial fulfillment of requirements for the Master's Degree at the University of Texas by E. D. Thomas, 1942.

(2) Present address: Harvard Medical School.

(3) General Aniline Fellow, 1942–1944.

(4) Lochte, Crouch and Thomas, THIS JOURNAL, **64**, 2753 (1942).

(5) Perrin and Bailey, *ibid.*, **55**, 4136 (1933).

(6) Emmert and Pirot, *Ber.*, **74**, 714 (1941).

(7) Crouch and Lochte, THIS JOURNAL, **65**, 270 (1943).

*Anal.* Calcd. for $(C_{10}H_{13}N)_2H_2PtCl_6$: Pt, 27.71. Found: Pt, 27.50.

### Synthesis of 2-Cyclopentylpyridine

**1-(2-Pyridyl)-cyclopentanol.**—This compound was prepared by the method of Emmert and Pirot.[6] Into a three-necked flask fitted with stirrer, condenser, and dropping funnel was placed 155 g. of pyridine, 30 g. of aluminum turnings, and a crystal of iodine. Twenty-three grams of mercuric chloride dissolved in 154 g. of cyclopentanone was placed in the dropping funnel. A reaction started after about 10 cc. of this solution had been added to the flask and the remainder of the solution was now added, a few drops at a time, at such a rate as to keep the reaction mixture refluxing slowly. Finally the mixture was stirred for five hours on a steam-bath before the mixture was poured into cold dilute sodium hydroxide. The base was extracted with ether, dried over potassium hydroxide, and distilled at 5 mm. pressure. The material boiling at 130–140° was collected. It solidified on cooling and was recrystallized from petroleum ether; yield 30.5 g. of white solid melting at 83°.

*Anal.* Calcd. for $C_{10}H_{13}ON$: C, 73.63; H, 8.03. Found: C, 73.63; H, 8.26.

**Dehydration of 1-(2-Pyridyl)-cyclopentanol.**—Six cubic centimeters of concentrated sulfuric acid was added drop by drop to 2 g. of the cyclopentanol. This solution was heated for one hour on a steam-bath, poured on ice, neutralized with sodium hydroxide, and extracted with ether. The yield was practically quantitative; however, when this operation was repeated with 14 times these quantities, a viscous tar formed from which only 8 cc. of 1-(2-pyridyl)-cyclopentene-1 could be isolated. The cyclopentene readily decolorized 2% potassium permanganate. It boiled at 238–239° (748 mm.).

**Hydrogenation of 1-(2-Pyridyl)-cyclopentene-1.**—An acetic acid solution of the cyclopentene was hydrogenated at atmospheric pressure in six hours over Adams catalyst. The resulting base was dried over potassium hydroxide and fractionated, b. p. 217–218° (750 mm.), $n^{20}D$ 1.5205.

The picrate after recrystallization from dilute ethanol and from 50% acetic acid melted at 106.5°. A mixture of this picrate with the picrates of the two petroleum base cyclopentylpyridines melted below 100° thus showing that neither of these was 2-cyclopentylpyridine.

*Anal.* Calcd. for $C_{16}H_{16}O_7N_4$: C, 51.06; H, 4.26; N, 14.89. Found: C, 51.17; H, 4.36; N, 15.03.

### Synthesis of 3-Cyclopentylpyridine

**Diethyl 2-Cyclopentyl-2-(2-cyanoethyl)-malonate.**—Following the general procedure of Bruson and Riener,[8] 19 g. of acrylonitrile was added to a stirred solution of 40 g. of cyclopentylmalonic ester,[9] 40 g. of dioxane, and 1.2 g. of sodium ethylate at 35–40°. The solution was stirred for one hour, the temperature raised to 50° for several hours or overnight with continued stirring. The reaction mixture was neutralized with 10% hydrochloric acid, and extracted with 100 cc. of benzene. The benzene layer was washed twice with 50-cc. portions of distilled water, and the benzene removed on a steam-bath. The residual oil was fractionated at 2 mm. pressure and 30 g. of the cyanoethylation product obtained, b. p. 162° at 2 mm., $n^{20}D$ 1.4612, $d^{20}_4$ 1.0614.

*Anal.* Calcd. for $C_{15}H_{23}O_4N$: C, 64.03; H, 8.24; N, 4.98. Found: C, 64.02; H, 8.26; N, 4.94.

**2-Cyclopentylglutaric Acid**[10] (low melting form).—One hundred grams of the cyanoethylation product obtained as above was hydrolyzed by refluxing with 300 cc. of concentrated hydrochloric acid for twenty hours. The solution was evaporated on a steam-bath and the residue extracted with ether. The ether was evaporated off and the residue heated to 200° *in vacuo* until carbon dioxide ceased to be liberated. The sirupy material remaining was distilled at reduced pressure yielding 44 g. of the very viscous acid, b. p. 176–177° at 1.5 mm. pressure. The acid solidified on standing and was recrystallized from petroleum ether (b. p. 60–75°) to a constant melting point of 69°.

*Anal.* Calcd. for $C_{10}H_{16}O_4$: C, 59.98; H, 8.06. Found: C, 60.03; H, 8.03.

**Diethyl 2-Cyclopentyl-2-(ethyl-3-propionate)-malonate.**—To a stirred solution of 90 g. (0.395 mole) of cyclopentylmalonic ester and 500 cc. of anhydrous xylene was added 8.5 g. (0.37 mole) of clean sodium and the mixture refluxed for three hours. A solution of 75 g. of ethyl 3-bromopropionate and 30 cc. of xylene was added slowly to the refluxing solution and the heating continued for fifteen hours. At the end of this time the solution was allowed to cool, 75 cc. of water added to dissolve the sodium bromide, and the aqueous layer removed. The xylene solution was washed twice with water and the xylene distilled under 40–50 mm. pressure. The residual liquid was fractionated at 2–3 mm. pressure. Sixty-seven grams of the tricarboxylic ester (72% conversion, with 25 g. of cyclopentylmalonic ester recovered) was obtained, b. p. 168–170° at 2.4 mm. pressure; $n^{20}D$ 1.4589; $d^{20}_4$ 1.068.

*Anal.* Calcd. for $C_{17}H_{28}O_6$: C, 62.17; H, 8.59. Found: C, 62.13; H, 8.57.

**2-Cyclopentylglutaric Acid** (high melting form).—Sixty-seven grams of the tricarboxylic ester was hydrolyzed by refluxing with 500 cc. of 10% aqueous potassium hydroxide for forty-eight hours. Concentrated hydrochloric acid was added to neutralize the solution which was then evaporated to dryness on a steam-bath in a stream of air. The sodium chloride–organic acid residue was extracted twice with an ether–alcohol solution, the two extracts combined, and the solvents evaporated on a steam-bath. The sirupy product which remained evolved carbon dioxide on continued heating at 100°. When carbon dioxide ceased to be evolved the residue was dissolved in boiling benzene–petroleum ether and the acid allowed to crystallize out of the solution. After two recrystallizations from petroleum ether 30 g. of 2-cyclopentylglutaric acid, m. p. 152.5°, was obtained.

*Anal.* Calcd. for $C_{10}H_{16}O_4$: C, 59.98; H, 8.06. Found: C, 59.84; H, 8.09.

**2-Cyclopentylglutaryl Dichloride.**—By a modification of Scheiber's[11] procedure 17 g. of the low melting cyclopentylglutaric acid was dissolved in 27.4 g. of thionyl chloride. The solution was warmed to 60° for three hours and finally refluxed for two hours. The excess thionyl chloride was removed under vacuum and the residual oil fractionated at 4–5 mm. pressure. Twenty grams (90%) of the dichloride was obtained, b. p. 140–142° at 4.5 mm. pressure.

*Anal.* Calcd. for $C_{10}H_{14}O_2Cl_2$: Cl, 30.10. Found: Cl, 29.93.

**2-Cyclopentylglutaryl Diamide.**—Eight grams of the acid chloride was poured slowly into 50 cc. of concentrated ammonia and the crystals, which formed after standing in the ice-box overnight, were filtered off. Recrystallization from concentrated ammonia gave 2 g. of white crystals which melted at 174° with the evolution of ammonia.

*Anal.* Calcd. for $C_{10}H_{18}O_2N_2$: C, 60.60; H, 9.13; N, 14.13. Found: C, 60.48; H, 9.18; N, 14.19.

**3-Cyclopentylglutarimide.**—Two grams of the diamide was heated to 200° at 5 mm. pressure in a 10-cc. flask equipped with an internal condenser until the evolution of ammonia ceased. A charred mass remained in the flask but a white solid, m. p. 131°, collected on the condenser. Recrystallization from petroleum ether gave 0.5 g. of white flakes melting at 131°.

*Anal.* Calcd. for $C_{10}H_{15}O_2N$: N, 7.73. Found: N, 7.84.

Eight grams of the cyclopentylglutaric acid (**high melting form**) was converted to the anhydride by refluxing one

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[8] Bruson and Riener, THIS JOURNAL, **65**, 23 (1943).

[9] Verwey, *Ber.*, **29**, 1996 (1896).

[10] Godchot and Taboury, *Compt. rend.*, **153**, 1011 (1911), oxidized 1-cyclopentyl-cyclopentanone-2 and obtained an oil which was identified as 2-cyclopentylglutaric acid merely by means of its copper salt.

[11] Scheiber, *Ber.*, **42**, 1322 (1909).

hour with 12 g. of acetyl chloride, after which the excess acetyl chloride and acetic acid were distilled *in vacuo*. Dry ammonia was passed into the residue at 130–140° for one hour and the product heated to 210° to form the imide which was then purified by recrystallization from benzene and petroleum ether. Four grams of the fine white flakes, m. p. 131°, was obtained. A mixture of this imide and that obtained from the diamide of the low melting cyclopentylglutaric acid showed no depression of melting point, thus showing the two imides to be identical.

*Anal.* Calcd. for $C_{10}H_{15}O_2N$: N, 7.73. Found: N, 7.85, 7.81.

**2,5,6-Trichloro-3-cyclopentylpyridine.**—By a modification of the procedure of Crouch and Lochte[7] an intimate mixture of 1.8 g. of 3-cyclopentylglutarimide and 6.4 g. of phosphorus pentachloride was warmed slowly in a water-bath to 43° at which temperature a vigorous reaction began. When this initial reaction had subsided the mixture was heated to 100° for fifteen minutes and the viscous liquid poured into shallow dishes and allowed to evaporate in a hood. The crystals, which soon formed, were washed into a beaker with ice-water, filtered off, and recrystallized from dilute ethanol and dilute acetic acid. Three grams of the trichloride was obtained, m. p. 141°.

*Anal.* Calcd. for $C_{10}H_{10}NCl_3$: N, 5.59; Cl, 42.46. Found: N, 5.62; Cl, 42.31.

**3-Cyclopentylpyridine.**—A methanol solution of 1.3 g. of the trichlorocyclopentylpyridine was reduced using hydrogen at 20 pounds pressure over palladium–charcoal[12] catalyst. Ninety-five per cent. of the calculated quantity of hydrogen was absorbed in four hours. The solution was now filtered, concentrated, and 15 cc. of 20% sodium hydroxide solution added. The oil, which immediately separated, was extracted with ether, separated from the aqueous layer, and the ether evaporated. The free pyridine base was dissolved in sulfurous acid solution and 1.5 g. of picric acid in a saturated aqueous solution was added. The picrate separated as an oil which crystallized on standing in the ice-box. After alternate recrystallizations from dilute acetic acid and dilute ethanol it melted at 118.7°.

*Anal.* Calcd. for $C_{10}H_{13}N{\cdot}C_6H_3O_7N_3$: C, 51.06; H, 4.26; N, 14.89. Found: C, 50.98, 51.03; H, 4.32, 4.24; N, 15.00, 14.97.

The picrate showed no depression in melting point when mixed with the petroleum base picrate melting at 117.5°, but did show a depression when mixed with the picrate of the isomeric petroleum base.

### Synthesis of 4-Cyclopentylpyridine

**Cyclopentyl Aldehyde.**—Cyclopentyl aldehyde was prepared by the action of magnesium bromide etherate on cyclohexene oxide according to the procedure of Clemo and Ormston.[13] One hundred and twenty grams of cyclohexene oxide gave 9 g. of cyclopentyl aldehyde, b. p. 136°, $n^{20}D$ 1.4432. Clemo and Ormston give the boiling point as 135°.

**3-Cyclopentyl-2,4-dicyanoglutaryl Diamide.**—Following the general procedure of Day and Thorpe,[14] 15.4 g. of recrystallized cyanoacetamide was dissolved in 75 cc. of water, 9 g. of cyclopentyl aldehyde added, the solution clarified by adding 35 cc. of alcohol, then 0.2 cc. of 50% potassium hydroxide added. The solution was shaken vigorously for a few minutes and allowed to stand for two days at room temperature. The white solid which separated was removed by filtration. After two recrystallizations from 95% alcohol 4 g. of a white powdery substance was obtained, m. p. 213° (effervescence).

*Anal.* Calcd. for $C_{12}H_{16}O_2N_4$: C, 58.22; H, 6.51; N, 22.62. Found: C, 58.00; H, 6.55; N, 22.62, 22.55.

**3-Cyclopentylglutaric Acid.**—To 3.3 g. of 3-cyclopentyl-2,4-dicyanoglutaryl diamide was added 8 cc. of concentrated hydrochloric acid and the mixture heated until the solid dissolved. Eight cubic centimeters of water was added and the solution refluxed for five hours. The mixture was allowed to cool and the acid extracted with 50 cc. of ether. After evaporating off the ether, the acid was recrystallized twice from petroleum ether to give 1.7 g. of 3-cyclopentylglutaric acid, m. p. 111.5°.

*Anal.* Calcd. for $C_{10}H_{16}O_4$: C, 59.98; H, 8.06. Found: C, 59.82; H, 8.09.

**4-Cyclopentylpyridine.**—One and one-half grams of 3-cyclopentylglutaric acid was refluxed with 5 g. of acetyl chloride for one hour, the acetic acid and excess acetyl chloride were distilled under vacuum, and dry ammonia passed into the anhydride at 130° for one hour. The product was heated to 210–230° for fifteen minutes to form the imide which was extracted with benzene. This extract gave 1 g. (damp weight) of the imide which was subsequently treated with phosphorus pentachloride to give the corresponding trichloropyridine as before.

The trichloro compound was hydrogenated in methanol–hydrogen chloride solution over palladium chloride–charcoal catalyst.[12] The resulting cyclopentylpyridine was removed as before and the picrate prepared. After several recrystallizations from water the melting point was constant at 146°. The picrate showed no depression in the melting point when mixed with the petroleum base picrate melting at 145°, but did show a depression when mixed with the picrate of the isomeric petroleum base.

## Summary

1. In an extension of a study of California petroleum bases boiling in the 210–213° range, 3-cyclopentyl- and 4-cyclopentylpyridine have been isolated and identified.

2. 2-, 3- and 4-cyclopentylpyridine have been synthesized and characterized.

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[12] Stevens, Beutel and Chamberlin, THIS JOURNAL, **64**, 1095 (1942).

[13] Clemo and Ormston, *J. Chem. Soc.*, 362 (1933).

[14] Day and Thorpe, *J. Chem. Soc.*, **117**, 1465 (1920).