Butyrophenone-α-d and α-ethylbutyrophenone-α-d. To 4.05 g. (0.0273 mole) of butyrophenone was added 210 ml. (0.0273 mole) of 0.130*M* ethereal sodium triphenylmethide. The color change from deep red to light yellow was rapid and the end point was sharp when the calculated volume had been added. The enolate solution was stirred for 3 hr. with 1.5 ml. (0.075 mole) of deuterium oxide. The ether layer was washed well with water and distilled through a 6-plate column to give six fractions, 3.7 g., 90%, of butyrophenone-α-*d*, b.p. 61–62° at 2 mm., n_D^{25} 1.5175. The infrared spectrum contained characteristic peaks at 4.63μ and 11.10μ which were lacking in the spectrum of butyrophenone. Several major peaks characteristic of butyrophenone were missing.

The conversion of α-ethylbutyrophenone to its enolate is a slow reaction. An end point was obtained when stoichiometric amounts of ketone and sodium triphenylmethide were stirred for several hours at 30°. The enolate from 4.07 g. (0.0231 mole) of ketone was stirred for 16 hr. with 2 ml. (0.10 mole) of deuterium oxide to give seven fractions, 3.5 g., 83%, of α-ethylbutyrophenone-α-*d*, b.p. 72–73.5° at 1 mm., n_D^{25} 1.5093. The infrared spectrum contained characteristic peaks at 4.65μ and 11.22μ which were lacking in the spectrum of α-ethylbutyrophenone. Major peaks characteristic of this ketone were lacking. All spectra were determined in carbon tetrachloride solution. The spectrum of the deuterated ketone was unchanged by shaking an ethereal solution with dilute aqueous sodium hydroxide for 30 min. at room temperature. This experiment shows the absence of H-D exchange during the washing procedure used in the equilibrium studies.

Equilibrium studies. The reaction of sodio-α-ethylbutyrophenone with butyrophenone is typical. The enolate was prepared from 5.29 g. (0.0301 mole) of the ketone and 203 ml. (0.0301 mole) of 0.148*M* ethereal sodium triphenylmethide. The addition with stirring to give a satisfactory end point required 1 hr. The solution was stirred for an additional 3 hr. after which 4.50 g. (0.0304 mole) of butyrophenone was added. After 28 hr., the reaction was quenched by the addition of 4 ml. of deuterium oxide. The ether layer was washed with five 10-ml. portions of water, the last of which was neutral to litmus. The solution was dried over Drierite and diluted with carbon tetrachloride. All of the ether and a portion of the carbon tetrachloride were removed through a short column, and the residue was diluted to 50.0 ml. with carbon tetrachloride for infrared analysis.

In the reverse process, 0.026 mole of sodio-butyrophenone was stirred for 26 hr. with 0.026 mole of α-ethylbutyrophenone and quenched with 0.10 mole of deuterium oxide.

Lithio-butyrophenone was prepared by stirring and refluxing for 5 days a concentrated ethereal solution of the ketone with excess powdered lithium hydride. The solution was filtered through sintered glass and diluted to 0.107*M* with anhydrous ether. A solution of 181 ml. (0.019 mole) of the enolate was stirred for 117 hr. with 3.42 g. (0.019 mole) of α-ethylbutyrophenone, the reaction quenched with 4 ml. of deuterium oxide and extracted as described.

Spectra were measured on a Perkin-Elmer Model-21 spectrophotometer. The four ketones and triphenylmethane were found to obey Beer's law at the wave lengths used for analysis. When triphenylmethane was present, the concentration of this hydrocarbon was estimated by its absorbance at 6.69μ, a wave length at which the absorbances of the four ketones are negligible. The amounts of triphenylmethane obtained agreed within 3% with those calculated from the quantities of sodium triphenylmethide employed. Spectra of the product mixtures starting with equal concentrations of either ketone-enolate pair were practically identical. The equilibrium is far to the left as indicated by the characteristic peaks of butyrophenone and α-ethylbutyrophenone-α-*d* which appear as small shoulders on the strong peaks of α-ethylbutyrophenone and butyrophenone-α-*d*. Absorbances were measured at peaks characteristic of each of the four ketones. These absorbances were corrected for absorbance due to triphenylmethane when present. Solution of four simultaneous equations gave the equilibrium concentrations from which values of K ranging from 0.006 to 0.02 were calculated for both forward and reverse processes. The equilibrium is too far to the left to obtain a more precise value for the equilibrium constant from these data.

COLLEGE OF CHEMISTRY AND PHYSICS
THE PENNSYLVANIA STATE UNIVERSITY
UNIVERSITY PARK, PA.

Use of Girard's Reagent "T" in the Separation of Derivatives of Chlorophylls *a* and *b*

H. R. WETHERELL AND M. J. HENDRICKSON

Received November 10, 1958

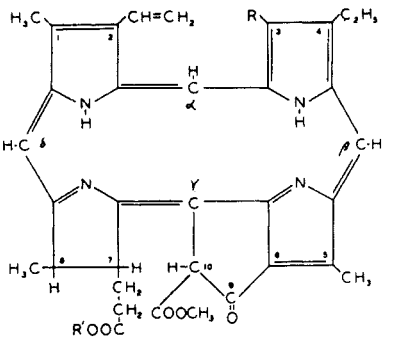
In view of the continuing interest in the chemistry of chlorophyll, we wish to report a new method for the separation of mixtures of *a* and *b* derivatives. The large scale preparative methods employed in this field separate chlorophyll derivatives according to their hydrochloric acid number[1] and their behavior toward buffers of different *p*H. The latter indicates the number of free carboxylic acid groups present.[2] In the method reported here, Girard's reagent "T" (carboxymethyltrimethylammonium chloride hydrazide)[3] is employed to resolve mixtures into groups of *a* compounds and *b* compounds, irrespective of their hydrochloric acid number or the number of carboxylic acid residues present. The 3-formyl group of the *b* compounds reacts readily with this reagent to form a water soluble derivative, whereas members of the *a* series, even those possessing a keto group, *i.e.*, pheophorbide *a* (I, R = CH_3; R′ = H) or purpurin 7*a* trimethyl ester (II, R = C(O)—$COOCH_3$) react very slowly if at all.

The experimental procedure is as follows: A mixture of *a* and *b* compounds containing about 15 mg. of the *b* member is dissolved in 30 ml. of a 90:10 (v/v) mixture of 95% ethanol:glacial acetic acid containing 150 mg. of Girard's reagent "T". The mixture is refluxed under nitrogen for 5 min., cooled, and poured into 1 l. of peroxide-free ether. (If refluxing is continued indefinitely some of the *a* derivative, if it possesses a keto group, does react.) This is then extracted with small (100 ml.) portions of distilled water until the aqueous extract is colorless. The *a* derivative, free of even traces of *b* contamination, remains in the ether layer. Partial hydrolysis of esterified compounds may occur, but treatment with diazomethane is sufficient to re-esterify them completely. The *b*

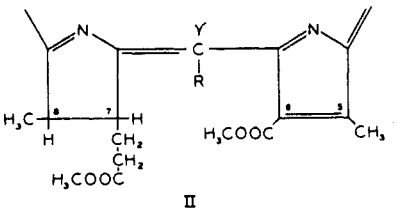
(1) R. Willstätter and A. Stoll, *Investigations on Chlorophyll*, translated from the German by F. M. Schertz and A. R. Merz, The Science Press Printing Co., Lancaster, Pa., 1928, pp. 237–245.

(2) M. J. Hendrickson, unpublished data.

(3) Purchased from Fisher Scientific Co.



I



II

fraction can be regenerated if desired by making the aqueous extract about 6% with respect to hydrochloric acid and heating at 85° for 15 min. It can then be driven into fresh ether and esterified.

This method has been tried on several different mixtures of *a* and *b* derivatives, *e.g.*, chlorin p_6 trimethyl ester (II, R = $COOCH_3$ in the *a* series) and *b*-chlorin p_6 trimethyl ester (II, R = $COOCH_3$, with a formyl group at position 3); purpurin 7*a* trimethyl ester and purpurin 7*b* trimethyl ester (II, R = C(O)—$COOCH_3$, with a formyl group at position 3), and has been found capable of effecting complete separations. We have been unable to separate pheophytin *a* (I, R = CH_3; R′ = phytyl) from pheophytin *b* (I, R = CHO; R′ = phytyl) however, presumably because the phytol residue renders the *b*-Girard compound somewhat ether soluble. Also, in the case of the pheophorbides (I, R = CH_3 or CHO; R′ = H), we are not certain that they do not suffer some slight degree of oxidation and/or allomerization at the 10- position, when the reaction is carried out as described. Although chromatographic analysis[4] shows only one *a* and one *b* component, and the respective phase tests are still positive, these two criteria alone are not conclusive proof, and examination of the products of a hot quick saponification under nitrogen (modified after Willstätter) should supply definitive evidence. It was noted however, that if the reflux time was extended to 20 min., an additional *a* and *b* component appeared on the chromatogram. The visible spectra of these compounds were similar to the respective pheophorbides, but they both gave a negative phase test.

The chlorophyll derivatives in the foregoing discussion were prepared according to Fischer and his co-workers.[5] They were characterized by means of their hydrochloric acid number, visible and infrared spectra, solubility in buffers of appropriate *p*H, and chromatographic behavior.

Department of Physiology and Pharmacology
University of Nebraska College of Medicine
Omaha, Neb.

(4) M. J. Hendrickson, R. R. Berueffy, and A. R. McIntyre, *Anal. Chem.*, 29, 1810 (1957).

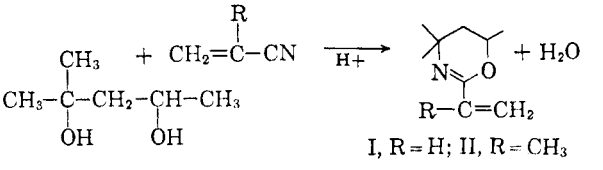
(5) H. Fischer and A. Stern, *Die Chemie des Pyrrols*, Hälfte 2, Bd. II, Akademische Verlagsgesellschaft, Leipzig, 1940.

2-Alkenyl-4,4,6-trimethyl-5,6-dihydro-1,3-oxazines

John W. Lynn

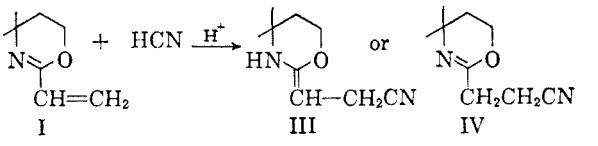
Received November 10, 1958

A novel polymerizable oxazine, 2-vinyl-4,4,6-trimethyl-5,6-dihydro-1,3-oxazine (I), was prepared by the reaction of acrylonitrile with 2-methyl-2,4-pentanediol in sulfuric acid; an extension of the general reaction described by Tillmanns and Ritter.[1] The 2-isopropenyl analog was also prepared by this reaction using methacrylonitrile. Similar 2-alkenyl-5,6-dihydro-1,3-oxazines may be prepared by the aluminum alkoxide catalyzed condensation of 1,3-alkanolamines with α,β-unsaturated esters.[2]



I, R = H; II, R = CH_3

The addition of hydrogen cyanide to I in refluxing acetic acid gave 2-(2′-cyanoethylidene)-4,4,6-trimethyltetrahydro-1,3-oxazine (III). The reaction of HCN could take place by 1,4- addition to give III, or by 3,4-addition to give IV. That III is the product (by direct 1,4- addition or by isomerization of initially formed IV) is clearly shown by the infrared spectrum. A sharp band at 3.00μ as well as absence of typical unconjugated C=N absorption at 6.25μ is in good agreement with structure III, and not at all in accord with IV.



I III IV

(1) E. Tillmanns and J. J. Ritter, *J. Org. Chem.*, 22, 839 (1957).

(2) P. L. de Benneville and L. S. Luskin, U. S. Patent 2,831,858, April 22, 1958