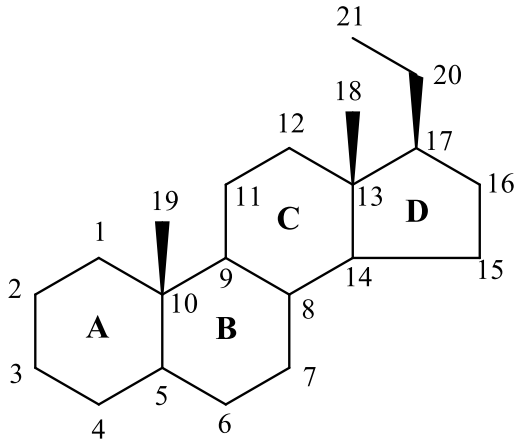
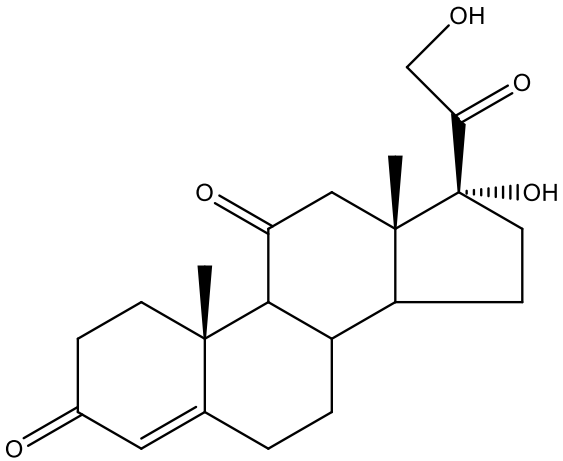
Remembering the Kalamazoo Steroid Chemistry Work (1950-1995)

Edward J. Hessler, Ph.D.

Bridge Organics Co.

Numbering of the carbon atom positions in the steroid skeleton





Cortisone

Donald S. Gilmore

Stigmasterol

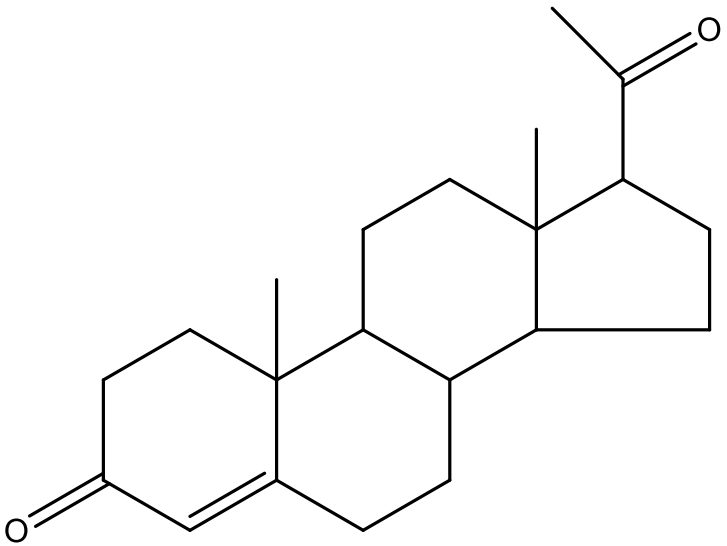
Heyl and Herr 1950 ↓ ozonolysis

C21-aldehyde

↓ 2 oxidations

↓

Progesterone



Conversion of steroids in soybean oil to hydrocortisone

Soybeans

↓ pressed

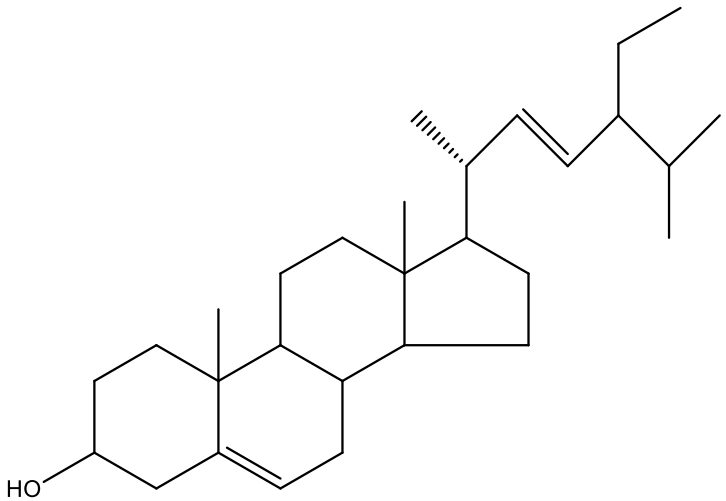
Soybean oil

↓ vacuum distillation

Henkel **Soy sterols**

Greiner and Fevig, early 50's ↓ fractional crystallization

Stigmasterol + sitosterol



Progesterone

Peterson and Murray 1952 — *Rhizopus nigricans*

↓

11-alpha-hydroxyprogesterone

Hogg, Beal, Nathan, Lincoln
WP Schneider, Magerlein
Hanze, Jackson, Korman
1955

↓

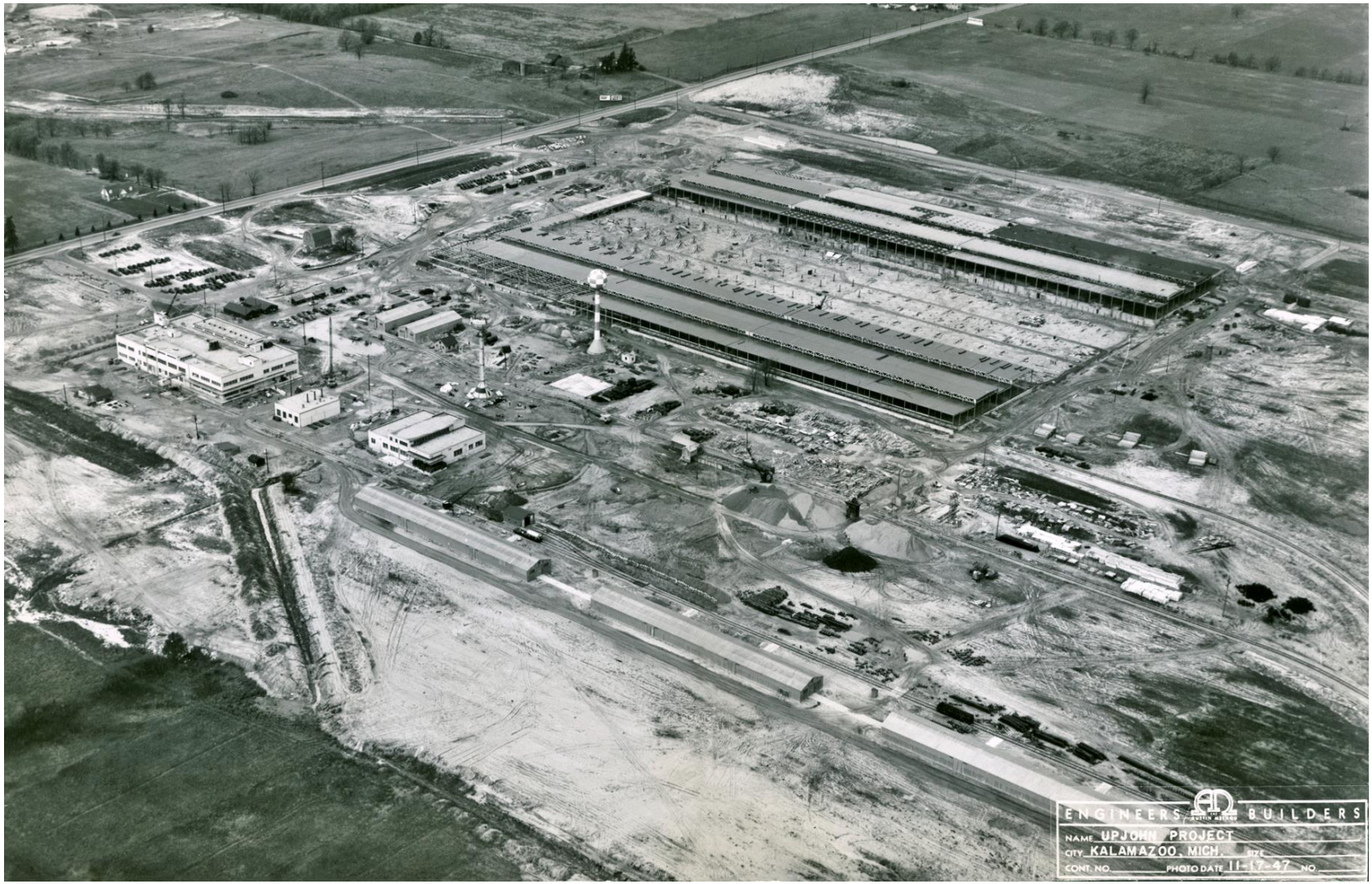
Favorski ester

↓

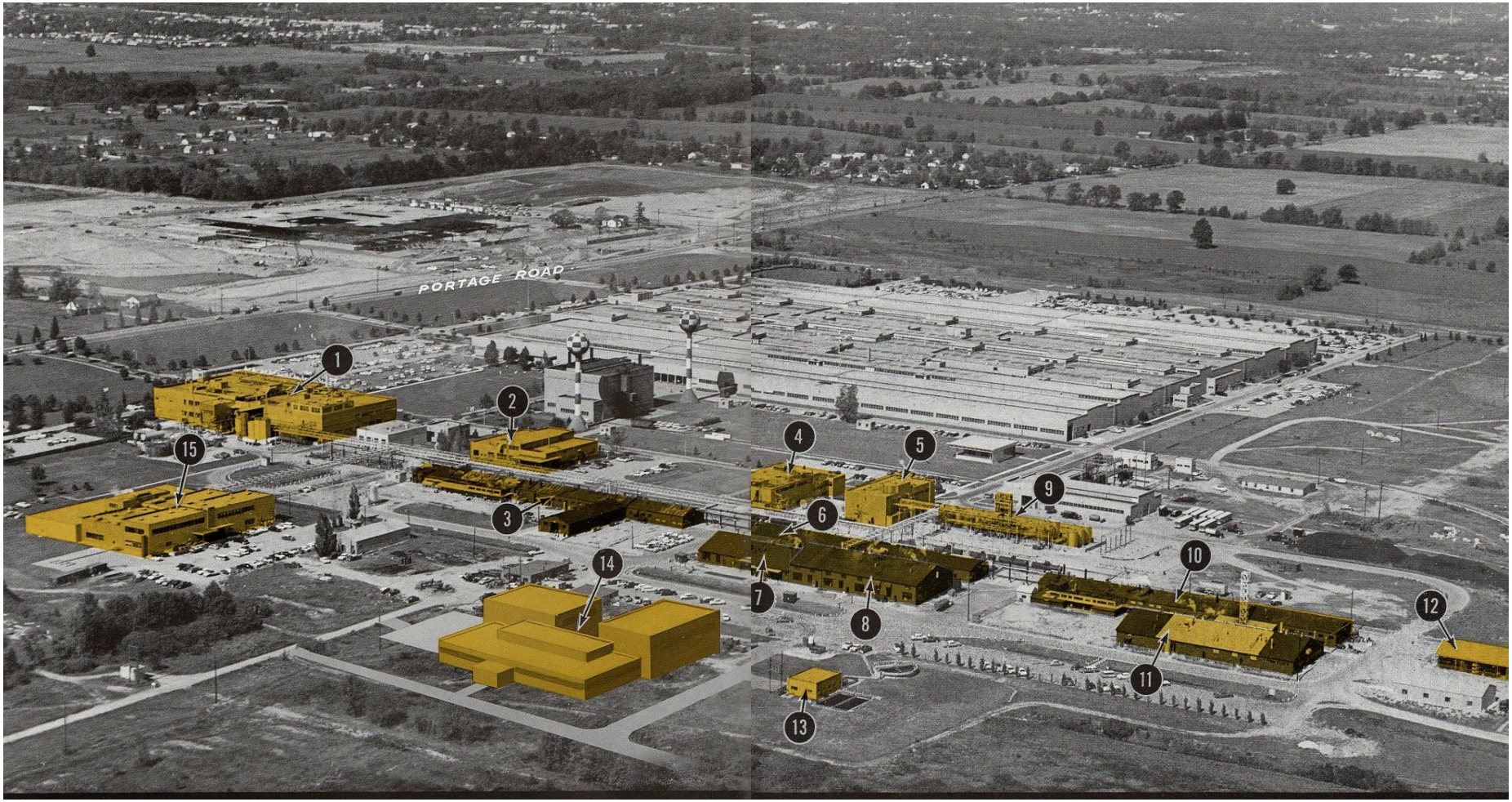
Dienediol acetate

↓

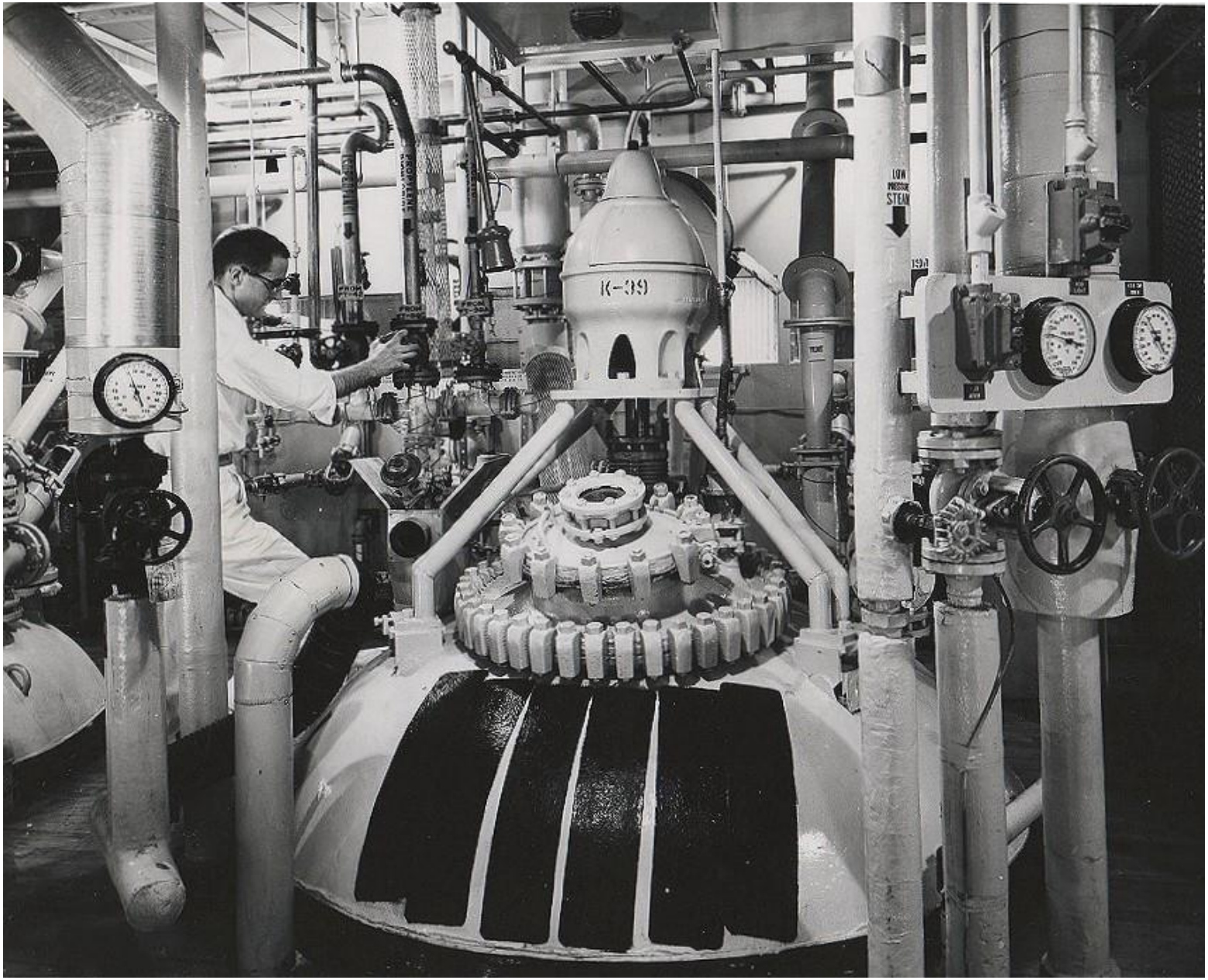
Hydrocortisone



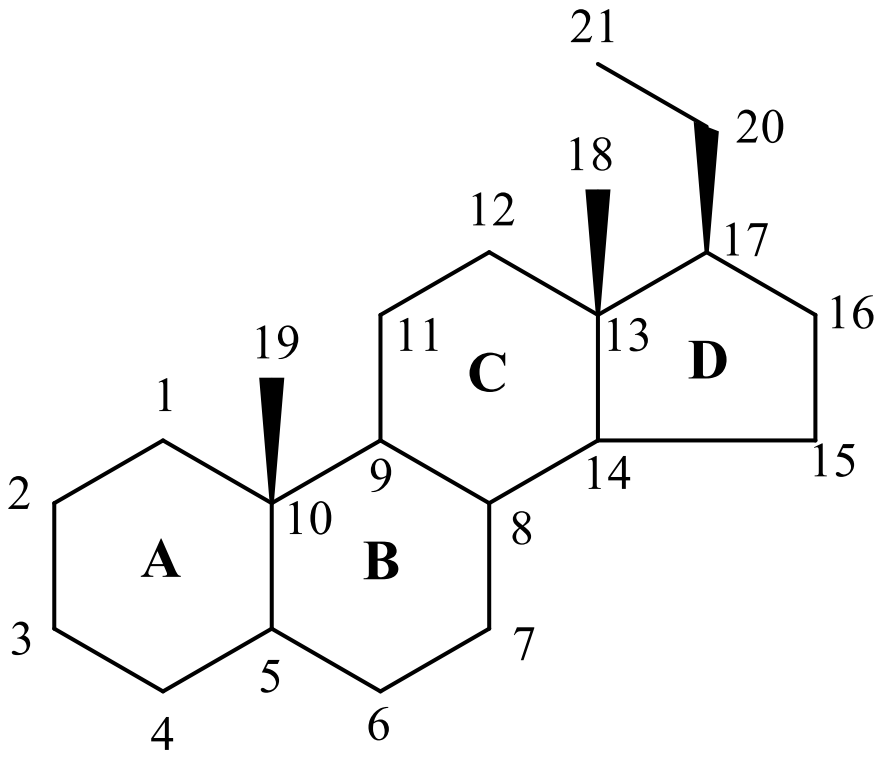
Beginnings of the Portage chemical facility



Portage chemical facility (1960)


K-39
LOW PRESSURE STEAM

Numbering of the carbon atom positions in the steroid skeleton



Dienediol acetate

↓

Dienediol hemisuccinate

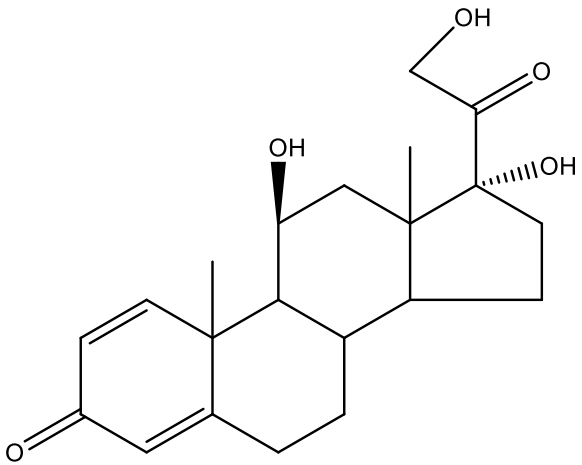
fermentation with S. affinis

↓

Trienediol

↓

Prednisolone products



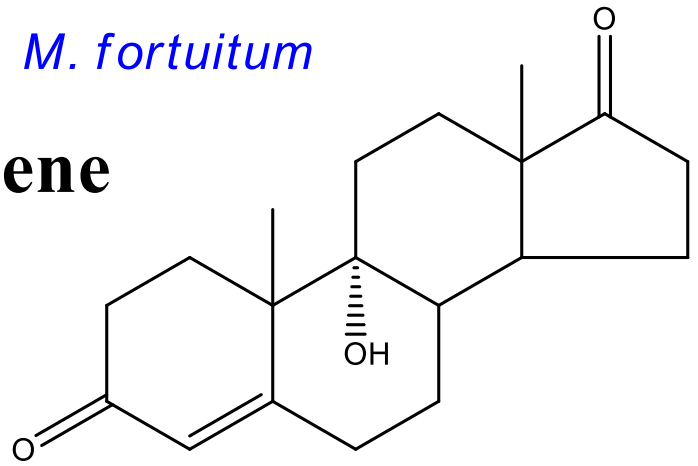
Allene sulfoxide route

Sitosterol

MG Wovcha et.al., 1978

M. fortuitum

9-hydroxyandrostene dione



Van Rheenen and Shephard, 1979

allene sulfoxide

17hydroxy-20-methylenolether

hydrocortisone acetate

9-alpha-hydroxyandrostenedione

KPShephard 1978

↓

4,9(11)-androstadienedione

fermentation by S. affinis

↓

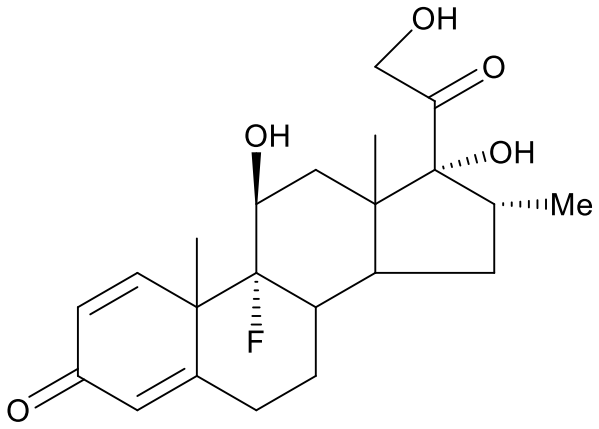
EJ Hessler, VH
Van Rheenen 1980

↓

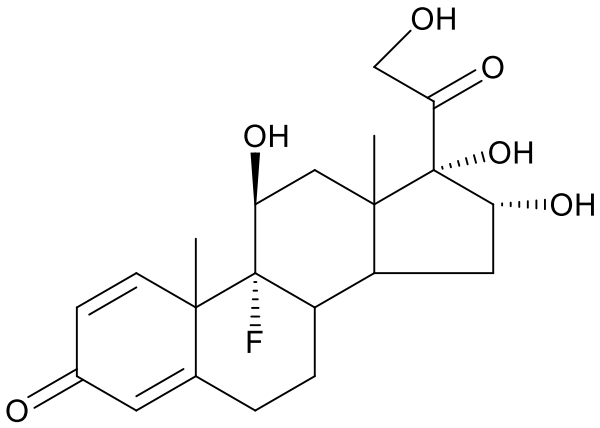
17-chloroaldehyde

↙ ↘

dexamethasone products



triamcinolone products



SNAP chemistry

DA Livingston, JE Petre, and CLBergh, 1990

9hydroxyandrostenedione

↓

4,9(11)-androstadienedione

↓

17-cyanohydrin

↓

O-chloromethylsilylated cyanohydrin

↓

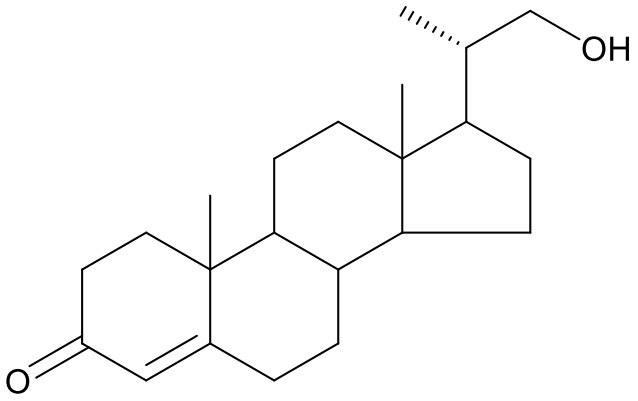
hydrocortisone acetate

Sitosterol

Merle Wovcha 1991 — *M. fortuitum mutant*

↓

21-alcohol



B. Hewitt

↓

21-aldehyde

↓ oxidation of enamine

Progesterone

The End of an Era

Questions?