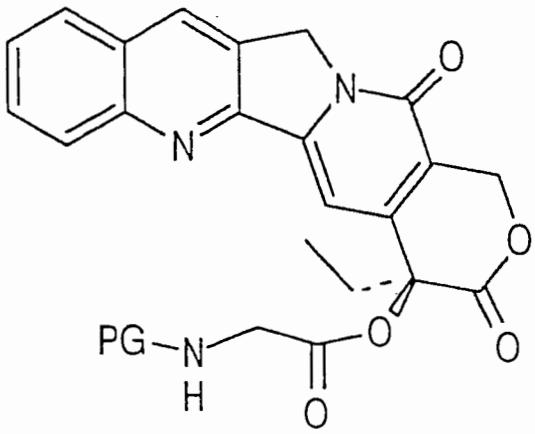
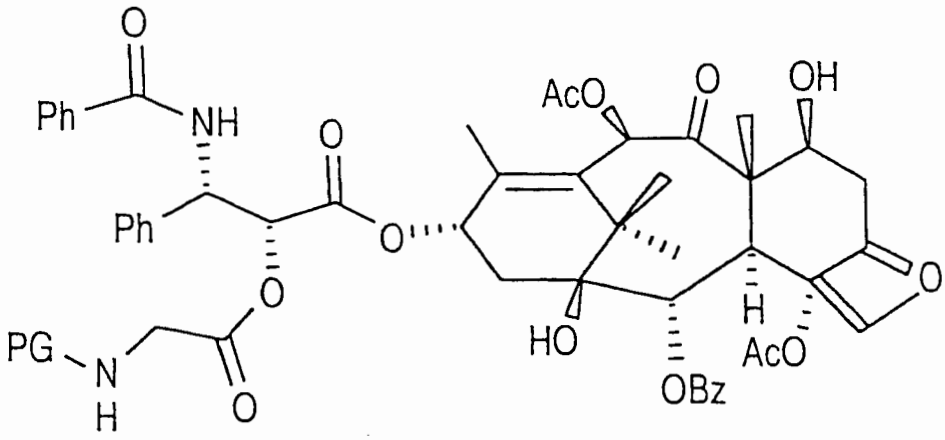
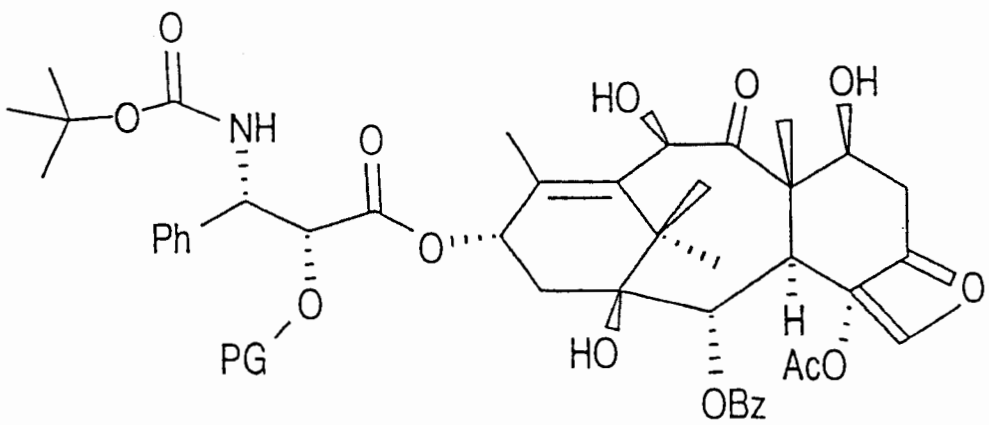
FIG. 1



POLY-L-GLUTAMIC ACID-GLYCYL-20(S)CAMPTOTHECIN



POLY-L-GLUTAMIC ACID-2'-(GLYCYL) PACLITAXEL



POLY-L-GLUTAMIC ACID-2'-DOCETAXEL

FIG. 2

MANUFACTURING SCHEME

POLY-L-GLUTAMIC ACID SODIUM SALT

1. DISSOLVE IN WATER
2. ACIDIFY TO pH 2 WITH 1M HCl
3. SEPARATE THE SOLID BY CENTRIFUGATION
4. WASH WITH WATER UNTIL pH >3.5
5. LYOPHILIZE

POLY-L-GLUTAMIC ACID

1. PACLITAXEL, DIMETHYLAMINOPYRIDINE, DIISOPROPYLCARBODIIMIDE, DIMETHYLFORMAMIDE, STIR UNTIL REACTION IS COMPLETE
2. DILUTE WITH 10% NaCl SOLUTION(VOLUME 2.5 TIMES OF DMF)
3. FILTER
4. WASH SEVERAL TIMES WITH WATER
5. LYOPHILIZE
6. SLURRY WITH MeCN
7. VACUUM DRY

CT 2103

YIELD = AVERAGE 87% FOR 10 LOTS

FIG. 3

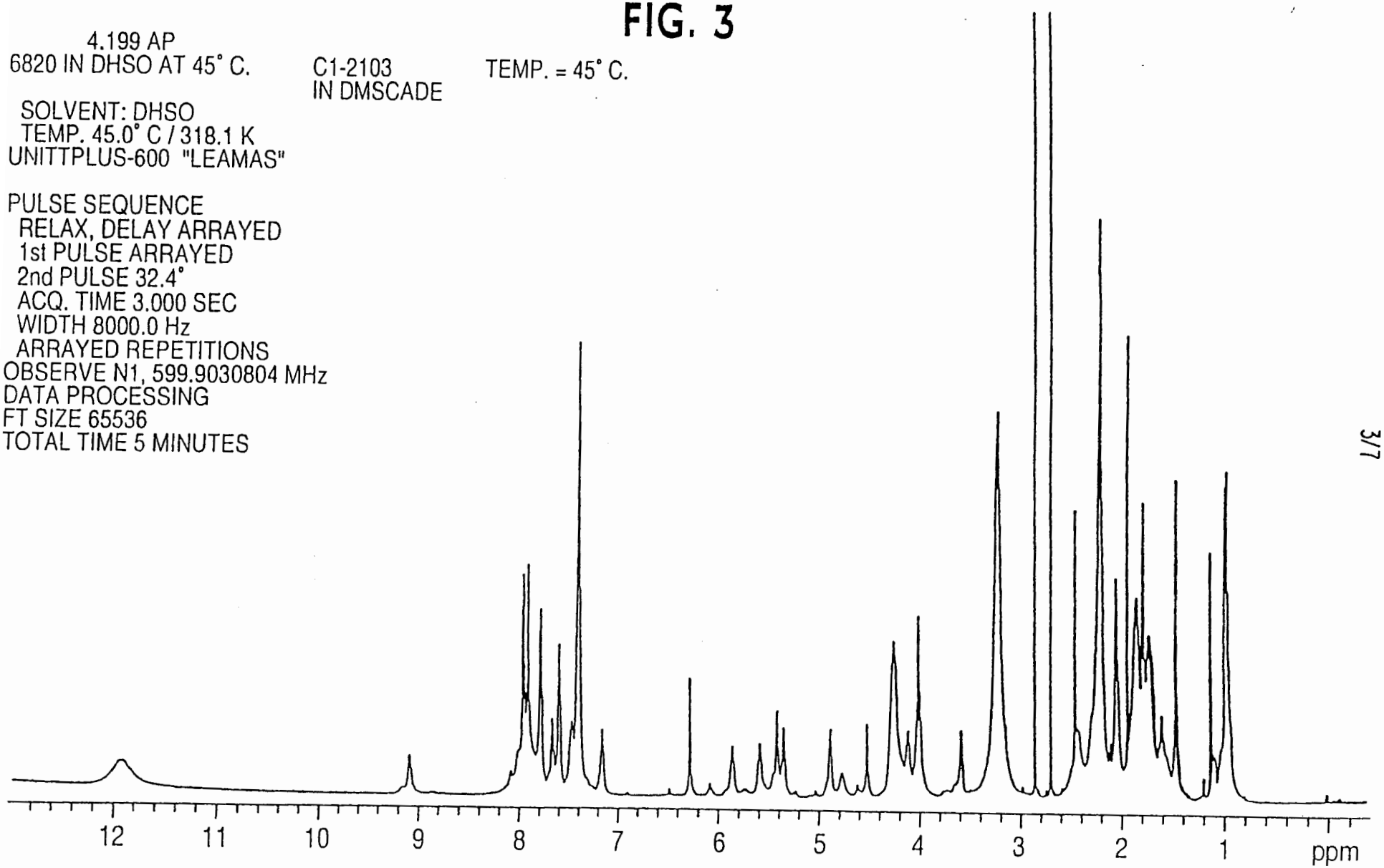
4.199 AP
6820 IN DHSO AT 45° C.

C1-2103
IN DMSCADE

TEMP. = 45° C.

SOLVENT: DHSO
TEMP. 45.0° C / 318.1 K
UNITTPLUS-600 "LEAMAS"

PULSE SEQUENCE
RELAX, DELAY ARRAYED
1st PULSE ARRAYED
2nd PULSE 32.4°
ACQ. TIME 3.000 SEC
WIDTH 8000.0 Hz
ARRAYED REPETITIONS
OBSERVE N1, 599.9030804 MHz
DATA PROCESSING
FT SIZE 65536
TOTAL TIME 5 MINUTES



3/7

FIG. 4

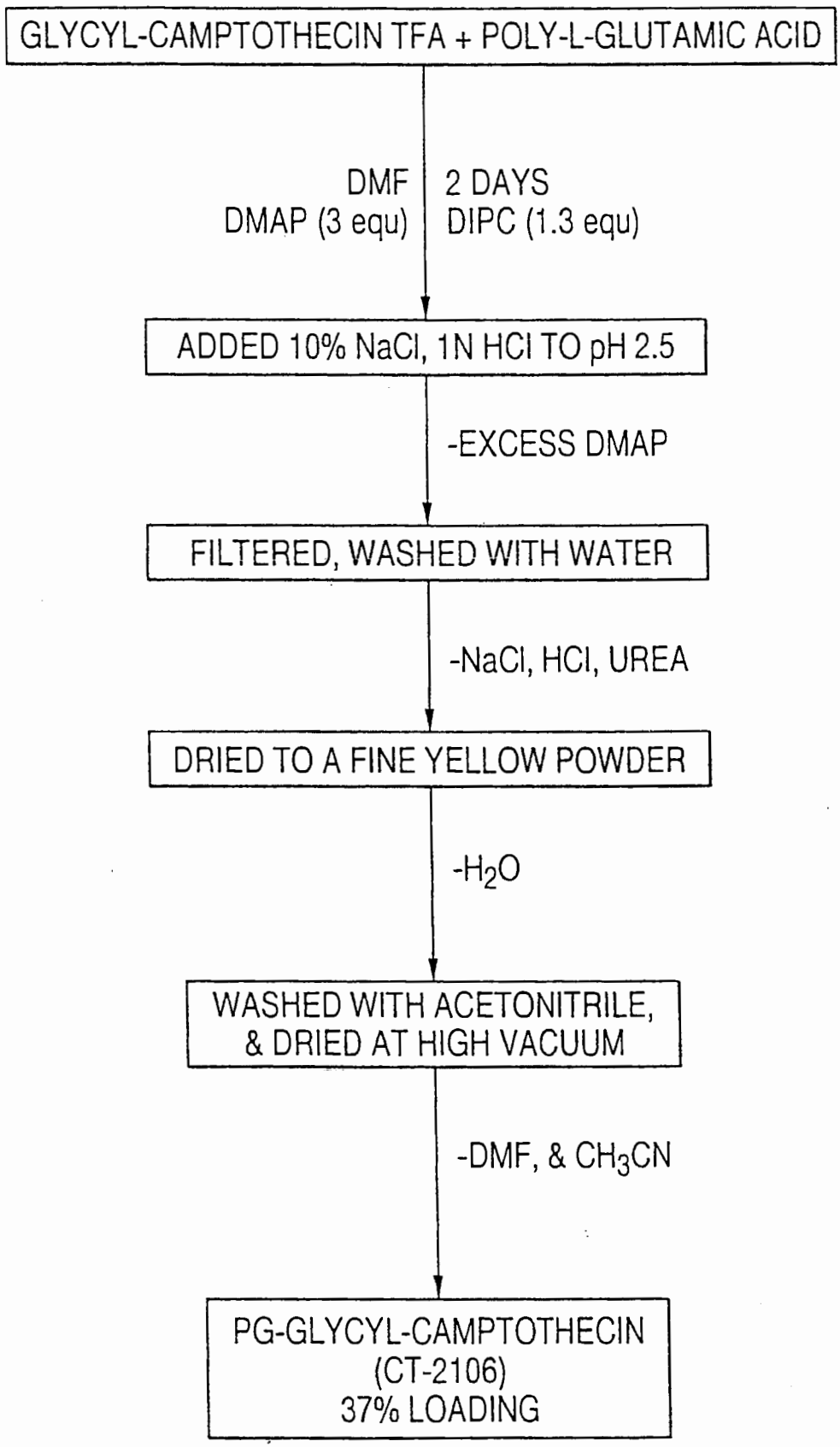

GLYCYL-CAMPTOTHECIN TFA + POLY-L-GLUTAMIC ACID
DMF
DMAP (3 equ)
2 DAYS
DIPC (1.3 equ)
ADDED 10% NaCl, 1N HCl TO pH 2.5
-EXCESS DMAP
FILTERED, WASHED WITH WATER
-NaCl, HCl, UREA
DRIED TO A FINE YELLOW POWDER
-H_2O
WASHED WITH ACETONITRILE, & DRIED AT HIGH VACUUM
-DMF, & CH_3CN
PG-GLYCYL-CAMPTOTHECIN (CT-2106) 37% LOADING

FIG. 5

REACTION SCHEME I

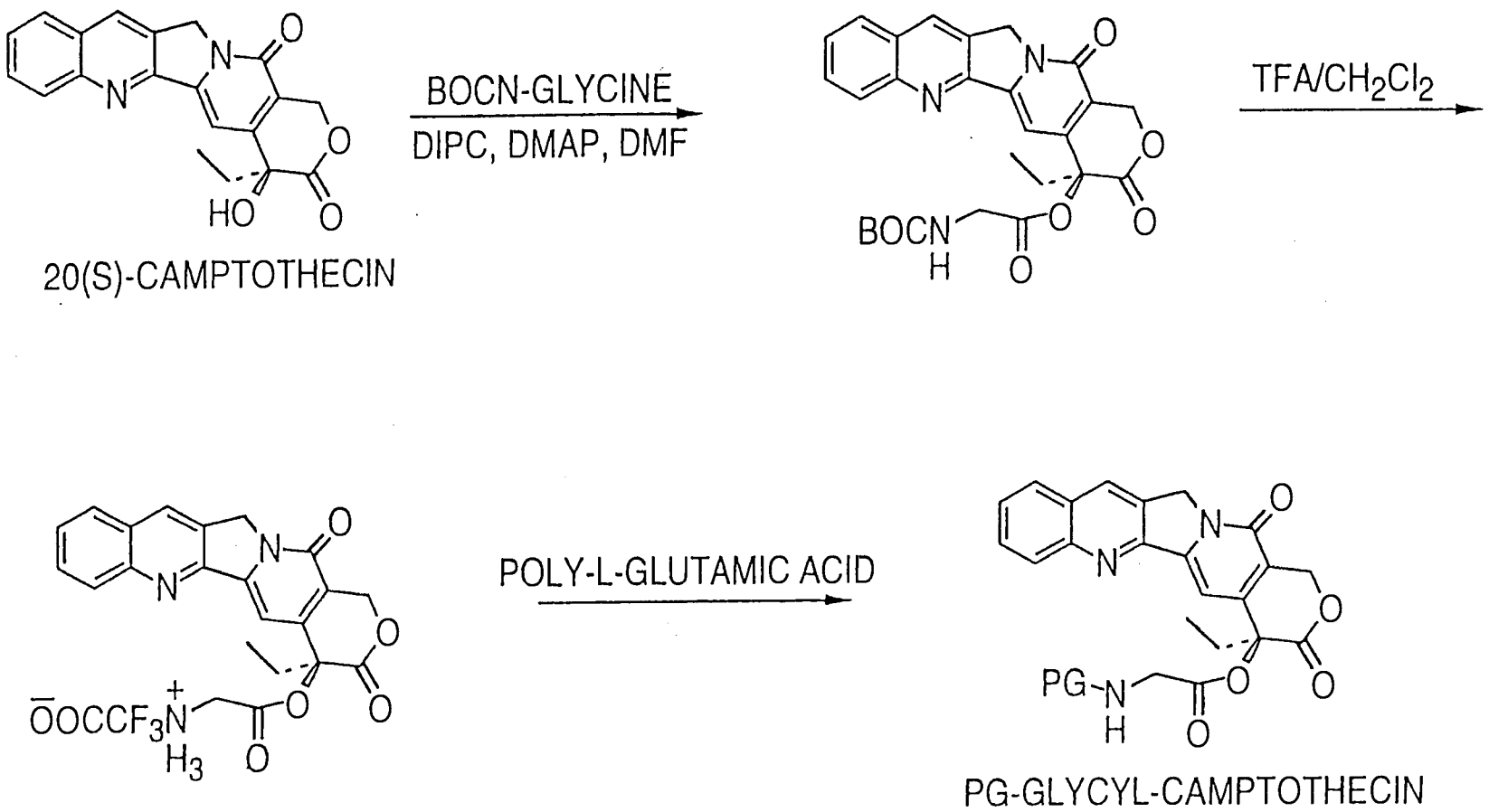
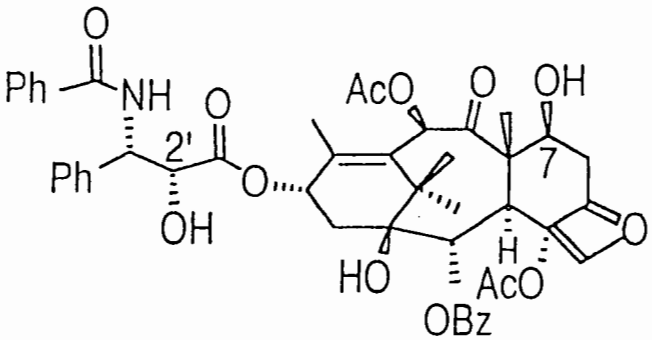


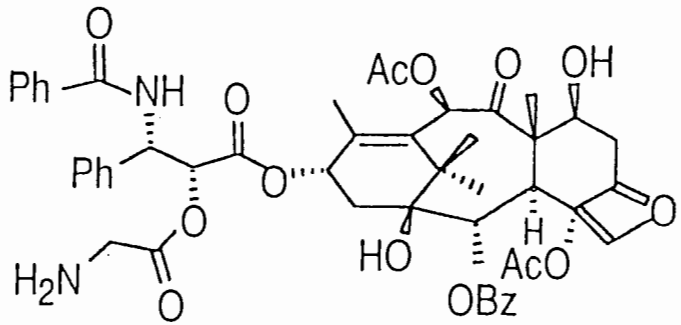
FIG. 6

REACTION SCHEME II



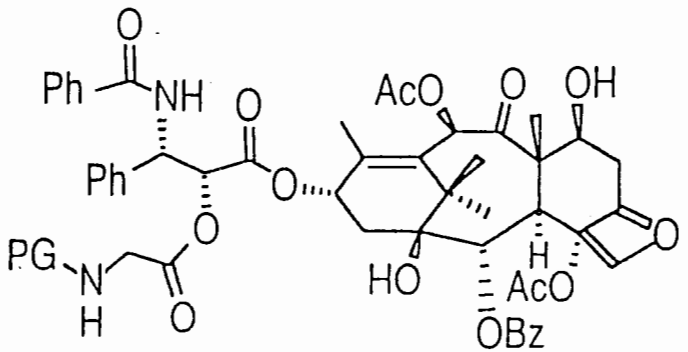
PACLITAXEL

1. BOCN-GLYCINE
   DIPC, DMAP, DMF
2. HCOOH
3. $NaHCO_3$



POLY-L-GLUTAMIC ACID

DIPC, DMAP, DMF



PG-2'-(GLYCYL)PACLITAXEL

FIG. 7

REACTION SCHEME III

