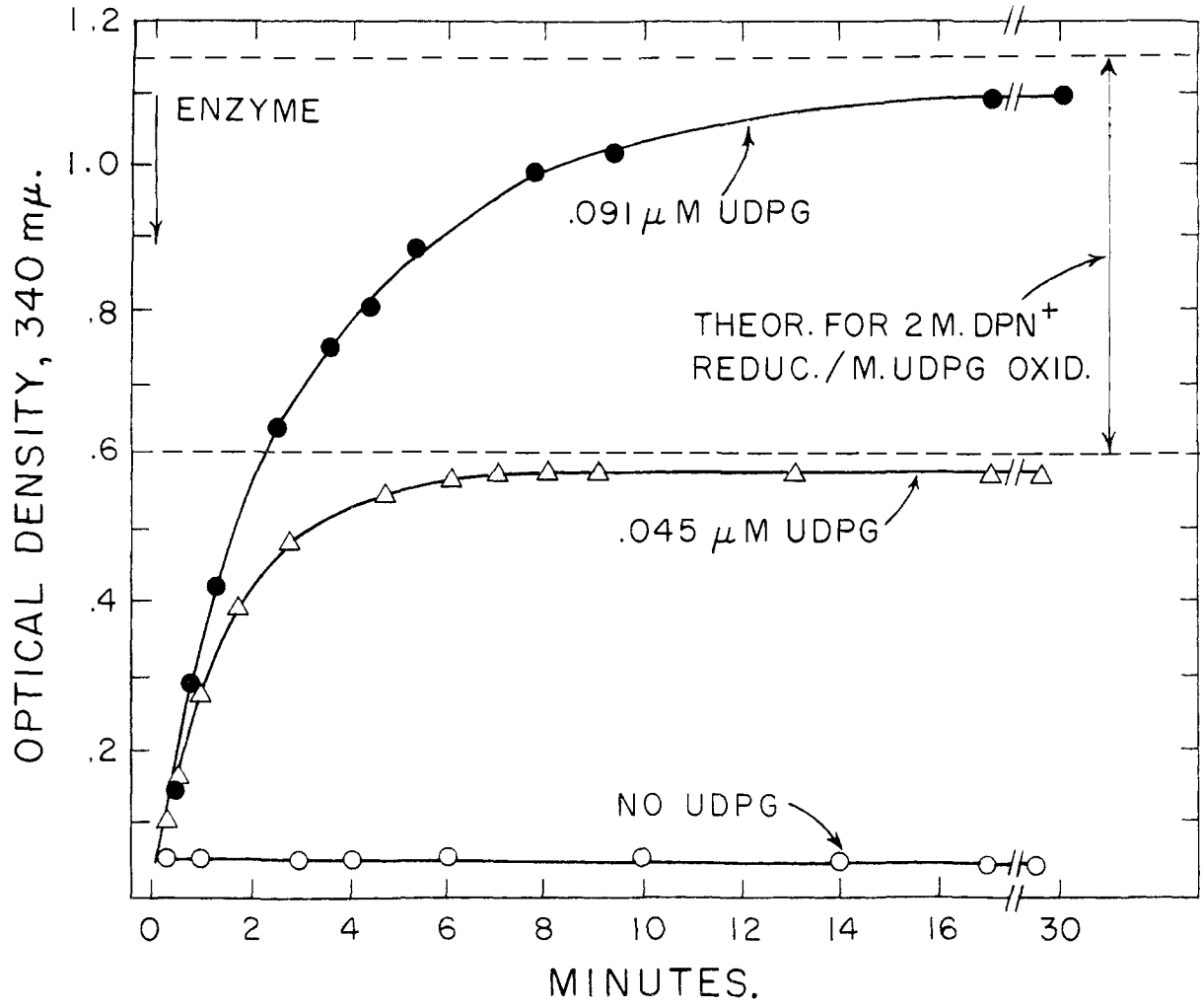

Fig. 1.—Reduction of DPN^+ by purified UDPG dehydrogenase. Each cuvette contained 0.1 *M* diethanolamine buffer, *p*H 9.0, 0.4 μM DPN^+, UDPG as indicated and enzyme in 1 cc.

column and eluted with an NaCl gradient in 0.01 *N* HCl. A zone in the region expected for UDPGA contained a UDP compound which gave carbazole color. For each mole of uridine (ultraviolet adsorption) 0.93 mole of glucuronic acid was present, based on the carbazole reaction. The enzymatic oxidation product of UDPG, even when generated in the presence of semicarbazide as an aldehyde trap, could be utilized to generate *o*-aminophenol glucuronide in the presence of washed microsomes and *o*-aminophenol (Table I). At least 75% of the generated UDPGA could be transferred to the acceptor. No evidence for the appearance of an intermediate compound at the oxidation level of aldehyde has so far been obtained; attempts to accumulate such a compound are in progress.

NATIONAL INSTITUTE OF ARTHRITIS AND METABOLIC DISEASES AND NATIONAL HEART INSTITUTE
U. S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
BETHESDA, MARYLAND
JACK L. STROMINGER
HERMAN M. KALCKAR[8]
JULIUS AXELROD
ELIZABETH S. MAXWELL

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(8) Visiting Scientist of the National Institutes of Health on leave of absence from the Institute of Cytophysiology, University of Copenhagen.

THE PARTIAL SYNTHESIS OF TOMATIDINE[1]

Sir:

The steroid alkaloid tomatidine,[2] derived by hydrolytic cleavage of the tetroside tomatine, native to certain species of *Lycopersicum*, has been shown to yield as important degradation fragments Δ^{16}-allopregnen-3β-ol-20-one[3] and tigogenin lactone.[4] These scission products, together with the secondary nature of the alkamine, diagnostic behavior under conditions of hydrogenation, and empirical composition $C_{27}H_{45}NO_2$, have supported the attribution of a skeletal formulation akin to that characteristic of solasodine, the structure of which has been confirmed by partial synthesis from kryptogenin[5] and from diosgenin.[6] Inasmuch as it is now known[7] that diosgenin and sarsasapogenin give rise,

(1) Supported in part by the United States Public Health Service and the Eugene Higgins Trust.

(2) T. D. Fontaine, J. S. Ard and R. M. Ma, THIS JOURNAL, **73**, 878 (1951).

(3) Y. Sato, A. Katz and E. Mosettig, *ibid.*, **73**, 880 (1951).

(4) R. Kuhn and I. Löw, *Ber.*, **85**, 416 (1952).

(5) F. C. Uhle, THIS JOURNAL, **75**, 2280 (1953).

(6) F. C. Uhle, *ibid.*, **76**, 4245 (1954).

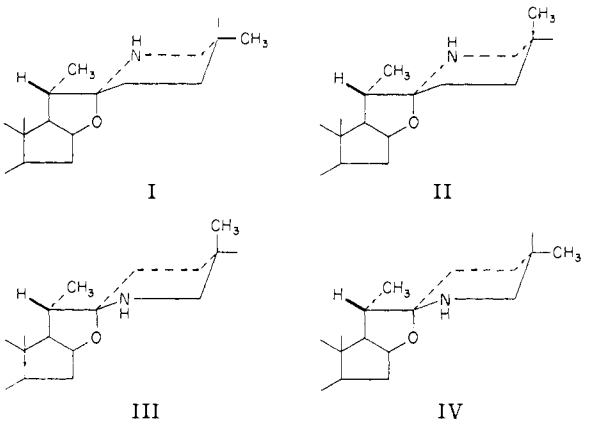
(7) I. Scheer, R. B. Kostic and E. Mosettig, *ibid.*, **75**, 4871 (1953); V. H. T. James, *Chem. and Ind.*, 1388 (1953).

respectively, to enantiomorphic forms of 2-methylglutaric acid which have been correlated with D- and L-glyceraldehyde, the "D" configuration at C-25 in the case of solasodine has, accordingly, been established. Furthermore, the partial synthesis of 5β-solanidan-3β-ol from sarsasapogenoic acid[8] serves to establish the "L" configuration at C-25 in this octahydropyrrocoline solanum alkaloid, and in its congeners, including demissidine, 5α-solanidan-3β-ol, which was recently shown to be the end-product of a series of transformations of tomatidine.[9] Since neither of these partial synthetic sequences would be expected to lead into version at C-25, the "L" configuration at this position in tomatidine may be assigned and the alkamine recently prepared from pseudosarsasapogenin[6] designated as the 5β-epimer of the tomato alkaloid.

We have now confirmed this formulation for tomatidine by synthesis from neotigogenin, a sapogenin originally encountered as a companion substance to tigogenin in *Chlorogalum pomeridianum*[10] and more recently isolated from the mother liquors accumulated subsequent to the crystallization of hecogenin from *Agave sisalana*.[11] Neotigogenin was shown[11] to yield L-2-methylglutaric acid following chromic acid oxidation of an appropriate derivative and to afford tigogenin on prolonged maintenance under reflux in ethanolic acid solution.

Pseudoneotigogenin,[12] m.p. 174–178°, has been transformed, following successive treatment with *p*-toluenesulfonyl chloride in pyridine and sodium iodide in diethyl ketone, to the C-27 phthalimido derivative, m.p. 98–100° (calcd. for $C_{35}H_{47}NO_4$: C, 77.02; H, 8.68; N, 2.57. Found[13]: C, 76.90; H, 9.02; N, 2.58) which, on treatment with hydrazine in ethanol, followed by phosphoric acid, has afforded tomatidine, m.p. 205–207° (calcd. for $C_{27}H_{45}NO_2$: C, 78.02; H, 10.91; N, 3.37. Found: C, 77.69; H, 10.83; N, 3.24), mixed melting point and infrared spectrum identical with that displayed by a sample of naturally occurring tomatidine[14]; hydrochloride, m.p. 265–270°; $[\alpha]^{25}D$ −5.3° (*c* 0.254 in methanol); calcd. for $C_{27}H_{46}NO_2Cl$: C, 71.73; H, 10.26; N, 3.10. Found: C, 71.35; H, 10.02; N, 3.11.

It is not possible, on the basis of the experimental evidence available at the present time, to unequivocally assign total spatial representations to rings E and F of the aminoketal alkaloids. As a consequence of the recent rather extensive discussion[7,15,16] of the stereochemical relationships at C-20, C-22 and C-25 in the spiroketal sapogenins, there appears to be general agreement that in those sapogenin isomers which are stable to moderately vigorous acid conditions, the C-21 methyl group may be assigned to the α-position. This consideration, together with the demonstration of the specific orientations at C-25, limits the configurational possibilities to formulations I and III for solasodine and to II and IV for tomatidine. If arguments advanced[16] in the sapogenin field may be considered germane to the case of the alkaloids, the partial expressions I for solasodine and II for tomatidine appear most probable.



I II III IV

DEPARTMENT OF PHARMACOLOGY
HARVARD MEDICAL SCHOOL
BOSTON 15, MASS. FREDERICK C. UHLE
RESEARCH DEPARTMENT JAMES A. MOORE
PARKE, DAVIS AND COMPANY
DETROIT 32, MICHIGAN

RECEIVED NOVEMBER 8, 1954

(8) F. C. Uhle and W. A. Jacobs, *J. Biol. Chem.*, **160**, 243 (1945).

(9) R. Kuhn, I. Löw and H. Trischmann, *Angew. Chem.*, **64**, 397 (1952).

(10) L. H. Goodson and C. R. Noller, THIS JOURNAL, **61**, 2420 (1939).

(11) R. K. Callow and V. H. T. James, *Chem. and Ind.*, 691 (1954).

(12) This substance will be fully described by Drs. Callow and James in a forthcoming publication. We wish to thank Dr. Callow of the National Institute for Medical Research, London, for the gift of a quantity of neotigogenin.

(13) Microanalyses and spectroscopic determinations by Dr. S. M. Nagy and associates of the Massachusetts Institute of Technology, Cambridge, Mass.

(14) We are indebted to Dr. T. D. Fontaine, U. S. Department of Agriculture, Philadelphia, for a specimen of naturally occurring tomatidine.

(15) M. E. Wall, C. R. Eddy and S. R. Serota, THIS JOURNAL, **76**, 2849 (1954); M. E. Wall and S. R. Serota, *ibid.*, **76**, 2850 (1954); J. B. Ziegler, W. E. Rosen and A. C. Shabica, *ibid.*, **76**, 3865 (1954).

(16) D. A. H. Taylor, *Chem. and Ind.*, 1066 (1954).

GLUCOSIDES FROM THE RHIZOMES OF *PODOPHYLLUM PELTATUM* LINN.

Sir:

It has long been known that podophyllotoxin (Ia)[1] is the most important component of the resin fraction obtained from the rhizomes of the North American *Podophyllum peltatum* Linn. and the Indian *Podophyllum emodi* Wall. (*Berberidaceae*). It is only recently, however, that this compound has gained in interest following the discovery of its ability to inhibit the growth of certain tumors. In both species of podophyllum a number of other compounds have been encountered which are similar both in chemical structure and in biological activity to podophyllotoxin. The Indian variety, for example, also contains 4′-demethyl-podophyllotoxin (Ib),[2] while the American variety contains α-peltatin (IIb) and β-peltatin (IIa).[3] Recently, we have been able to show that the two compounds podophyllotoxin and demethyl-podophyllotoxin, which are present in the resin fraction, also occur

(1) V. Podwyssotzki, *Arch. Exp. Path.*, **13**, 29 (1880); *Ber.*, **15**, 377 (1882). Regarding the constitution, see in particular: J. L. Hartwell and A. W. Schrecker, THIS JOURNAL, **73**, 2909 (1951).

(2) M. V. Nadkarni, P. B. Maury and J. L. Hartwell, *ibid.*, **74**, 280 (1952); M. V. Nadkarni, J. L. Hartwell, P. B. Maury and J. Leiter, *ibid.*, **75**, 1308 (1953).

(3) J. L. Hartwell, *ibid.*, **69**, 2918 (1947); J. L. Hartwell and W. E. Detty, *ibid.*, **70**, 2833 (1948); **72**, 246 (1950).