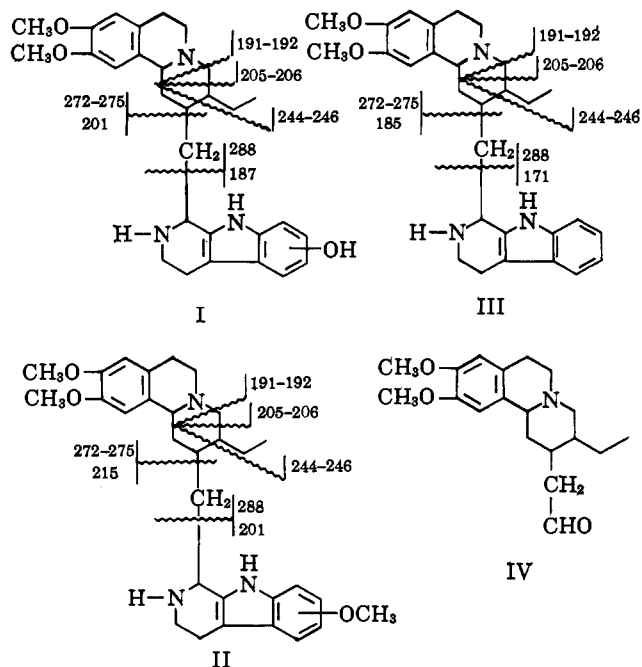


stituent. This approach has been used successfully for structure proposals of many indole alkaloids.⁸



Second, the noncrystalline product (II) from the methylation of tubulosine with diazomethane gave a mass spectrum in which all the peaks originating from the quinolizidine moiety were also present, but the peaks at m/e 201 and 187 were shifted to m/e 215 and 201 (base peak). The observed peak movements (see II) are in full accord with the proposed structure of tubulosine. Mechanistic proposals for the formation of the fragments indicated schematically in structures I-III may be found in the original literature^{4,5} dealing with emetine.

In the biogenesis of Ipecacuanha alkaloids it is assumed that the isoquinoline nucleus is formed from a phenylethylamine precursor, which (formally speaking) condenses with another intermediate which can be represented by protoemetine (IV).⁹ By substituting a tryptamine precursor for the phenylethylamine component, the biogenetically plausible, but hitherto unencountered, structure of tubulosine (I) is created.

Acknowledgment.—We thank Dr. W. Simon (E. T. H., Zürich) for the pK_{MCS} determinations, Prof. A. R. Battersby (University of Liverpool) for the generous gift of a sample of the hydrochloride of III, Dr. M. J. Vernengo (University of Buenos Aires) for assistance in part of this work, and Dr. D. P. Hollis (Varian Associates) for the n.m.r. spectrum. The work at Stanford University was supported by grant No. AM-04257 from the National Institutes of Health of the U. S. Public Health Service.

(8) See H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Structure Elucidation of Natural Products by Mass Spectrometry," Vol. I, Holden-Day, Inc., San Francisco, Calif., 1964.

(9) A. R. Battersby and B. J. T. Harper, *J. Chem. Soc.*, 1748 (1959); C. Szántay and L. Tóke, *Tetrahedron Letters*, 1323 (1963).

DEPARTAMENTO DE QUÍMICA ORGÁNICA P. BRAUCHLI
FACULTAD DE CIENCIAS EXACTAS Y NATURALES V. DEULOPEU
BUENOS AIRES, ARGENTINA
DEPARTMENT OF CHEMISTRY H. BUDZIKIEWICZ
STANFORD UNIVERSITY CARL DJERASSI
STANFORD, CALIFORNIA

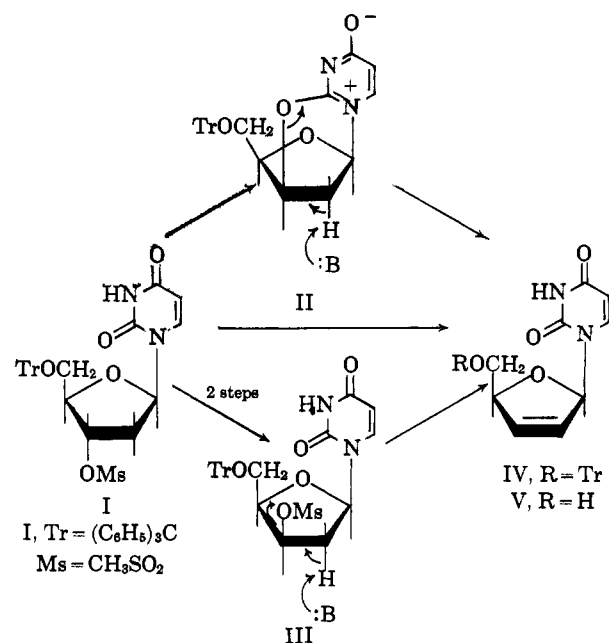
RECEIVED MARCH 6, 1964

Nucleosides. VI. The Introduction of Unsaturation into the Carbohydrate of a Pyrimidine Nucleoside *via* a 2,3'-Anhydro Bond

Sir:

We wish to report the introduction of a 2',3'-double bond into the carbohydrate moiety of a pyrimidine nucleoside *via* a novel, base-catalyzed elimination reaction in which a uracyloxy group behaves as a leaving group.¹ The unsaturated derivatives are viewed as potentially useful intermediates for the synthesis of a number of unusual pyrimidine nucleosides.

3'-*O*-Mesityl-5'-*O*-trityl-2'-deoxyuridine² (I) was readily converted to 2,3'-anhydro-1-(2'-deoxy-5'-*O*-trityl- β -D-lyxosyl)uracil (II)³ in high yield on treatment with 1 equiv. of sodium hydroxide in ethanol.⁴ The reaction of II with potassium *t*-butoxide in dimethyl sulfoxide at room temperature for 0.5 hr. afforded a solid (70% yield) with properties consistent with 1-(5'-*O*-trityl-2',3'-dideoxy-2'-ene- β -D-glycero-pentofuranosyl)uracil⁵ (IV), m.p. 194–196°, $[\alpha]^{25}_D -56^\circ$



(c 0.4, ethanol), $\lambda_{\max. \text{min}}^{\text{EtOH}}$ (m μ) 261, 242 (ϵ 9770, 6000). The same base-solvent system (2 equiv. of base) applied to either 1-(3'-*O*-mesityl-5'-*O*-trityl-2'-deoxy- β -D-lyxosyl)uracil (III)⁶ or I gave a product identical in every respect with IV. The corresponding detritylated product V, m.p. 155–156° dec., $[\alpha]^{25}_D -88^\circ$ (c 0.3, water), $\lambda_{\max. \text{min}}^{\text{H}_2\text{O}}$ (m μ) 261, 231 (ϵ 10,380, 2300), was obtained in 81% yield on treatment with 1 equiv. of hydrogen chloride in chloroform.

(1) The concept of an anhydro bond comprising a leaving group was first advanced by K. C. Murdock and R. B. Angiers [*J. Am. Chem. Soc.*, **84**, 3748 (1962)] in connection with the formation of a halogenated 1-cyclopentane derivative of thymine (a thymidine isostere) from an anhydro intermediate. It was proposed that a positive charge (acid solution) on the anhydro oxygen atom enables a thyminyloxy group to behave as a leaving group.

(2) J. P. Horwitz, J. Chua, M. Noel, and M. A. DaRooze, *J. Med. Chem.*, **7**, 385 (1964).

(3) Analytical values for all compounds described in this work were consistent with the indicated structures.

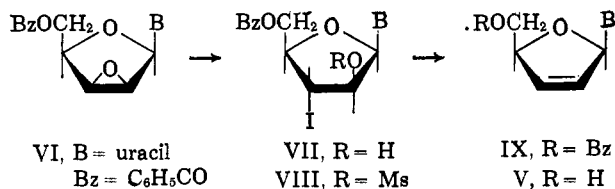
(4) The procedure is essentially the same as that described previously [J. P. Horwitz, J. Chua, J. A. Urbanski, and M. Noel, *J. Org. Chem.*, **28**, 942 (1963)] for the synthesis of 5'-*O*-trityl-2,3'-anhydrothymidine.

(5) This nomenclature is in accord with that employed by R. K. Ness and H. G. Fletcher, Jr.; *ibid.*, **28**, 435 (1963).

(6) The mesylation of 1-(5'-*O*-trityl-2'-deoxy- β -D-lyxofuranosyl)uracil (see ref. 2) gives III in good yield.

The identity of V was established by independent synthesis which utilized 1-(5'-*O*-benzoyl-2',3'-epoxy- β -D-lyxosyl)uracil (VI)⁷ as starting material and a method described recently for the introduction of a 2,3-double bond into a hexose.⁸ Scission of the epoxide ring in VI with sodium iodide in acetone containing 1 equiv. of acetic acid gave a single isolable iodohydrin (55% yield), m.p. 198–200° dec., $[\alpha]^{25D} +41^\circ$ (*c* 1.0, acetone) $\lambda_{\max}^{\text{EtOH}}$ (m μ) 261, 229 (ϵ 8710, 19,640), $\lambda_{\min}^{\text{EtOH}}$ (m μ) 248, 214 (ϵ 7330, 16,730), to which the structure 1-(5'-*O*-benzoyl-3'-deoxy-3'-iodo- β -D-arabinosyl)uracil (VII) has been tentatively assigned.⁹ The latter was converted to a 2'-*O*-mesylate (VIII, 50% yield), m.p. 114–116°, $[\alpha]^{20D} +41^\circ$ (*c* 0.8, acetone), $\lambda_{\max}^{\text{EtOH}}$ (m μ) 260, 232 (ϵ 10,100, 14,300), $\lambda_{\min}^{\text{EtOH}}$ (m μ) 249 (ϵ 8760), and treated with sodium iodide in acetone. Reaction occurred at 0° with elimination of iodine and the methanesulfonyloxy group to give 1-(5'-*O*-benzoyl-2',3'-dideoxy-2'-ene- β -D-glycero-pentofuranosyl)uracil (IX) in 70% yield, m.p. 139–140°, $[\alpha]^{25D} -107^\circ$ (*c* 0.5, acetone), $\lambda_{\max}^{\text{EtOH}}$ (m μ) 261, 230 (ϵ 9330, 14,320), $\lambda_{\min}^{\text{EtOH}}$ (m μ) 246, 217 (ϵ 7300, 12,005). Saponification of the benzoate ester in IX gave a solid which proved to be identical in every respect with V.

Studies are currently in progress to expand the scope of elimination reactions as applied to anhydro nucleosides. The results will be described in detail in the near future.



Acknowledgment.—This work was supported in part by research grants CA-02903 and CY-5943 from the National Cancer Institute, Public Health Service, and in part by an institutional grant from the United Foundation of Greater Detroit allocated through the Michigan Cancer Foundation.

(7) J. F. Codington, R. Fecher, and J. J. Fox, *J. Org. Chem.*, **27**, 163 (1962).

(8) N. F. Taylor and G. M. Riggs, *J. Chem. Soc.*, 5600 (1963).

(9) This assignment is in accord with the normal course of opening of sugar- or nucleoside-2,3-epoxides which occurs predominantly at C-3 [see C. D. Anderson, L. Goodman, and B. R. Baker, *J. Am. Chem. Soc.*, **81**, 898 (1959)]. However, it is to be noted that either of the two possible *trans* iodohydrins should lead to the introduction of a 2',3'-double bond in this alternate synthesis of V.

ROLLIN H. STEVENS MEMORIAL
LABORATORY

DETROIT INSTITUTE OF CANCER RESEARCH
DETROIT, MICHIGAN 48201

JEROME P. HORWITZ
JONATHAN CHUA
IRWIN L. KLUNDT
MARGARET A. DAROOG
MICHAEL NOEL

RECEIVED FEBRUARY 26, 1964

Photolysis of Thiobenzophenone in the Presence of Olefins: A Novel Reaction

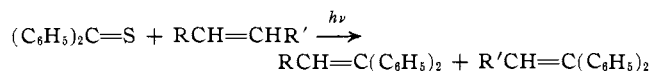
Sir:

A study of the light-catalyzed reactions of thiobenzophenone in alcoholic solvents was reported recently.¹

(1) G. Oster, L. Citarel, and M. Goodman, *J. Am. Chem. Soc.*, **84**, 703 (1962).

Its photolytic behavior was found to differ considerably from that of benzophenone²; irradiation with near-ultraviolet light in the absence of oxygen gave the reduction products benzhydryl mercaptan, dibenzhydryl disulfide, and a tetrasulfide from thiobenzophenone, whereas dibenzopinacol is produced from benzophenone.

The addition of carbonyl compounds to olefins under the influence of light to give oxetanes is a well known reaction.^{3–6} In view of the contrast presented by the photochemical results for thiobenzophenone and benzophenone which have been noted above, it was of interest to us to determine what course the irradiation of the thioketone in the presence of olefins would take. In the present communication we report the novel photolytic reaction which thiobenzophenone undergoes with olefins, as described below for *cis*-2-butene and 1-hexene.



cis-2-Butene (Matheson) and nitrogen were bubbled continuously through a solution of thiobenzophenone⁷ (2.2 g.) in cyclohexane (170 ml.) which was irradiated with a Hanovia No. 608A-36 lamp.⁸ After 4 hr. the thioketone had completely reacted, as evidenced by the disappearance of its blue color. The solvent and excess *cis*-2-butene were removed under reduced pressure, and the residue was distilled at 0.5 mm. giving a light blue-tinged liquid. Chromatography of the liquid on Woelm Activity Grade 1 acid alumina with petroleum ether (b.p. 30–60°) as the eluent gave a white crystalline solid (0.71 g.), m.p. 47–49°. Recrystallization of the solid from 95% ethanol yielded pure 1,1-diphenyl-1-propene (0.5 g., 23% yield based on thiobenzophenone), m.p. 49–50°; a mixture melting point with an authentic sample prepared by the dehydration of 1,1-diphenyl-1-propanol was undepressed (lit.^{9,10} m.p. 51°, 51–52°). When the photolysis was carried out using *trans*-2-butene, the same reaction occurred, yielding an equal amount of 1,1-diphenyl-1-propene.

In order to ascertain what, if any, specificity thiobenzophenone exhibits in its reactions with olefins, it was treated photochemically with the terminal olefin, 1-hexene. A mixture of thiobenzophenone (2.0 g.) and 1-hexene (65 ml., Phillips 99 mole %) was irradiated for 5 hr. while a slow stream of nitrogen was bubbled through. The solvent and 1-hexene were removed under reduced pressure, and the residue was distilled at 0.1 mm. giving a clear liquid. Chromatography on

(2) J. N. Pitts, R. L. Letsinger, R. P. Taylor, J. M. Patterson, G. Recktenwald, and R. B. Martin, *ibid.*, **81**, 1068 (1959).

(3) E. Paterno and G. Chieffii, *Gazz. chim. ital.*, **39**, 341 (1909).

(4) G. Büchi, C. G. Inman, and E. S. Lipinsky, *J. Am. Chem. Soc.*, **76**, 4327 (1954).

(5) R. Srinivasan, *ibid.*, **82**, 775 (1960).

(6) J. F. Harris, Jr., and D. D. Coffman, *ibid.*, **84**, 1553 (1962).

(7) R. H. Abeles, R. F. Hutton, and F. H. Westheimer, *ibid.*, **79**, 712 (1957).

(8) The reaction did not proceed when a Pyrex filter was placed between the lamp and the photolysis mixture. However, the reaction was not affected by the placement of a Vycor filter between the lamp and the photolysis mixture. This suggests that the reaction observed is due to irradiation with light in the range 210–280 m μ . It has been previously shown in ref. 1 that thiobenzophenone in an inert solvent, cyclohexane, and in the absence of oxygen undergoes a net chemical change when irradiated with far-ultraviolet light (254 m μ). However, the products of this reaction were not isolated.

(9) R. Lagrave, *Ann. chim. (Paris)*, [10] **8**, 386 (1927).

(10) K. V. Auwers, *Ber.*, **62**, 693 (1929).