was completely filled with white crystals melting at 143°. A single recrystallization from ethyl alcohol gave 14.7 g. of a compound melting sharply at 153°. This substance was identified as the benzoate of triphenyl-vinyl alcohol; first, by a mixed melting point determination with some of the same compound synthesized after the manner described by Biltz,[1] and second, by saponification with alcoholic potash and identification of the triphenyl-vinyl alcohol and benzoic acid so formed.

Yield of the benzoate of triphenyl-vinyl alcohol based on 10.2 g. of diphenyl ketene, 79%.

Compound Melting at 248°.—The very sparingly soluble compound formed in small quantities was crystallized from hot ethyl alcohol. It contained neither magnesium nor halogen. The compound was found to undergo no change when refluxed for 8 hours with alcoholic potash. This proved that the compound was not the supposed polymer of diphenyl ketene, tetraphenyl-diketo-cyclobutane. Staudinger and Göller[2] found their compound melting at 244–245° to hydrolyze on even milder treatment to tetraphenyl acetone and diphenyl acetic acid.

Likewise, this proved that the compound is not diphenyl-dibenzoyl methane. This compound would be expected if the Grignard reagent had added to the ethylenic linkage of the ketene. 1,3-Diketones are readily hydrolyzed under these conditions to acids and monoketones.

Summary.

The benzoate of triphenyl-vinyl alcohol was obtained when the addition compound of diphenyl ketene and phenyl magnesium bromide was treated with benzoyl chloride. This proves that the Grignard reagent adds to the carbonyl group and not to the ethylenic linkage in ketenes.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF CASE SCHOOL OF APPLIED SCIENCE.]

THE CONSTITUTION OF THE ORGANIC NITROGEN BASES OF CALIFORNIAN PETROLEUM.

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The acid washings of crude Californian petroleum contain a mixture of organic nitrogen bases. By neutralization of the diluted acid these may be made to separate as a heavy, dark brown oil which possesses an odor closely resembling that of an empty cigar box. Californian crudes, according to Engler and Höfer,[3] have the highest nitrogen content of any known petroleum, 2.39%. Japanese oil follows closely with 2.25%

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[1] *Ber.*, 32, 655 (1899).

[2] *Ibid.*, 44, 530 (1911).

[3] "Das Erdöl," 1, 1913.

nitrogen, and Algerian with 2.17%, but, in general, 1.5% is the maximum found. Thus, on the basis of an average molecular weight, there may be as high as 20% of the crude oil composed of organic nitrogenous bases.[1]

The problem of isolating individual bases is, however, no easy task. The mixture of compounds resembles petroleum itself in containing what are apparently whole series of related, homologous substances which can be only approximately separated by many repeated fractional distillations *in vacuo.*

In 1899 careful distillations were carried out by one of the authors on the basic constituents of a Santa Paula, California, oil.[2] The final main fractions, obtained by distillation under 50 to 90 mm. pressure were, according to analysis and molecular weight determinations as follows:

Fraction 130–40° as $C_{12}H_{17}N$.
Fraction 197–99° as $C_{13}H_{18}N$.
Fraction 209–11° as $C_{14}H_{19}N$.
Fraction 215–17° as $C_{15}H_{19}N$.
Fraction 223–25° as $C_{16}H_{19}N$.
Fraction 270–75° as $C_{17}H_{21}N$.

Chlopin concluded[3] that the nitrogen bases of Galician oil consist of a "whole series of substances which have similar properties such as do homologous members of a chemical group," after the analyses of a series of fractionally precipitated double chloroplatinates of the bases.

Very briefly, the previous chemical knowledge of these basic petroleum constituents may be summarized as follows. They form illy-defined precipitates from acid solution with platinum, palladium, mercuric, cadmium, and ferric chlorides, potassium dichromate, ferro- and ferricyanides, and picric and oxalic acids. By oxidation with potassium permanganate in alkaline solution the nitrogen of the bases is evolved in part as ammonia and in part as free nitrogen. Oxidation with chromic acid forms free nitrogen and, in some cases, a small amount of acetic acid. Ethyl iodide adds to the bases if heated with them in a sealed tube. The bases are volatile with steam; they have an odor variously described as "pyridine-," "quinoline-," and "nicotine-like;" they possess rather weakly basic qualities; and, while nearly immiscible with water, they dissolve readily in alcohol, ether, benzol, carbon disulfide, etc.

The conclusion was drawn by Mabery[4] in 1900 from as much data as was at that time obtained, that the bases of Californian petroleum consist of more or less hydrogenated quinolines, for example, tetrahydroquinoline. The experimental facts described in the following show: (1) that by the

[1] C. F. Mabery, This Journal, 28, 426 (1906).

[2] C. F. Mabery, *J. Soc. Chem. Ind.*, 19, 505 (1900).

[3] *Ber.*, 33, 2837 (1900).

[4] *Loc. cit.*

careful oxidation with potassium permanganate of the various members of the series of fractions obtained by the vacuum distillation of the basic mixture from Californian petroleum, *pyridine pentacarboxylic acid* and methyl *pyridine tetracarboxylic acid* are obtained; (2) that no aliphatic acid is formed in an appreciable amount by this permanganate oxidation, and that the very small quantity (trace) which is actually produced has only the properties of the lowest aliphatic acids and not those of butyric acid or higher; (3) that by chromic acid oxidation of one of the members of the series of fractions, and subsequent dry distillation of the calcium salts of the organic acids thus formed, β-methyl quinoline is produced; (4) that by reduction of various members of the series of fractions with nascent hydrogen and with hydriodic acid, hydrogen atoms are added, and that the nitrogen atom of the molecule is thereby converted from a tertiary to a secondary atom; (5) that the elementary composition of 2 more completely purified fractions corresponds to that of alkylated quinolines (or isoquinolines); and (6) that the general chemical behavior of the bases is not contrary to that which might be expected of highly alkylated quinolines (or isoquinolines).

The conclusion is then drawn that the organic bases of Californian petroleum consist mainly of an indefinite mixture of alkylated quinolines (or isoquinolines), which, as regards the nitrogen-containing ring are completely alkylated, and the alkyl side chains of which consist of small groups only.

Experimental.

The bases from Santa Paula, California oil were fractioned in 1899, at first under atmospheric pressure, then immediately, because some decomposition was evident, under partial vacuum, so that none of the 15 or so final fractions was ever distilled under atmospheric pressure. After many careful distillations at 50 to 90 mm. pressure, 2 to 4° fractions were finally collected covering a range of 130 to 283°. The best fractions were analyzed for carbon, hydrogen and nitrogen; their molecular weights and specific gravities determined; platinum double salts prepared; and various oxidation decomposition reactions attempted, the latter mainly with negative results.

In 1916–17, when the present work was carried out, these samples were brown, viscous to very viscous liquids, one or two of the highest fractions becoming amorphous, resinous solids when cooled with ice. Some of the fractions were much lighter in color and less viscous than their immediate neighbors. The odor of all was nicotine-like. They were nearly insoluble in, and much heavier than water, but readily dissolved in alcohol, ether, acetone, chloroform, carbon disulfide, etc. They were also readily soluble in dil. and conc. acid, separating again on the addition of alkali.

Various representative fractions were first submitted to regulated oxidation by neutral permanganate, with the result that pyridine penta- and methyl-pyridine tetracarboxylic acids were formed.

The permanganate oxidations and isolation of the silver salts of the organic acids thus formed were carried out in the following way:

Three g. each of representative fractions was boiled with 2% potassium permanganate solution until the liquid became decolorized. More permanganate, in concentrated solution, was then added to the liquid, the boiling continued until decolorization again took place, and so on, until the color of the solution produced by fresh portions of permanganate disappeared only very slowly indeed. From 25 to 40 g. of permanganate according to the basic fraction used, was necessary to accomplish this result in from 2 to 3 days. A 2-liter, round-bottomed flask, provided with reflux condenser, was used. A second small tube reached to the bottom of the flask, and through this a slow current of air could be drawn to agitate the heavy precipitate, and prevent extreme bumping. The manganese dioxide and a small amount of unattacked base which always remained, were filtered off and the filtrate made somewhat acid with 2 cc. of conc. nitric acid, beyond the neutral point. The acidified liquid was reduced to a small volume by distillation, the distillate serving for the detection of any volatile acids which might have been formed by the oxidation reaction, and the residue for the non-volatile ones.

We shall consider first the identification of the latter, the non-volatile organic acids. For this purpose, the concentrated liquid was transferred to an evaporating dish and evaporated to complete dryness. The residue of dry salts was pulverized and thoroughly extracted for 3 hours with boiling alcohol in a Soxhlet apparatus. Into the alcohol passed resinous colored products, some potassium nitrate, and an organic, nitrogen-containing acid which, on the addition of a silver nitrate solution, formed a voluminous, white precipitate of the difficultly soluble silver salt. This product will be mentioned later.

That portion of the dry salt residue which had not dissolved was then freed from alcohol, and taken up in 200 cc. of hot water. To this aqueous solution is now added an excess of silver nitrate solution, which forms a white, voluminous precipitate, somewhat more soluble with increasing acidity of the solution.

To effect at least a partial purification of this precipitate, it was filtered off and dissolved, insofar as possible, in boiling hot 1% nitric acid solution. The insoluble residue which always remained in varied small amounts was filtered off. Upon cooling the hot filtered solution, a precipitate re-formed, but the main portion separated only after the addition of sodium acetate to reduce the acidity. The product was now filtered off, washed, and dried to constant weight at 120–5°.

This product was examined with little hope at first that it would represent an individual product of the oxidation. When prepared, however, from the basic fractions of the most varying range and with quite radical modifications in the conditions of the reaction, quite the same analytical values were obtained.

The silver salts thus obtained were nearly white, do not darken at all upon boiling the water in which they are suspended, nor easily upon exposure to the light, nor upon heating them in a dry state to a temperature as high as 130°. They do, however, decompose explosively upon ignition. A distinct odor of pyridine, along with other aromatic odors, is produced by their decomposition, and a voluminous residue of silver and carbon is left. The explosive character of these salts made necessary the admixture of fine copper oxide powder in the analyses of them for carbon and hydrogen.

"Base 176–78°," requiring for 3 g. 30 g. of $KMnO_4$, gave, from its "alcohol insoluble" product, a silver salt of the following composition: C, 16.40, 16.27; H, 0.37, 0.25; N, 2.38; Ag, 60.54, 60.51.

The silver salt similarly prepared by the oxidation of 3 g. of "Base 130–32°," requiring 28 g. $KMnO_4$, contained: C, 16.43, 16.30; H, 0.40, 0.10; N, 2.25, 1.90; Ag, 60.66.

That from 3 g. of "Base 200–2°," which required 40 g. $KMnO_4$ for complete oxidation, contained: C, 15.62, 15.41; H, 0.18, 0.27; N, 1.61, 1.55; Ag, 59.80, 59.65.

That from 3 g. of "Base 209–11°," which required 38 g. $KMnO_4$, gave: C, 16.11, 15.86; H, 0.23, 0.24; N, 1.91, 1.77; Ag, 60.59, 60.37.

The values may be tabulated as follows:

	Average %.	C. %.	H. %.	N. %.	Ag. %.	O. %.
From Base	130–2°"	16.37	0.25	2.08	60.66	20.64
	176–8	16.34	0.31	2.38	60.53	20.44
	200–2	15.52	0.23	1.58	59.73	22.94
	209–11	15.99	0.24	1.84	60.48	21.45
Grand average,		16.06	0.26	1.97	60.35	21.37
$C_{10}HNAg_4O_{10}$ (calc.),		16.51	0.14	1.93	59.41	22.01

$C_{10}HNAg_4O_{10}$ represents the tetra-silver salt of pyridine pentacarboxylic acid. A difference of one methyl group would cause a variation of 1.3% in the carbon content, whereas the greatest variation from the mean, and also the greatest variation of the averages from the calculated value is in the case of carbon which is 0.5%.

The silver content of an acid salt might well be expected to deviate from any exact atomic proportion. Because it was of greater importance in this case to learn the composition of the acid to which the silver atoms were combined than to know which salt of that acid might be present, the percentage of silver was deducted from 100%, and the carbon, hydrogen, nitrogen, and oxygen values for the "organic residue" calculated on that basis. This has been done for the average percentages given above.

Average % for	C.	H.	N.	O.
"Organic residue" of product	40.50	0.64	4.97	53.99
$C_{10}HNO_{10}$ calc	40.68	0.34	4.74	54.25
Difference	—0.18	+0.30	+0.20	—0.26

Although the analytical errors have been doubled, we find a striking closeness between the 2 sets of figures. The acid which corresponds to the silver-containing compound, insofar as one may judge from the analytical figures, may well be *pyridine pentacarboxylic acid.* A confirmation of the pyridine nucleus of this acid was accomplished by the preparation of pyridine itself from the barium salt of the same acid.

Identification of the Pyridine Nucleus.—For this purpose the barium salt of the acid was prepared and dry-distilled, whereupon a distillate was obtained whose chief component was pyridine.

To obtain an aqueous solution of the acids, the same procedure as before in oxidation was followed. Barium chloride solution was added to the acidified filtrate after the addition of sodium acetate. The barium salt was a pure white, voluminous precipitate, which was dried and dry-distilled. The distillate was completely soluble in water, and possessed a strong, distinct pyridine odor. The distillate was acidified with hydrochloric acid, and warmed with an excess of sodium nitrite solution to decompose all ammonium hydroxide present. The solution was now evaporated to $^1/_2$ its volume, and distilled with an excess of conc. sodium hydroxide solution. The distillate was then redistilled once. An excess of picric acid, in alcoholic solution, was added to the solution, which was heated and then cooled. The voluminous precipitate of long, slender, yellow needles which formed, was recrystallized from hot alcohol, washed, and dried. The m. p. was found to be somewhat unsharp at 158–159°.

It appears that the m. p. of pyridine picrate is only with difficulty brought up to its maximum and correct value. Recrystallization of the picrate was, therefore, not attempted, but, instead, some was mixed with an equal amount of pyridine picrate prepared from pure pyridine and picric acid, and recrystallized from alcohol. The m. p. of the pure picrate was 160–2°, that of the mixture 158–60°, and that of the unknown picrate, as just stated, was 158–9°. It is apparent that the admixture of pyridine picrate with the unknown picrate raised, if anything, the m. p. of the latter, and that the unknown picrate did not appreciably lower the m. p. of the pure pyridine picrate when intimately mixed with it. The crystals of the 2 picrates were, moreover, indistinguishable in form from one another.

The base formed by the distillation of the barium salt of the acids which correspond to the analyzed silver salts of the acids is, therefore, identified with certainty as pyridine. This fact, in conjunction with the above analyses, demonstrates that pyridine pentacarboxylic acid is formed by the oxidation of each of 4 representative fractions of the bases.

The Silver Salt from the Alcohol-Soluble Salt Residue.—To return now to the silver salt which had been prepared from the alcohol-soluble portion of the dried, potassium-salt residue. After reprecipitation from hot water, this silver salt gave indications, by its analysis, that it was an acid salt of methyl-pyridine tetracarboxylic acid. (See Analysis No. 1 below.)

Also, what is apparently the same compound was obtained in a somewhat different manner. The salt residue was treated twice with hydrochloric acid, and the excess acid and water again expelled. The pulverized residue was now exhaustively extracted with ether. Finally, $^3/_4$ g. in all of a viscous, yellow or brown oil was obtained which would not crystallize either on long standing or after $^1/_2$ hour in a freezing mixture. A silver compound was prepared from one of its components, however, by the addition of silver nitrate to its solution. To purify the precipitate thus formed, as much of it as possible was dissolved in boiling water, the insoluble residue filtered off hot, and the salt separated by cooling the filtrate. The product was washed and dried, at first in an oven, then, as darkening was noticed, in a vacuum desiccator to constant weight.

Average % for	C.	H.	N.	Ag.	O.
No. 1. From "alcohol-soluble".........	25.7	1.8	3.8	43.0	25.7
No. 2. From "ether-extracted"........	25.3	1.8	3.3	44.1	25.5
Grand average........................	25.5	1.8	3.6	43.5	25.6
$CH_3C_5N(COOAg)_2$ $(COOH)_2$(calc.)......	24.8	1.0	3.0	44.7	26.5

These figures indicate, when taken in conjunction with what has preceded, that a product is extracted from the salt residue, after oxidation, by alcohol, and after further acidification, by ether, which gives the disilver salt of *methyl-pyridine tetracarboxylic acid.* It is of value to note here that the amount of this product was found to be much greater in the earlier experiments in which, as it now proves, somewhat less than the maximum amount of permanganate was used, while in the later experiments, in which the oxidation was carried further, the amount of this product was so small that it was not worth working upon.

As the results obtained in the oxidation of the bases by permanganate show that the final stage is pentacarboxy pyridine, the assumption is here reasonable, on the basis of the analytical figures, that the salt which corresponds to the alcohol- and ether-soluble portion is one of methyl-pyridine tetracarboxylic acid.

It may be mentioned here that the total weight of the *purified* silver salts obtained was about $^1/_2$ of the theoretical amount from 3 g. of the basic fractions.

The organic acids themselves, which correspond to these silver and barium salts, were obtained in the following manner: One g. of a basic fraction was oxidized by hot, dilute potassium permanganate solution as before, and the filtrate from the manganese dioxide evaporated to dryness. An excess of hydrochloric acid was now added to the residue, and it was again carried to complete dryness. The residue was now extracted a number of times with ether, and from the ether there was obtained, by evaporation, a few mg. of white, fern-like crystals. The amount could not be increased beyond this point as further ether extraction took out more and more of a brown impurity from which the crystals separated with greater and greater difficulty.

The crystals were those of an organic acid, very easily soluble in water and alcohol, but dissolving only with much difficulty in ether. The aqueous solution gave with ferrous sulfate a deep wine-red coloration which faded to yellow on the addition of ferric chloride. (All known pyridine acids possessing at least one carboxyl group in the α-position give a red color with ferrous sulfate solution.) Its hydrochloric acid solution did not precipitate platinic chloride, either with or without the simultaneous addition of alcohol. Its aqueous solution evolved carbon dioxide rapidly from silver, calcium, barium, etc., carbonates, and when filtered hot from the excess of metal carbonate, gave a precipitate of metal salt in each case on cooling. The silver salt formed a voluminous, white precipitate, the barium and calcium ones are rather more granular. The calcium salt was the more soluble, and on evaporation, thin, colorless plates of right angle cleavage separated at the edges of the concentrated solution.

A small amount of white, needle-shaped, acid crystals were obtained by extraction from the acid residue from the oxidation of "Base 142–6°." These were pressed out on a porous plate, moistened several times with a drop or two of water, and air-dried. A melting-point determination made upon them showed them to melt with darkening and gas evolution between 160 and 170°.

Although the melting points of the pyridine carboxy acids are not sufficiently definite and characteristic in general to lend themselves well to the purposes of identification, several careful attempts were made to prepare a pure sample of the organic acid through the barium and silver salts. The former was treated in solution with an amount of sulfuric acid exactly equivalent to its barium content; and the latter, finely ground, was suspended in boiling water while hydrogen sulfide gas was bubbled through the liquid for 5 hours. Only semi-liquid or amorphous products were obtained, however, in place of the acids.

No appreciable amount of aliphatic acid is formed by the permanganate oxidation. Other evidence afforded by permanganate oxidation of the bases was obtained by the examination of the distillates from the acidified filtrates in each case. To each one was added a slight excess of alkali carbonate, and the solution was evaporated to dryness. The salt residue was decomposed by conc. hydrochloric or sulfuric acid in slight excess, and the acid solution extracted with ether, the ether evaporated, and the residue examined for acid.

The amount of carbonate required was, in all cases, very small, notwithstanding the fact that some mineral acid always distilled over, and the organic acid residue from the evaporated ether, consisting of an aqueous solution of the volatile acids, was never greater than a drop or two.

Several residues were tested with alcohol and conc. sulfuric acid for ester formation. The odor in each case tried was distinctly that of acetic ester, except in that of "Base 164–166°," of which the odor seemed to be richer, more like that of propionic or butyric ester. In no case, however, was a rancid-smelling, volatile acid obtained from these distillates; they had always the sharp, biting odor of conc. acetic acid.

There was always present, in greater or lesser amounts, an insoluble, steam-volatile product which contaminated the lighter acid. An attempt to prepare the pure *p*-toluide of the volatile fatty acid for its melting point identification was not successful, as the amount of acid was too small, and it was too impure. One can safely affirm, however, that from none of the fractions ranging from "Base 132–134°" to "Base 270–283°" were appreciable amounts of higher fatty acids formed. A molecular amount from an average base would be about $^1/_2$ g. from 3 g. of base.

These facts argue against the presence in the molecule of side-chains of any considerable length.

Chromic acid oxidation gave an organic acid product which, when distilled from lime, gave β-methyl quinoline. Potassium dichromate, added to a solution of one of the bases in sulfuric acid, precipitates a yellow, finely divided oil, which soon collects and clings to the side of the test tube as a brown, viscous mass. On warming the mixture, a peppery odor similar to that obtained by *acid* oxidation with permanganate is noticed.

Three g. of "Base 166–168°," dissolved in dil. sulfuric acid, was oxidized by 25 g. of chromic oxide, also contained in dil. sulfuric acid. The oxidizing agent was added in portions, the flask heated between additions, then cooled before the next treatment. At first, the double acid chromate separated upon each fresh addition, and only gradually disappeared on heating. After the oxidation, the sulfuric acid was partially neutralized with lime, the precipitate filtered off hot, lime then added to the filtrate in excess, the mixture evaporated to complete dryness, the mass pulverized, and the small amount of unattacked base remaining completely extracted out of the solid residue by ether.

The mass was then submitted to careful dry distillation. The distillate consisted of an aqueous portion and oily drops. It was acidified, the oily drops dissolving, and boiled to a diminished bulk after the addition of an excess of sodium nitrite solution to destroy the ammonia which interferes with the identification of organic picrates. Now, by distillation with caustic, the other basic constituents were recovered, and were then converted into their picrates by the addition of an alcoholic picric acid solution. The first m. p. of the product was very unsharp, between 170 and 180°, but, after several recrystallizations from hot alcohol, it was raised to a sharp m. p. at 187–188°. This is, in all probability, the picrate of β-methyl-quinoline, m. p. 187°.

β-Methyl-quinoline may represent a β-methyl-carboxy quinoline which is known to be a resistant stage in the oxidation before the disruption of the quinoline nucleus in certain other cases.

Reduction of the bases converts the tertiary atom into a secondary one. Nascent hydrogen from sodium amalgam and alcohol, from zinc and acetic acid, and from tin and hydrochloric acid, as well as the action of hydriodic acid at 290–300° reduces the various basic fractions by hydrogen addition. As an example is the following:

22 g. of "Base 164–166°" was reduced by the use of mossy tin and conc. hydrochloric acid. The reduction occupied one day, and 200 cc. of the acid was used, 50 g. of tin being added in each portion at intervals. A large part of the hydrochloric acid was then evaporated off, the remainder neutralized with an excess of caustic, and steam-distilled. This last process was so slow that the separation was finally made by benzene extraction. The solvent was then evaporated, and the residue distilled *in vacuo*. The most constant fraction, 208–210°, at 90 mm. was a light, reddish brown, rather mobile oil. When analyzed for its carbon and hydrogen content it gave

	C.	H.	N (diff.).
No. 1	83.30	9.81	
No. 2	82.58	9.66	
Average	82.94	9.74	7.32

This composition corresponds nearly to that of an alkylated quinoline, $C_{14}H_{17}N$, *plus* 3 or 4 hydrogen atoms. Thus, the calculated composition of the latter would be:

	C.	H.	N.
For $C_{14}H_{21}N$	82.75	10.35	6.90
For $C_{14}H_{20}N$	83.16	9.91	6.93
The product analyzes as	82.94	9.74	7.32

It is certain that in the reduction process some of the base escaped action because of the formation of an insoluble double compound of tin chloride and base hydrochloride. This separates from even the conc. acid, is soluble in benzene, and was found in the residues in the flask from the above described distillation in the form of a dark brown, viscous oil, from which the tin is not to be precipitated by hydrogen sulfide.

That reduction has taken place upon the nitrogen ring and upon the nitrogen atom, is strongly indicated by a comparison of the actions of nitrous acid upon the basic fractions before and after treatment with nascent hydrogen. To a hydrochloric acid solution of one of the basic fractions before reduction, add a solution of sodium nitrite. An extremely small amount, if any, of an insoluble oil separates, and neutralization of the solution gives again the original base apparently unchanged by the reaction. Thus, its nitrogen atom is evidently a tertiary one.

If, however, a sodium nitrite solution be added to the solution, in acid, of one of the *reduced* bases, a reddish oil is formed in generous quantities which may be taken up in ether. The ether solution has a light color, and, on evaporation, a red liquid is left which is difficultly soluble in even conc. hydrochloric acid. Upon boiling this strongly acid solution for some minutes, and then making it alkaline, only a brownish oil, apparently the reformed base, separates.

The reddish oil which nitrous acid has formed gives, after it has been separated by the use of ether, the ether then washed thoroughly with dil. acid and evaporated off, a bright greenish blue product on treatment with phenol and sulfuric acid. (Liebermann's color reaction of nitroso amines.)

From all the evidence it seems that the nitrous acid forms a nitroso compound, a nitroso amine, of a base possessing one hydrogen atom attached to its nitrogen atom, and that reduction has taken place upon the nitrogen-containing ring and nitrogen atom of the base.

The elementary analysis of a redistilled basic fraction, and of an acid ferrocyanide gave carbon, hydrogen and nitrogen ratios of alkylated quinolines (or isoquinolines). 26 g. of a rather viscous fraction was distilled under reduced pressure. The largest fraction, which came over mainly between 188 and 195° at 14 mm. pressure, was yellowish in color with a very slight greenish fluorescence, and was somewhat viscid. Upon analysis it gave

Calc. for an alkylated quinoline containing 15 C atoms: C, 84.51; H, 8.92; N, 6.57.
Found: C, 85.25; H, 8.61; N, by diff., 6.14.

This analysis confirms the values given by the analysis of the same distillate collected under a lower pressure in the earlier work: C, 84.39; H, 8.97; N, 6.25, and the formula $C_{15}H_{19}N$ shown by its molecular weight 209, calculated 213.

It must be mentioned, however, that some of the lower boiling basic fractions undoubtedly contain too little hydrogen to correspond exactly in composition to an alkylated quinoline, while some of the higher boiling ones contain somewhat too much. Taken all in all, the conclusion to be drawn from the elementary analysis of the basic fractions may be only that the average composition agrees as well as might be expected with the carbon-hydrogen ratio of an alkylated quinoline.

The second method which was used for determining the carbon-hydrogen ratio was by the analysis of the greenish colored acid ferrocyanide which is formed by the addition of potassium ferrocyanide solution to an acid solution of a base.

To 3.5 g. of "Base 196–198°" in dil. hydrochloric acid solution was added 8 g. of potassium ferrocyanide in aqueous solution. A yellow-green, finely crystalline precipitate, more soluble in hot water than in cold, was formed. This was filtered off, and washed, then dissolved in boiling water. Upon cooling the solution, a dark green, somewhat sticky precipitate formed. This was filtered off, and to the filtrate 5 cc. of conc. hydrochloric acid was added. This separated out a light yellow-green precipitate which was filtered off, washed, and dried. Analysis gave, as an average of two determinations

C, 65.31; H, 6.12; N, 19.11; Fe, 9.31.

The basic fraction used in the preparation of this acid ferrocyanide is, according to its carbon-nitrogen ratio, and molecular weight, a C_{13} base. The formula of an alkylated quinoline containing 13 carbon atoms is $C_{13}H_{15}N$, and its acid ferrocyanide, $(C_{13}H_{15}NH)_2H_2Fe(CN)_6$, would have the calculated composition C, 65.55%; H, 5.81%; N, 19.11%; Fe, 9.53%.

If the base be assumed to contain one more hydrogen atom than an alkylated quinoline, its acid ferrocyanide, $(C_{13}H_{16}NH)_2H_2Fe(CN)_6$, would contain C, 65.33%; H, 6.13%; N, 19.05%; and Fe, 9.49%. The composition of the base "C_{13}" lies, therefore, near that of the alkyl quinoline ratio $C_{13}H_{15}N$.

The gummy, dark green precipitate first mentioned, quite evidently impure, contained C, 70.5%; H, 8.1%; Fe, 8.7%.

Additional Reactions.

Bromine.—If liquid bromine be added to one of any of the bases, a vigorous reaction takes place; hydrogen bromide is evolved in large amounts, and a dark, resinous product is formed which can not be obtained in a crystalline condition.

On the other hand, if a solution of bromine in chloroform or carbon disulfide be added to one of the bases dissolved in the same solvent, no hydrogen bromide is given off; a dark brown oil separates, and much heat is evolved. The oil is slightly soluble in conc. hydrochloric acid, and more so when heated. It may be dissolved in hot alcohol, but on cooling the solvent, it again separates as an oil. Conc. sulfuric acid decomposes it with evolution of hydrogen bromide; heating does this as well. Fuming nitric acid has little or no apparent action even upon continued heating.

A brominated preparation was analyzed. The solvent, carbon disulfide, had been cooled during the addition of the bromine, and the solvent and excess bromine evaporated at the room temperature. The more brominated, less basic, product was separated from the less brominated by treating with conc. hydrochloric acid, washing with dil. hydrochloric acid and water, each time acting over a thin layer of the insoluble oil and manipulating it to get as thorough action as possible. The product was then dried in a vacuum desiccator over calcium chloride for 2 days, and analyzed by Carius' method for bromine.

The average bromine content found was 60.3%. $C_{14}H_{17}NBr_4$ is calculated to contain 61.6% of bromine ("C_{14}" because it was this fraction used, and "H_{17}" because the bromine content varies but little on variation of 2 or 3 hydrogen atoms, and this represents the quinoline ratio). It therefore appears that this product is mainly $C_{14}H_{17}NBr_4$.

The addition of bromine to quinoline in carbon disulfide solution also gives a tetrabromo-quinoline of unknown orientation, which is soluble in water and dil. acids, but, unlike this product, is easily soluble in alcohol, ether, and carbon disulfide.[1]

The compound is slightly soluble in acidified water, as, on the addition of alkali to dil. acid which has been agitated with it, a fine emulsion appears. Silver nitrate solution forms silver bromide from a sample of the brominated product which has been thoroughly freed from uncombined bromine. With conc. sulfuric acid, or by heating, hydrogen bromide is freely evolved from the brominated base. The residue from which no more hydrogen bromide is evolved, does not give a silver bromide precipitate upon heating it with conc. nitric acid and thereupon diluting and adding silver nitrate solution.

Iodine.—Iodine in chloroform solution separates a brown, amorphous mass from the chloroform solution of any of the bases. This product can not be recrystallized from any solvent in a solid form. Apparently the same product is formed when hydriodic acid is used for the purpose of reducing the bases.

Hydriodic Acid.—One of the basic fractions was heated 3 hours at 290–300° with 52% hydriodic acid solution in a sealed tube. Only reduced base, as shown by test with nitrous acid on the acid-soluble portion of the product, and an iodine addition product were obtained.

Phthalic Anhydride.—Phthalic anhydride condenses with the basic fractions in what is evidently a phthalone formation. Alkylated quinolines possessing a methylene group in the α-position are known to be capable of condensation with phthalic anhydride; quinaldine, for example, α-methyl quinoline, forms in this manner phthalone itself or "quinoline yellow," $C_6H_4NCHCOCC_6H_4$.

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[1] Claus and Isetel, *Ber.*, **15**, 820 (1882).

The experiment with one of the petroleum bases was carried out as follows: 2 g. of a medium fraction was heated with one equiv. (1.5 g.) of phthalic anhydride and one g. of zinc chloride for 4 hours at 160–170° in an open flask on a sand bath. Without the zinc chloride the condensation did not occur, even with severe heating with a free flame. The product is a dark, resinous mass which may be crystallized from alcohol. The alcoholic solution colors cloth and paper a brilliant yellow which is fast to washing.

The action of fuming sulfuric acid and of bromine in chloroform solution regenerates phthalic acid from this condensation product.

Fuming Sulfuric Acid.—Experiments with several of the basic fractions showed that one of the lower fractions was capable of sulfonation without great difficulty, whereas a medium fraction was found to be extremely resistant.

"Base 134–136°" was heated overnight at 120–130° with an excess of fuming sulfuric acid. A portion of the acid solution was diluted with water, whereupon some very finely divided charred matter separated. The acid was neutralized with an excess of barium carbonate. During this part of the process the great emulsifying power of the solution was noted in the permanent froth acquired by shaking it. After the last addition, a small amount of free base was liberated. The solution was filtered while boiling hot, and the filtrate evaporated to a small bulk; a generous amount of thin, flat, transparent crystals of a barium sulfonate of the base separated.

To the remainder of the solution an excess of alkali was added, and the unsulfonated base extracted with ether. The unattacked base amounted to about $^1/_4$ of the weight of base originally taken.

A small quantity of a much higher boiling basic fraction, "Base 192–194°," was heated at 125 to 130° with an excess of fuming sulfuric acid for 14 hours. From the large amount of charred and recovered base, and the small amount of soluble barium sulfonate, it was evident that this higher basic fraction was much more resistant than the lower one to the action of fuming sulfuric acid.

Nitric Acid.—Fuming nitric acid reacts violently with the bases. Conc. nitric acid has no action in the cold, but apparently has some action on continued heating. Dil. nitric acid has no apparent action, either in the hot or cold.

Platinum Chloride.—Chloroplatinates of the bases were desired for identification and analysis. The hydrochloride of "Base 192–194°" forms a very finely granular, yellow precipitate with platinic chloride, which is soluble in hot, and difficultly soluble in cold water. Its m. p. was unsharp at 120–125°. On attempting to recrystallize this precipitate from hot water, decomposition was noted, and a brown, resinous substance separated. On account of the instability thus indicated these salts were not used.

The brominated base does not give a precipitate with platinum chloride.

Phosphorus Pentachloride and Potassium Permanganate on the Benzoylated and Acetylated Reduced Bases. Attempts to Break Open the Nitrogen Ring for Purposes of Orientation.—The use of phosphorus pentachloride in breaking open the nitrogen ring of piperidine and of tetrahydroquinoline and of similar compounds, after the stability of the nitrogen-containing ring has been first diminished by benzoylation of the base is the method of von Braun.[1] As an illustration of this method is the conversion, thereby, of benzoyl piperidine to benzoyl-chloro-amyl-amine, $C_6H_5CONH(CH_2)_5Cl$, and to dichloro-pentane, $Cl(CH_2)_5Cl$.

4.5 g. of "Base 164–166°" which had been reduced by nascent hydrogen, was shaken with 15 g. of benzoyl chloride in portions in the presence of an excess of 10% sodium hydroxide solution. At the end of the reaction ether was added, and the ether layer repeatedly washed with caustic solution, then twice with dil. hydrochloric acid and with water. A sticky, oily, sweetish-smelling, brown residue was left, which, in ether solution, was dried overnight with powdered calcium chloride. After filtration through a cotton plug, and evaporation of the ether in a vacuum desiccator, 3.2 g. of a reddish gum of a sweetish odor was left. It may be mentioned here that since the basic fractions themselves resist benzoylation, it is necessary to first reduce them for benzoylation.

According to the suggestion of von Braun, purification of this substance was not attempted at this stage. It was heated with phosphorus pentachloride without further treatment. This last operation, by chlorination, might be expected to break open the nitrogen-containing ring, the stability of which has been diminished, as von Braun showed in analogous cases, by the influence of the benzoyl group and quinquivalence of the nitrogen in an intermediate product.

The 3.2 g. of benzoylated product was heated with the calculated weight of phosphorus pentachloride to 120°. The reaction which took place was very vigorous, accompanied by gas evolution, and, after its intensity had diminished, the temperature was increased to 150 to 160° for $^1/_2$ hour. After cooling the flask, ice water was added in portions until all phosphorus halogen compounds had been decomposed. The remaining oil was treated with the smallest possible amount of hot, absolute alcohol, which dissolved it easily, but from which it did not crystallize of itself, nor by the aid of precipitants.

As no pure product could be crystallized out and identified, the decomposed, benzoylated, reduced base was investigated by oxidation with

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[1] *Ber.*, 37, 2818 (1904).

permanganate. All of these results were negative in result, as were those of the oxidation by permanganate of some of the acetylated reduced bases.

Conclusion.

The chemical evidence as to the nature of these bases isolated from Californian petroleum supports the following views:

They consist mainly of alkylated quinolines (or isoquinolines).

Three alkyl groups are united to the α-, β- and γ-carbon atoms of the nitrogen-containing ring in all from the lowest to the highest members. Formation of pentacarboxy and methyl-tetracarboxy pyridine; the production of methyl-quinoline also agrees with this.

In the lowest fraction, $C_{12}H_{13}N$, since 3 side chains must be present, these must consist of 3 methyl groups, as the quinoline radical itself accounts for 9 out of the 12 carbon atoms.

Phthalone formation also requires a $—CH_2$ or a $—CH_3$ group in the α- or γ-position in the nitrogen-containing ring.

None of the alkyl groups represents a long side chain (more than 4 carbon atoms), even in the bases of high molecular weight, as indicated by the absence of propionic, butyric, or higher fatty acids in the oxidation products.

The behavior of the basic fractions with bromine, iodine, hydriodic acid, fuming sulfuric acid, platinic chloride, phthalic anhydride, nascent hydrogen, nitrous acid, acetylating and benzoylating agents, and mild and strong oxidizing agents is in entire conformity with these conclusions, and no fact was discovered which was antagonistic to them.

If the bases are then as simple substances as are the alkylated quinolines and isoquinolines, it may be asked why their identification could not follow from the preparation of simple salts as picrates, chloroplatinates, and double mercury compounds. It appears that this is because all of the fractions of the series of bases represent mixtures which can be fairly well separated into stages as regards molecular weights, but are difficult to separate into individual substances. The facts cited in experimental evidence for the character of the compounds represent what might be expected from a mixture of quinoline and possibly isoquinoline derivatives, a small part more, a small part less highly alkylated than the average, and containing perhaps a small percentage of hydrogenated nuclei or of pyridine derivatives.

These admixtures would, no doubt, easily prevent the crystallization of the bases constituting the main portions, as these, under favorable circumstances, are difficultly enough solidified; and also would prevent the crystallization of products of reactions in which all of them might take part, or in which the products are, at best, difficult to crystallize.

The mixture of even 90% of an individual base with a total of 10% of isomers, homologs, and near homologs, would give a mixture which would have all of the propertes found in the experimental work. Such a mixture might reasonably be expected to be formed in petroleum production.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS AND FROM THE ABBOTT LABORATORIES, OF CHICAGO, ILLINOIS.]

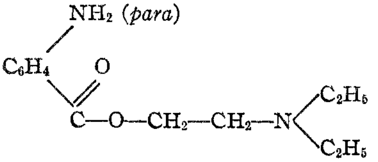
THE RELATIONSHIP BETWEEN CHEMICAL CONSTITUTION AND PHYSIOLOGICAL ACTION IN LOCAL ANESTHETICS.

I. HOMOLOGS OF PROCAINE.

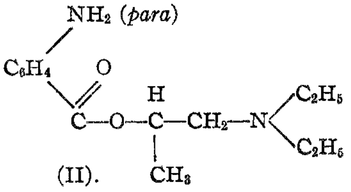
BY OLIVER KAMM.

Received February 23, 1920.

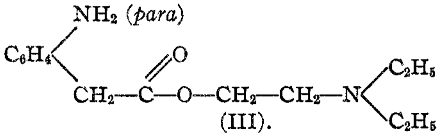
Several simple homologs of the well-known anesthetic, procaine (Formula I),[1] have been described in the literature. The formulas for compounds of this type which differ from the parent substance in that they possess one more carbon atom are represented structurally as follows:



(I).



(II).



(III).

Compound II is described in the German patent literature,[2] but the writer is not aware of published data recording the physiological action of this individual. Compound III has been synthesized more recently by Pyman[3] and has been found to be inactive as an anesthetic. It is to be noted that the latter compound is an amino-alcohol ester of an aliphatic acid (*p*-aminophenyl *acetic* acid) whereas a maximum anesthetic effect appears to develop when the carbonyl group is united directly to the aromatic nucleus. Such a type of linkage is, however, not essential, provided that the carbonyl group of the ester be united to an unsaturated carbon atom,[4] such as is illustrated by Formulas IV and V. Both of these

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[1] This is the formula of the free base. Procaine (also called novocaine) is the monohydrochloride of this compound.

[2] Friedlaender, **8**, 995; *D. R. P.* 179,627.

[3] *J. Chem. Soc.*, **111**, 167, 1119 (1917).

[4] For exceptions see Fourneau, *J. pharm. chim.*, [7] **2**, 337, 397 (1910).