The mung bean particulate preparation thus contains a 4-epimerase capable of converting UDP glucuronic acid to UDP galacturonic acid, and a decarboxylase which decarboxylates the UDP uronic acid (or acids) to UDP pentose (or pentoses).

Particulate preparations from asparagus shoots, radish roots and leaves, and spinach leaves were also found to catalyze these reactions.

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16-ALKYLATED CORTICOIDS. II. 9α-FLUORO-16α-METHYLPREDNISOLONE 21-ACETATE[1]

Sir:

A recent report[2] on preliminary clinical trials of 9α-fluoro-16α-methylprednisolone prompts us to describe our synthesis of its 21-acetate (I) from sapogenin intermediates. The biological activity of I in animal and human studies is similar to that reported for the corresponding alcohol. Additional pertinent animal and clinical data for the acetate are recorded below.

16α-Methylpregnenolone[3] was hydrogenated with palladium in acetic acid to 3β-hydroxy-16α-methylallopregnan-20-one, m.p. 203–205°, $[\alpha]_D$ +68.2° (all rotations in dioxane). *Anal.* Found: C, 79.42; H, 11.31. Enol acetylation at C-20 followed by treatment with peracetic acid, then alkaline hydrolysis, gave 3β-17α-dihydroxy-16α-methylallopregnan-20-one, m.p. 257–259°, $[\alpha]_D$ +11.9°. *Anal.* Found: C, 75.91; H, 10.04. Bromination and acetoxylation at C-21 produced 21-acetoxy-3β,17α - dihydroxy - 16α - methylallopregnan-20-one, m.p. 181–185°, $[\alpha]_D$ +21.0. *Anal.* Found: C, 70.59; H, 8.51. Oxidation with chromium trioxide–acetone–sulfuric acid gave 21-acetoxy - 17α - hydroxy - 16α -methylallopregnane-3,20-dione, m.p. 205–207°, $[\alpha]_D$ +46°. *Anal.* Found: C, 71.15; H, 8.74. Dibromination at C-2 and C-4, then dehydrobromination with dimethylformamide produced 21-acetoxy-17α-hydroxy-16α-methyl-1,4-pregnadiene-3,20-dione (16α-methyl-1-dehydro-Compound S 21-acetate) which without purification was hydrolyzed with sodium hydroxide to the 21-alcohol, m.p. 209–212°, $[\alpha]_D$ +45.7°, λ_{max}^{MeOH} 244 mμ (ε 14,900). *Anal.* Found: C, 73.98; H, 8.38. 11α-Hydroxylation with *Pestalotia foedans*[4] gave 11α,17α,21-trihydroxy-16α-methyl-1,4-pregnadiene-3,20-dione, m.p. 236–238°, $[\alpha]_D$ +23.9°, λ_{max}^{MeOH} 247 mμ (ε 18,200). *Anal.* Found: C, 70.56; H, 8.02. 21-Monoacetate: m.p. 188–190°, $[\alpha]_D$ +45.6, λ_{max}^{MeOH} 247 mμ (ε 19,000). *Anal.* Found: C, 66.96; H, 7.64 (1 mole ethyl acetate). 11α-Tosylate-21-acetate: m.p. 182–184° (dec.), $[\alpha]_D$ +87.7°, λ_{max}^{MeOH} 229.5 mμ (ε 22,200), shoulder at 241 mμ. *Anal.* Found: C, 65.53; H, 6.78. Dehydrotosylation with sodium acetate in acetic acid gave 21-acetoxy-17α-hydroxy - 16α - methyl - 1,4,9(11) - pregnatriene-3,20-dione, m.p. 210–213°, λ_{max}^{MeOH} 238 mμ (ε 15,500). *Anal.* Found: C, 72.68; H, 7.65. Addition of hypobromous acid (N-bromoacetamide and perchloric acid) gave a 9α,11β-bromohydrin, which was epoxidized by sodium acetate treatment to 21 - acetoxy - 17α - hydroxy - 16α - methyl - 9β,11β-epoxy-1,4-pregnadiene-3,20-dione, m.p. 198–200°, $[\alpha]_D$ +40.1°, λ_{max}^{MeOH} 249 mμ (ε 15,600). *Anal.* Found: C, 69.55; H, 7.18. Ring opening with hydrogen fluoride in chloroform–tetrahydrofuran produced the desired product, 9α-fluoro-16α-methylprednisolone 21-acetate (I), m.p. 229–231°, $[\alpha]_D$ +77.6, λ_{max}^{MeOH} 239 mμ (ε 14,500). *Anal.* Found: C, 66.27; H, 7.18.

Eosinopenic activity in the mouse, dog, and man, shows this compound to be at least four to six times as active as prednisone and prednisolone. In the granuloma pouch test,[5] I is 6.5 times as active as prednisolone acetate, while thymus involution studies in rats and the nitrogen excretion in dogs reveals this compound to be about twenty-five times as active as prednisolone acetate and prednisone, respectively, in these tests.

Metabolic balance studies[6] carried out with I in a human subject in doses of 15 mg. and 25 mg. per 24 hours caused an average increase over control values in urinary excretion per 24 hours of (1) phosphorus: 53 mg. at 15 mg. dose and 387 mg. at 25 mg. dose; (2) nitrogen: 3 g. at 15 mg. dose and 6.4 g. at 25 mg. dose; (3) sodium: 13.4 meq. at 15 mg. dose and 26.4 meq. at 25 mg. dose; (4) potassium: 8.9 meq. at 15 mg. dose and 17.9 meq. at 25 mg. dose.

Fasting blood sugar levels were consistently elevated above 120 mg. per cent. throughout the period of administration of I in doses of 15 mg. and 25 mg. per 24 hours. This is in marked contrast to the results obtained with prednisone at doses up to 70 mg. per 24 hours.

(1) After submission of this manuscript, a Communication appeared [G. Arth, J. Fried, D. Johnston, D. Hoff, L. Sarett, R. Silber, H. Stoerk and C. Winter, THIS JOURNAL, **80**, 3161 (1958)] describing the preparation of 9α-fluoro-16α-methylprednisolone 21-acetate from bile acid intermediates.

(2) E. W. Boland, *Cal. Med.*, **88**, 417 (1958).

(3) R. E. Marker and H. Crooks, THIS JOURNAL, **64**, 1280 (1942).

(4) Canadian Patent 507,009.

(5) A. Robert and J. E. Nezamis, *Acta Endocrinol.*, **25**, 105 (1957).

(6) E. C. Reifenstein, F. Albright and S. Wells, *J. Clin. Endocrinol.*, **5**, 367 (1945).

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STUDIES OF THE PHOSPHOGLYCERIC ACID MUTASE REACTION WITH RADIOACTIVE SUBSTRATES

Sir:

In a previous communication it was confirmed that diphosphoglyceric acid (DPGA) activated phosphoglyceric acid mutase and that during the reaction one of the phosphate groups was transferred to a suitable acceptor.[1] There was observed,

(1) L. I. Pizer and C. E. Ballou, THIS JOURNAL, **79**, 3612 (1957).