

Press. He believes that unless it is given the prompt consideration which the exigencies of the case seem to demand, the American Pharmaceutical Association will have lost its greatest opportunity for a larger service to all of American Pharmacy.

WORTLEY F. RUDD.

CHEMISTRY OF HEPTANE AND ITS SOLUTION.

BY EDWARD KREMERS.

1. INTRODUCTORY REMARKS.

The object of this brief introduction is not to describe the preliminary survey which has been made during the past four years, much less to dwell on the theoretical aspects of the subject. Its purpose is merely to acquaint those interested with the subject how few and short were the steps that led from the investigation of certain phases of plant chemistry to the general study of chemistry as it reveals itself within the narrow aspects of so highly selective a solvent as this saturated hydrocarbon. Those theoretical aspects that seem to demand immediate attention, will be considered briefly in connection with the respective chapters. After the preliminary survey, that has been made hastily and for the most part qualitatively thus far, will have been supplemented by more carefully repeated experiments, conducted quantitatively wherever possible and whenever desirable, it may seem apropos to dwell on the more general theoretical phases of this "new chemistry" as it has been called.

Even to phytochemists and to those interested in the chemistry of the "terpenes and camphors," to use a phrase made familiar by Wallach's one hundred and more classical contributions to organic chemistry published in the *Annalen*, it may not be generally known that as early as 1871, Wenzell,¹ an ex-pharmacist in San Francisco, revealed some of the peculiar properties of abietene, erasine and aurantine, by which names the oil from the Digger's pine, *Pinus sabiniana*, was locally known. Wenzell's publication attracted the attention of Thorpe, who demonstrated by elementary analysis and the study of its physical properties that this unusual oil consisted principally of normal heptane. Somewhat later, under the guidance of Schorlemmer, whose classical researches on the methane hydrocarbons qualified him particularly to direct the investigation, the same scientist proved chemically that his physical determinations had led him to a correct conclusion.

Ever since the occurrence of heptane in quantity had been demonstrated in the Digger's pine, it has been of special interest to phytochemists. The discovery of the same hydrocarbon in another California species, namely the Jeffrey pine, *Pinus Jeffreyi*, also its discovery in the fruits of *Pittosporum resiniferum* of the Philippines, known as petroleum nuts, has added to the phytochemical interest in this hydrocarbon.

Though there are said to be thousands of acres of forests of *Pinus sabiniana* and *Pinus Jeffreyi* in the mountains of California, it has been by no means an

¹ For a review of the early history of heptane from conifers, see W. T. Wenzell, on "Abietene," *Pharm. Rev.*, 22, 408, 1904.

easy matter to secure an abundance of this material. Thanks to the coöperation of the Forest Products Laboratory and of the District Forester, also of Mr. D. F. Fryer, of Santa Rosa, California, it has been possible in recent years to secure larger amounts of the oils from both species, though the product was at times mixed with the oil of Western Yellow pine, with which the Digger's pine grows and with which it is apt to be confounded by the workmen who box the trees and collect the oleoresin.

Phytochemically, the writer's interests were at first directed to the study of the approximately two percent of constituents other than heptane, also to the study of the resin which results after the volatile constituents have been removed from the oleoresin by distillation. As soon as the heptane was obtainable in liter quantities, its use for a laboratory experiment in elementary organic chemistry suggested itself. Although all of our organic texts point out the importance of chlorine substitution in connection with the saturated hydrocarbons of the methane series, there appears to be not a single laboratory manual which gives an experiment to impress the student with this important property. What could be more instructive to the beginner in organic chemistry than to repeat Schorlemmer's classical experiments on the constitution of the methane hydrocarbons in connection with this pure heptane. Hence, whenever material was available, it was used for this purpose in the laboratory.

In his general phytochemical work, the writer has long emphasized the importance of computing percentage composition with reference to absolutely dry material. In this connection he also pointed out that the older methods for drying were often unsatisfactory and, when applied to such products as cloves, altogether wrong and beneath criticism. Hence, his classes in phytochemistry have been made acquainted with the xylene method, as applied to moisture determinations of woods impregnated with creosote, a problem analogous to that encountered in drugs and other materials rich in volatile oils such as the cloves already referred to.²

A more careful study of this problem, however, revealed certain disadvantages in the use of xylene, disadvantages that were at times increased rather than diminished by the substitution of such substances as the terpenes for xylene. Heptane, with its boiling point so closely approximating that of water, suggested itself as an ideal substitute. Experience soon taught that it also has its limitations, but it also taught something far more important.

So highly mucilaginous a drug as squill is exceedingly unsatisfactory when its moisture content is determined by the older methods. The use of the heptane modification of the xylene method proved much more satisfactory. Its application also revealed a fact of greatest importance to phytochemical analysis, *viz.*, that, as a highly selective solvent, its use in the moisture determination may casually reveal the presence of other constituents than water. In the case of squill, the "scillain," or whatever the substance may have been, crystallized out from the residual heptane in beautiful crystals.

Highly satisfactory as was this observation, the suggestion naturally presented itself at once that other constituents of the examined material might re-

² Unpublished results deposited as theses in the Library of the University of Wisconsin.

main in solution. Thus while crystallization from the filtered and cooled heptane solution would naturally be more than welcome, there was no reason why a heptane solution, free from most of the admixtures which are found in alcoholic and similar extracts, should be discarded without at least an effort to ascertain something about the nature of the dissolved constituents.

In order to ascertain something about the nature of such solutions, the most promising line of attack seemed to be the study of alkaloidal drugs, or, better still, of the alkaloids themselves, since even very small amounts can be detected readily by general alkaloidal reagents. Thus a beginning was made with morphine and other alkaloids. No sooner had this line of investigation been begun than it became apparent that the use of alkaloidal reagents not in aqueous solution, but in heptane solution, became desirable. Hydrogen chloride in heptane solution having been prepared for this purpose, what more natural than to prepare a solution of ammonia in heptane and bring these two heptane solutions together and witness the precipitation of ammonium chloride resulting from the addition of hydrogen chloride to ammonia both in heptane solution. Simple and self-evident as is this phenomenon to the investigator, to the chemist who thinks, it becomes a matter of significance.

From this insignificant beginning to a thousand and one experiments is a story of four years of "playing" at chemistry. Yet it was a playing that was rich in interesting observations and oftentimes in surprising results. Indeed, each and every new experiment performed suggested ten new experiments, so that the mind at times became overstimulated and a respite of shorter or longer duration had to be taken.

With such an irrepressible stimulus to pass from one new experiment to another, careful study of individual reactions and products became a mental, if not a physical, impossibility. Hence, the detail work had to be assigned to others. Practical applications had to be ignored almost entirely for the time being. In order to cover the field in a rational way, the reverse order of the periodic system was taken as guide, with this exception, however, that the hydrohalogens were studied before the halogens. The practical reason for this is apparent without comment to every chemist at all acquainted with the chemistry of the hydrocarbons of the methane series. In reporting certain phases of the work, the order just indicated may not always be followed.

The writer is by no means unaware that others have worked with petroleum hydrocarbons as solvents. Indeed, twenty-five years ago, while physical chemists of the Ostwald school knew of but one chemistry only, namely that of the aqueous solution, and this only in extreme dilution, he advocated the use of the non-aqueous solvent. The study of the peculiar behavior of a group of isomeric nitrosochlorides: true simple nitrosochlorides, isonitrosochlorides and bisnitrosochlorides, also of related compounds, in different organic solvents had even then impressed upon him the importance of the chemistry of solutions other than the aqueous; though the dilute aqueous solution at that time was the only orthodox one. The significance of heptane as a solvent is at least three-fold.

It is a saturated hydrocarbon of the limit series and in this respect differs materially from the other hydrocarbons that have been used by various investigators.

So far as the previous use of hydrocarbons of the methane series is concerned mixtures only have been employed. The heptane from both the Digger's and Jeffrey pines appears to be devoid of isomers and homologues and the small amount of impurities present in the natural products can be removed by a variety of new ways, as has been ascertained in the preliminary survey already alluded to. In heptane, a distinctively chemical unit, capable of a high degree of purity, is now made available; hence not only more satisfactory qualitative work can be done, but, what is possibly more important, quantitative work as well.

Heptane is not only volatile, but its boiling point lies very close to that of water, the most common solvent used. Moreover, its boiling point lies only twenty degrees higher than that of alcohol, the most common of the organic solvents employed in chemical work.

A disadvantage of the heptane, namely, its highly selective solvent property, frequently turns out an advantage, for it is remarkable how many substances can be prepared in this solvent by the precipitation method. Indeed, in many of the innumerable organic reactions performed, the writer was again and again reminded of his early chemical work in qualitative inorganic analysis. So simple were many of the reactions that the writer has referred to his work as "playing" at chemistry. This does not imply, however, that many of the precipitates are as simple as at first supposed. Indeed, much painstaking detail work will have to be done in order that the secrets of this chemistry of the heptane solution may be properly revealed.

CHEMISTRY OF THE HEPTANE SOLUTION.

BY EDWARD KREMERS.

2. REVISION OF THE PHYSICAL CONSTANTS OF HEPTANE.

BY ROLAND E. KREMERS.

The physical constants for normal heptane, so painstakingly determined by Thorpe for the hydrocarbon obtained from the Digger's pine, are possibly among the most accurate on record for a hydrocarbon of the methane series. However, if one stops to consider that the hydrocarbon so carefully investigated physically by Thorpe had an optical rotation of $6.9'$, it becomes apparent at once that the material examined by him must have been impure. Normal heptane should be optically inactive. The angle of rotation can readily be accounted for by assuming that in the collection of the oleoresin, the collector did not discriminate sufficiently between *Pinus sabiniana* and other species of pine yielding pinene, *e. g.*, *Pinus ponderosa*.¹ That such mistakes have been made has since then been demonstrated repeatedly. Thus, *e. g.*, an oleoresin presumably from Jeffrey pine, which likewise produces heptane in place of pinene, contained about one-third or more of the oleoresin of *Pinus ponderosa*, with which this species is readily confounded by the workmen. This oleoresin was distilled and the oil examined in this laboratory by R. J. Harnon.² In like manner the admixture of a pinene oleoresin with the oleoresin of *Pinus sabiniana* has since then been observed in the Forest Products Laboratory.³ Hence, with an unusually pure heptane at our disposal, it seemed highly desirable to re-determine the physical constants and to compare them with those of Thorpe.