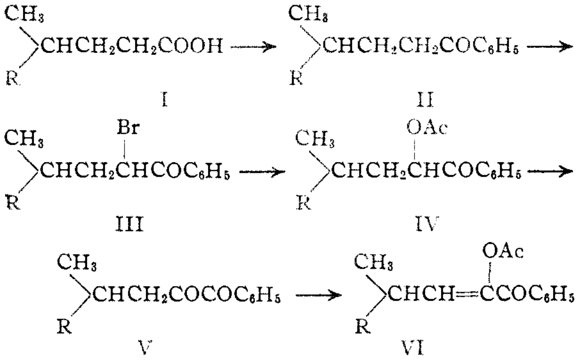
A NEW METHOD FOR THE DEGRADATION OF BILE ACID DERIVATIVES

Sir:

I wish to report in outline form a promising new procedure for degrading the characteristic γ-substituted *n*-valeric acid side chain (I) of the bile acids and their derivatives in the preparation of suitable starting materials for steroid hormone partial syntheses.

The excellent method of Gilman and Nelson[1] when applied to the acid chloride of I provides the phenyl ketone (II) in 70 to 75% yield if diphenylcadmium is used. Bromination of the ketone yields a mixture of isomeric 23-bromo compounds (III) which upon acetolysis forms the corresponding 23-acetoxy derivatives (IV). The latter, after hydrolysis to the α-ketols, can be oxidized with copper sulfate in aqueous pyridine to the α-diketone (V) in 65 to 70% over-all yield from the monoketone. Acetylation of the diketone then forms the expected enolacetate (VI) which is suitable for oxidative cleavage to *bisnor*-acid derivatives.

(R = Substituted steroid ring system)



Of the many new compounds which have been characterized in the course of these studies, those arising as intermediates in the degradation of cholic acid are typical:

(II) Cholophenone (*nor*-cholyl phenyl ketone), m. p 174–176.5°; $[\alpha]^{20}\text{D}$ +26°.[2] *Anal.* Calcd. for $C_{30}H_{44}O_4 \cdot {}^1/_2H_2O$: C, 75.43; H, 9.50. Found: C, 75.35; H, 9.48.
  Cholophenone triacetate, m. p. 120.3–121°; $[\alpha]^{20}\text{D}$ +79°
  Cholophenone 2,4-dinitrophenylhydrazone, m. p. 221–222.5°
  Cholophenone oxime, m. p. 214–217° dec.

(III) 23(β)[3]-Bromo-cholophenone triacetate, m. p. 108.5–111.5°; $[\alpha]^{20}\text{D}$ +95°. *Anal.* Calcd. for $C_{36}H_{49}O_7Br \cdot H_2O$: C, 62.51; H, 7.43. Found: C, 62.86; H, 7.19. Calcd. for $C_{36}H_{49}O_7Br$: C, 64.18; H, 7.33. Found: (sintered *in vacuo*), C, 64.05; H, 7.35.

(IV) 23(α)[3]-Acetoxy-cholophenone triacetate, m. p. 180–182°; $[\alpha]^{20}\text{D}$ −10°. *Anal.* Calcd. for $C_{38}H_{52}O_9 \cdot {}^1/_2H_2O$: C, 68.96; H, 8.07. Found: C, 69.15; H, 8.09.

(V) *bisnor*-Cholyl benzoyl ketone triacetate, m. p. 166–169° (after drying, 161.5–166°); $[\alpha]^{20}\text{D}$ +92°. *Anal.* Calcd. for $C_{38}H_{48}O_8$: C, 71.02; H, 7.95. Found: C, 70.92; H, 7.88.
  bisnor-Cholyl benzoyl ketone 7,12-diacetate, m. p. 201–203.5°; $[\alpha]^{20}\text{D}$ +80°. *Anal.* Calcd. for $C_{34}H_{46}O_7$: C, 72.05; H, 8.18. Found: C, 72.16; H, 8.34.
  2-*bisnor*-Cholyl-3-phenyl-quinoxaline triacetate, m. p. 217–218.5°.

Work now in progress indicates that the application of this degradation scheme to substituted *nor*-bile acids will result in the formation of pregnane-20-one derivatives in much higher yields than heretofore obtainable.

NATIONAL INSTITUTE OF HEALTH
BETHESDA, MARYLAND ROBERT P. JACOBSEN

RECEIVED MARCH 21, 1944

---

[1] Gilman and Nelson, *Rec. trav. chim.* **55**, 518 (1936).

[2] Rotations measured in chloroform.

[3] Configuration tentatively assigned.

DESTRUCTION OF RIBOFLAVIN IN MILK BY SUNLIGHT[1]

Sir:

The phenomenon of photochemical destruction of riboflavin has been adequately demonstrated by György and coworkers[2] and Roscoe,[3] and more recently by Williams and Cheldelin.[4] The latter workers demonstrated that as much as 26% of the riboflavin of milk was destroyed by light when the milk was exposed for as short a time as five minutes at 100°. These findings suggested that in all probability appreciable amounts of riboflavin would be lost in milk bottled in the standard type retail glass milk bottle when exposed to sunlight at ordinary temperatures.

Experiments were conducted from mid-morning until mid-afternoon on sunny days. Fresh milk obtained the same day was bottled in pint milk bottles with the usual type cap and exposed to direct sunlight on an open porch. Riboflavin concentrations were determined fluorometrically with the Coleman electronic photometer (Model 12), using essentially the technic of Hand[5] except that 10 cc.

TABLE I

DESTRUCTION OF RIBOFLAVIN IN MILK BY SUNLIGHT

Series	Original riboflavin content, γ/cc.	Riboflavin content after 1 hr. exposure, γ/cc.	Destruction %
I	1.86	1.13	39
	1.51	0.97	36
II	1.98	1.13	43
	2.29	1.40	39
	2.29	1.60	30
III	0.83	0.38	54
	1.94	1.30	33
IV	2.43	1.65	32
	2.60	1.90	27
	1.28	0.66	48

---

[1] Published with the approval of the Director of the North Carolina Agricultural Experiment Station as Paper No. 182 of the Journal series.

[2] P. György, R. Kuhn and T. Wagner-Jauregg, *Naturwissenschaft*, **21**, 560 (1933).

[3] M. H. Roscoe, *Biochem. J.*, **27**, 1540 (1933).

[4] R. R. Williams and V. H. Cheldelin, *Science*, **96**, 22 (1942).

[5] D. B. Hand, *Ind. Eng. Chem., Anal. Ed.*, **11**, 306 (1939).