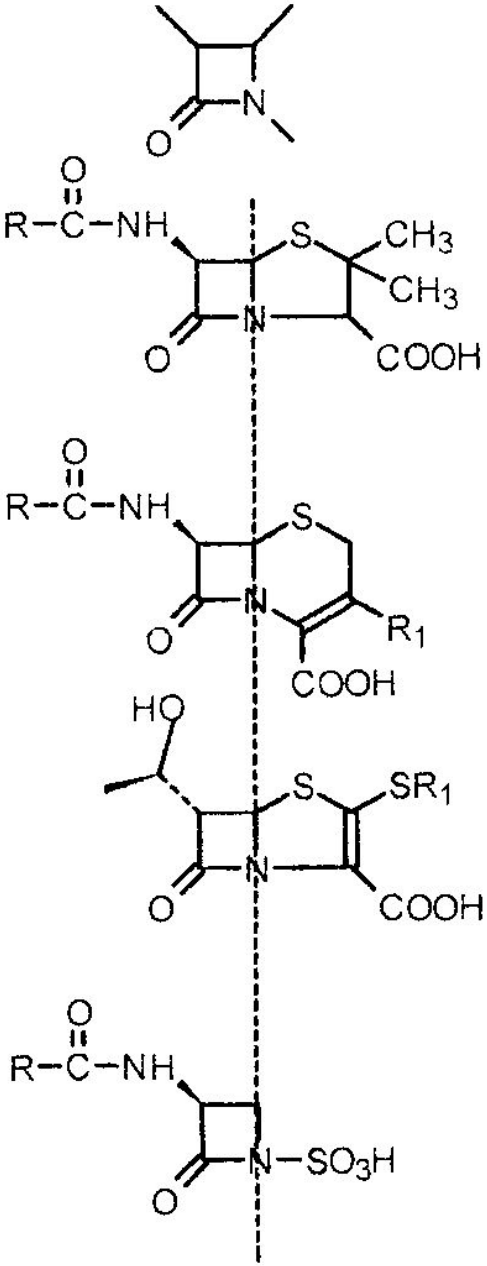
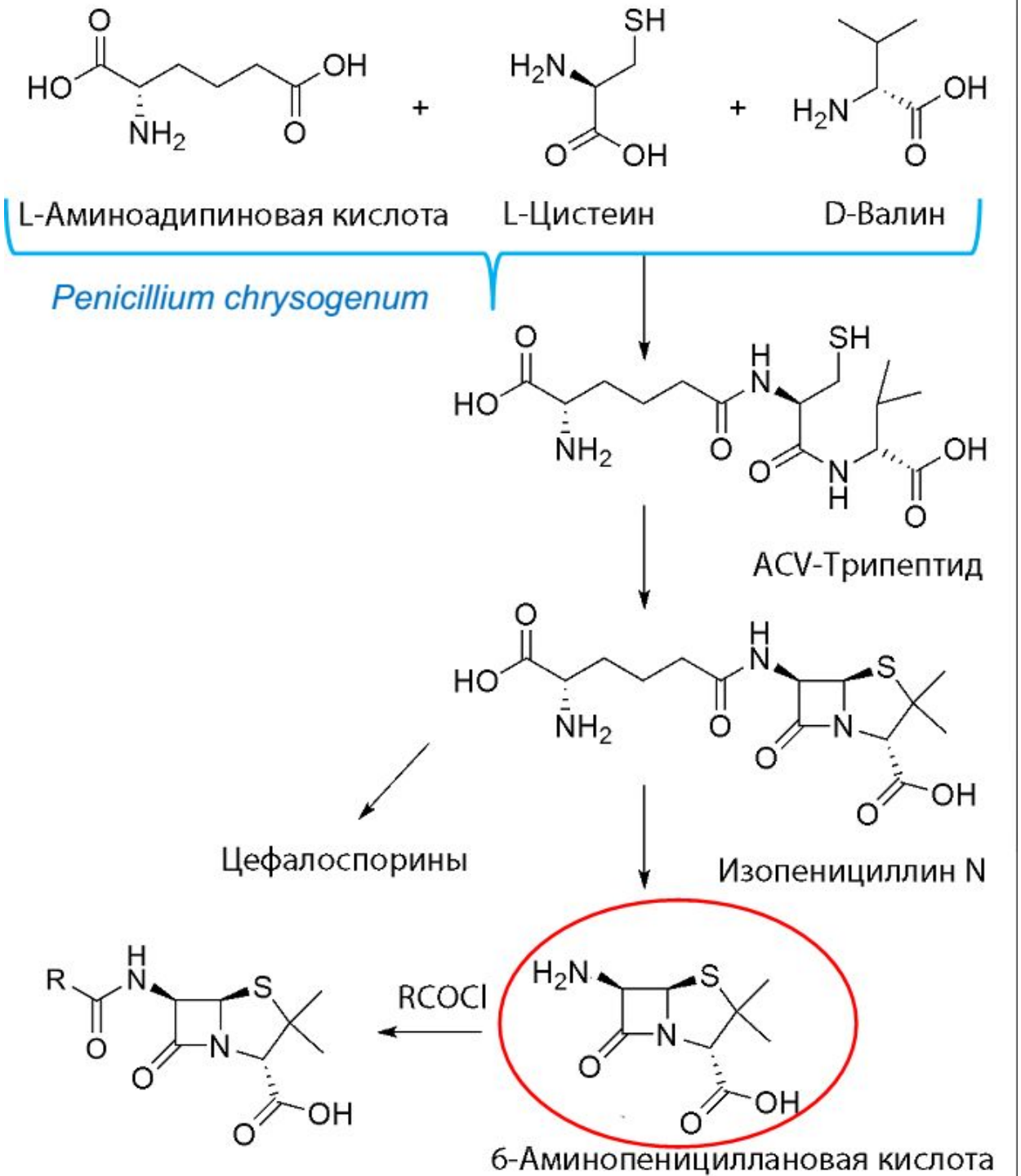
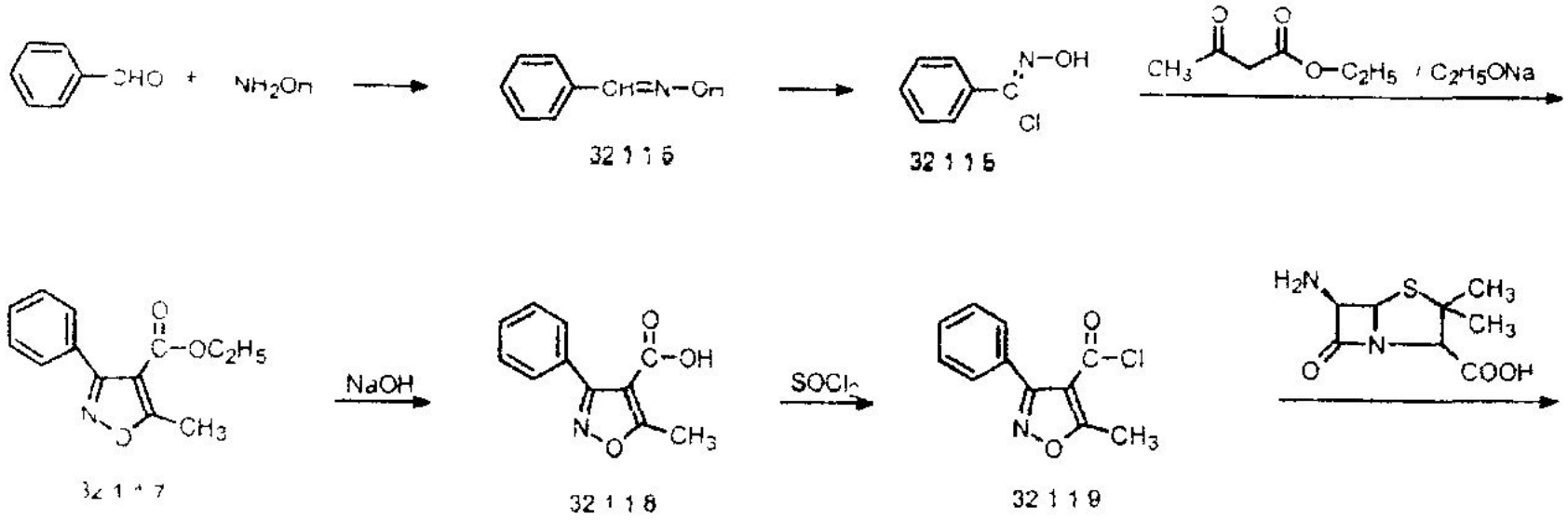
ПОЛУЧЕНИЕ АНТИБИОТИКОВ

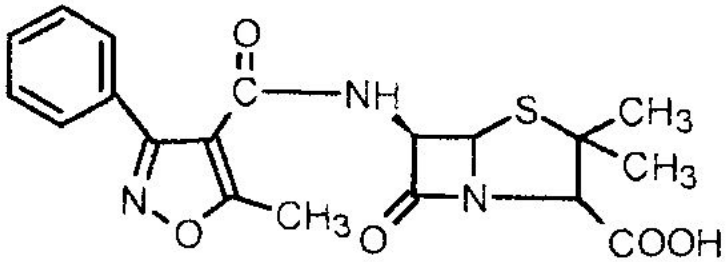
БЕТА-ЛАКТАМНЫЕ АНТИБИОТИКИ




L-Аминоадипиновая кислота
L-Цистеин
D-Валин
Penicillium chrysogenum
ACV-Трипептид
Цефалоспорины
Изопенициллин N
RCOCl
6-Аминопенициллановая кислота

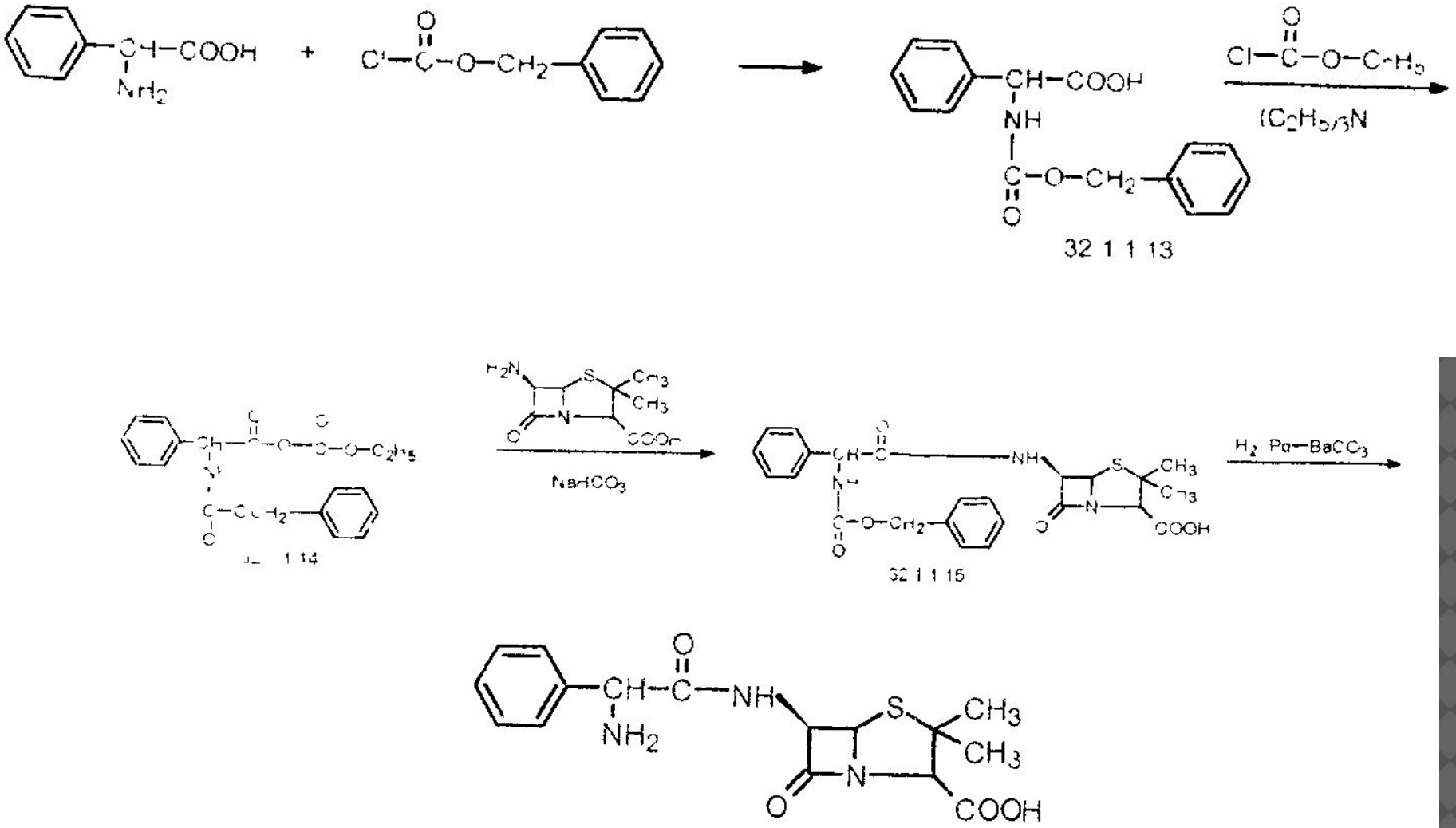
ОКСАЦИЛЛИН

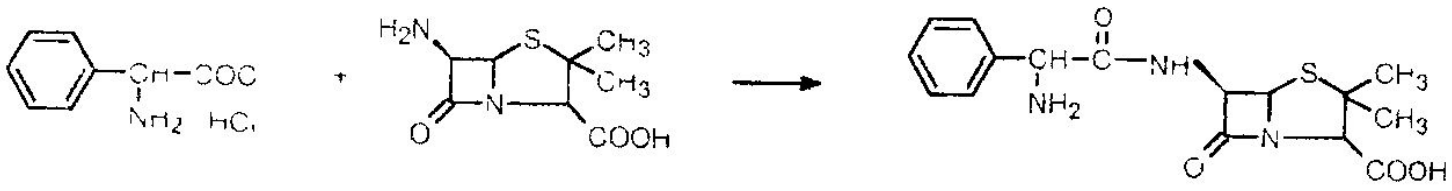




32 1 1 10

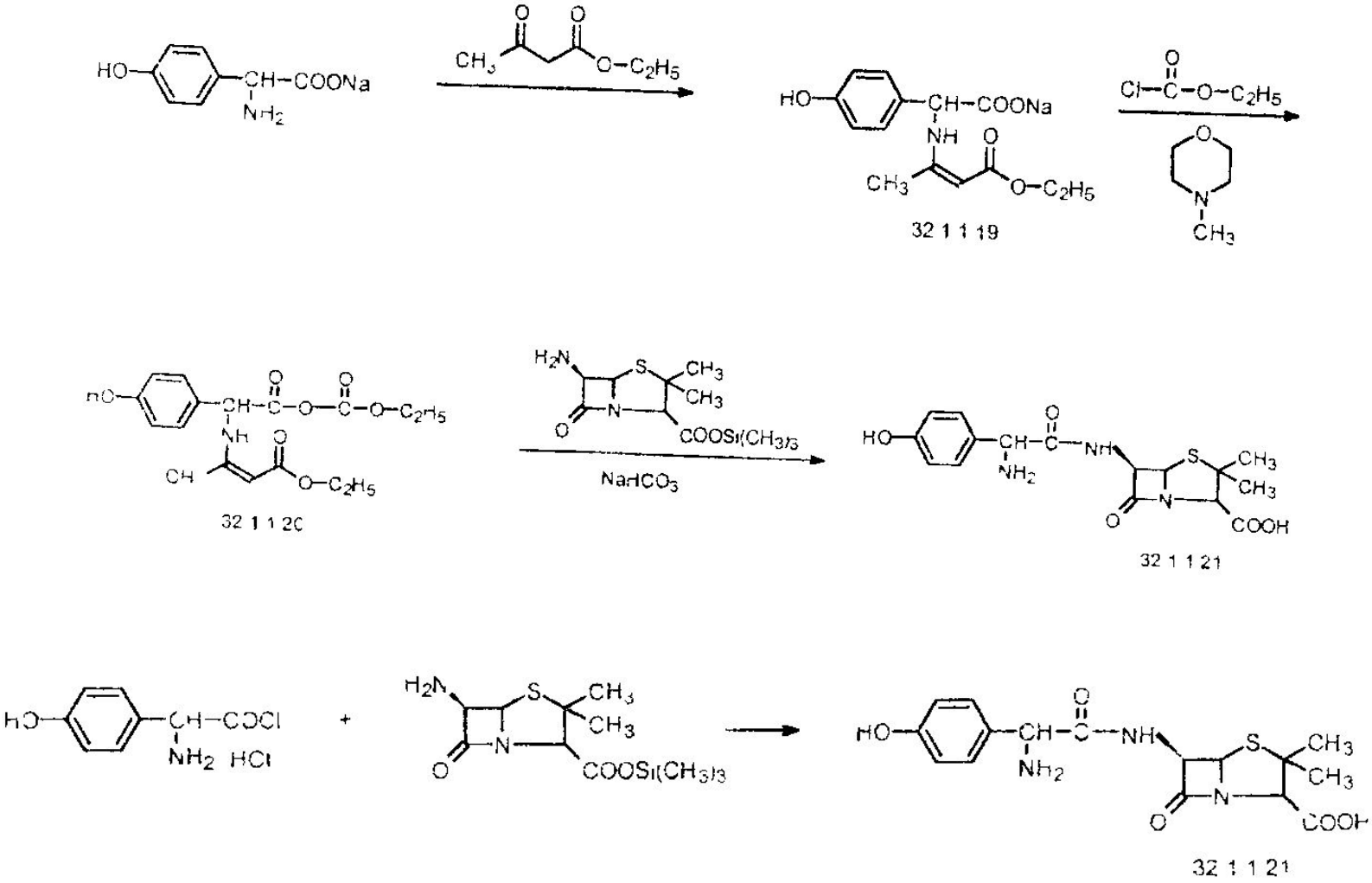
АМПИЦИЛЛИН


CH–COOH
NH2
+
Cl–C–O–CH2
CH–COOH
NH
C–O–CH2
32 1 1 13
Cl–C–O–C2H5
(C2H5)3N
NaHCO3
NH
S
CH3
CH3
COOH
32 1 1 15
H2 Pd–BaCO3
32 1 1 16

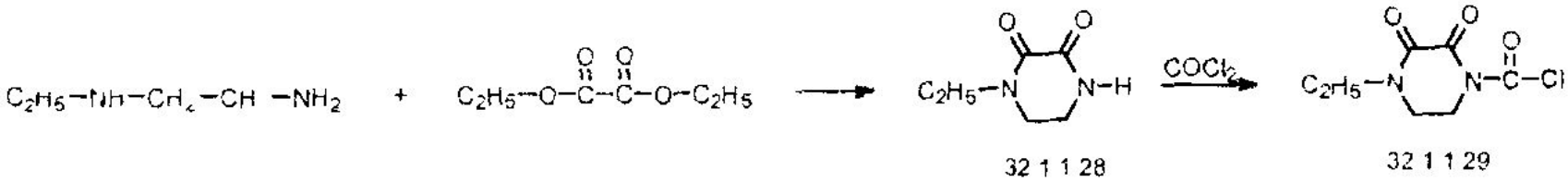


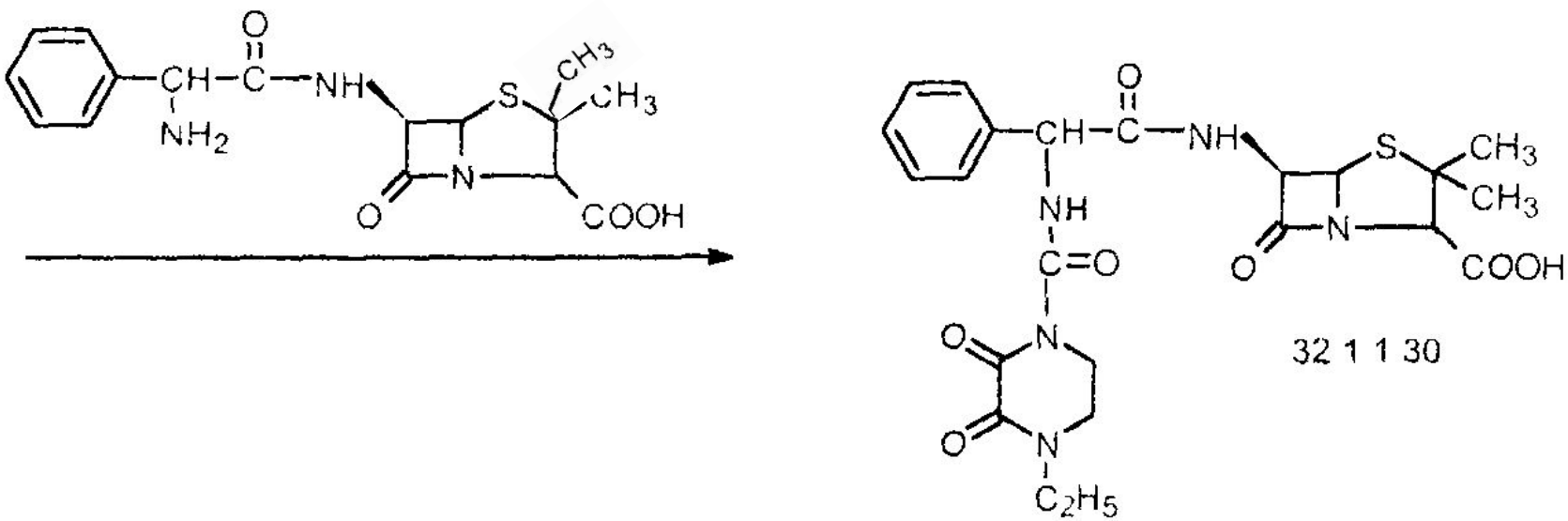
32 1 1 16

АМОКСИЦИЛЛИН

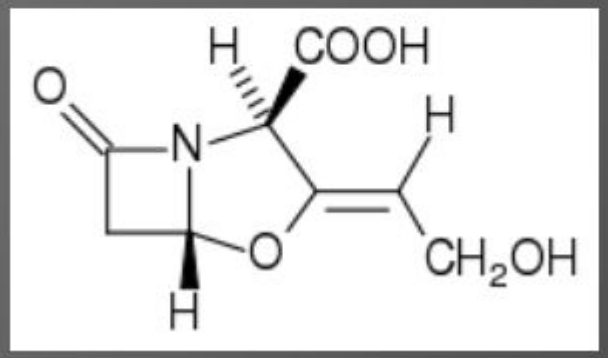


ПИПЕРАЦИЛЛИН

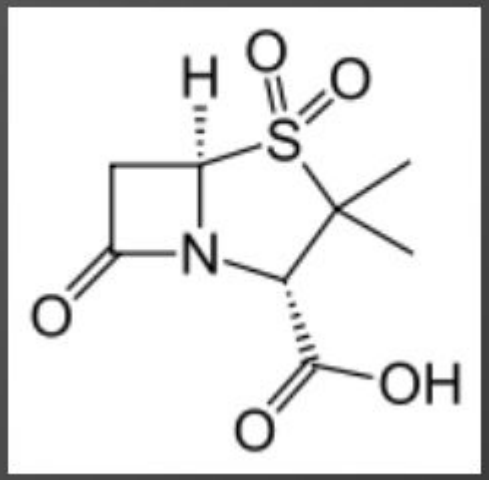




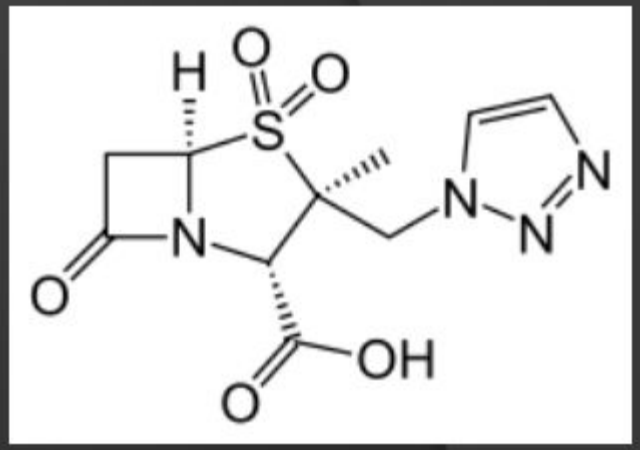
Клавулановая кислота



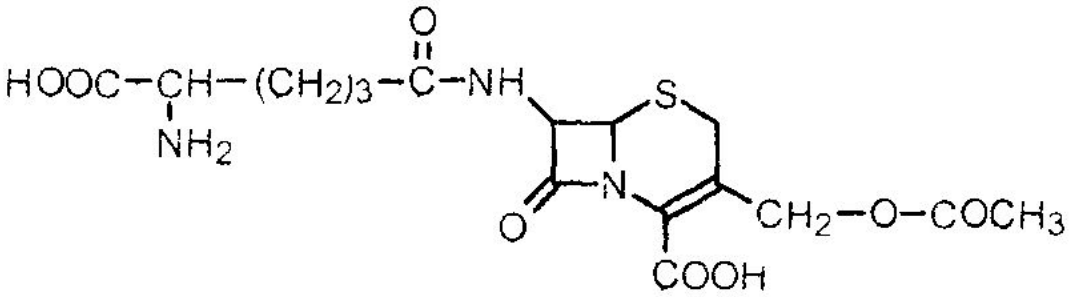
Сульбактам



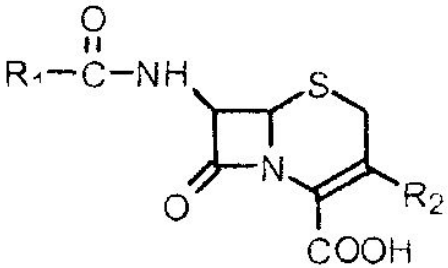
Тазобактам



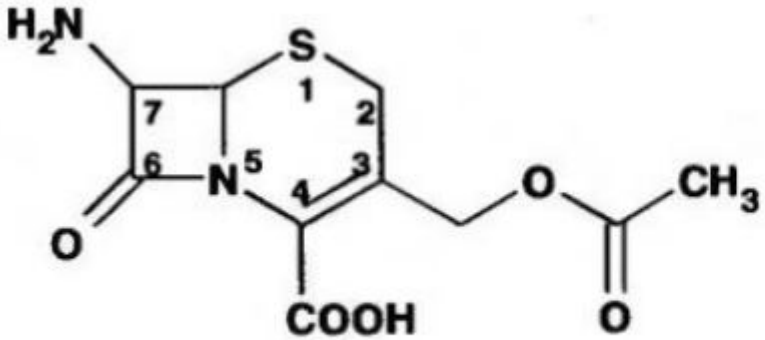
ЦЕФАЛОСПОРИНЫ



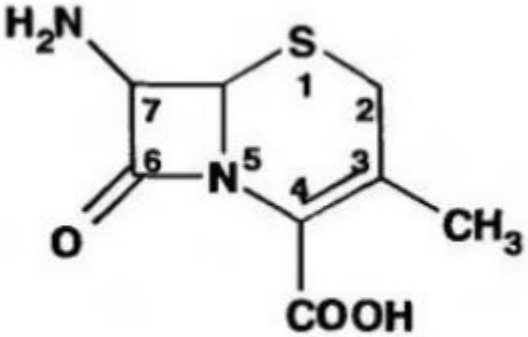
цефалоспорин С



полусинтетические цефалоспорины



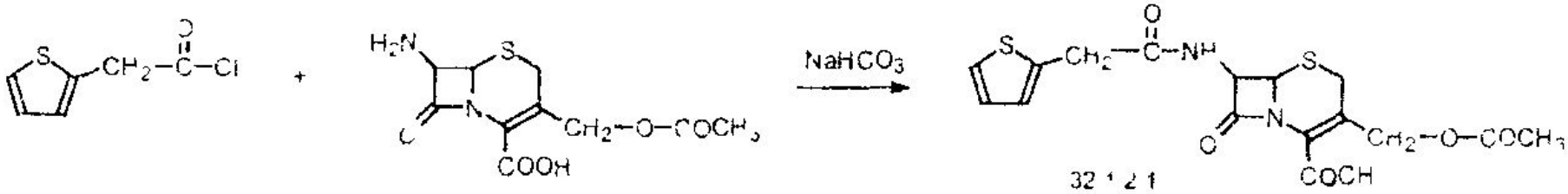
7-АЦК



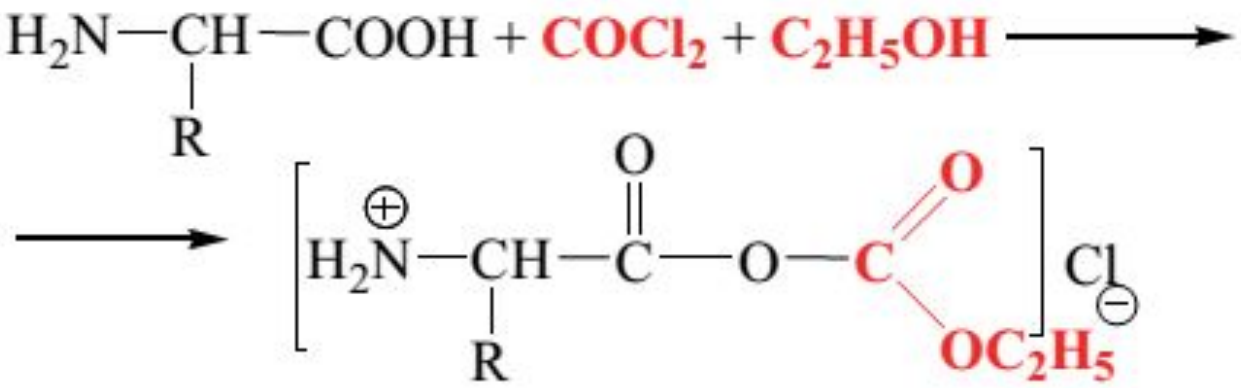
7-АДЦК

ЦЕФАЛОСПОРИНЫ I ПОКОЛОЕНИЯ

ЦЕФАЛОТИН

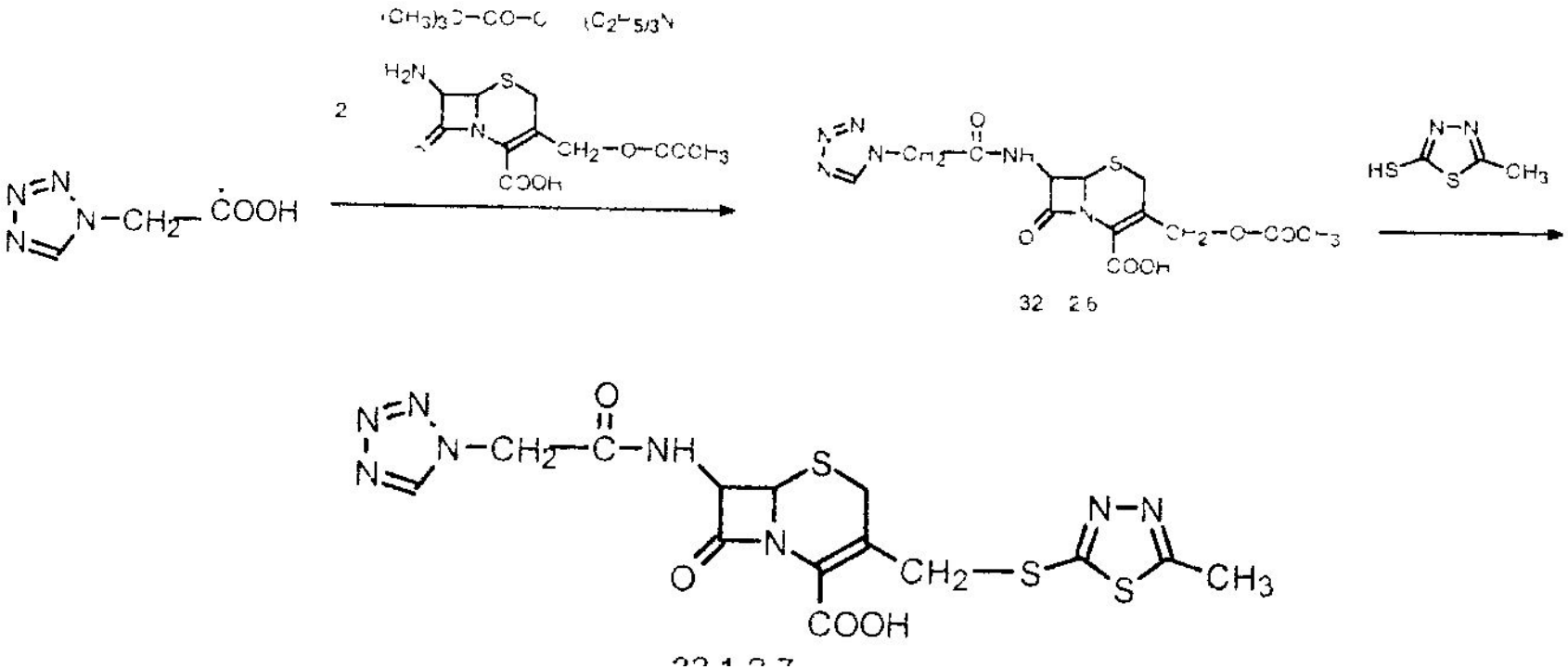


Активация COOH- путем превращения их в смешанные ангидридные группировки с угольной кислотой используются как метод усиления электрофильных свойств карбоксильных групп (активация) в пептидном синтезе:

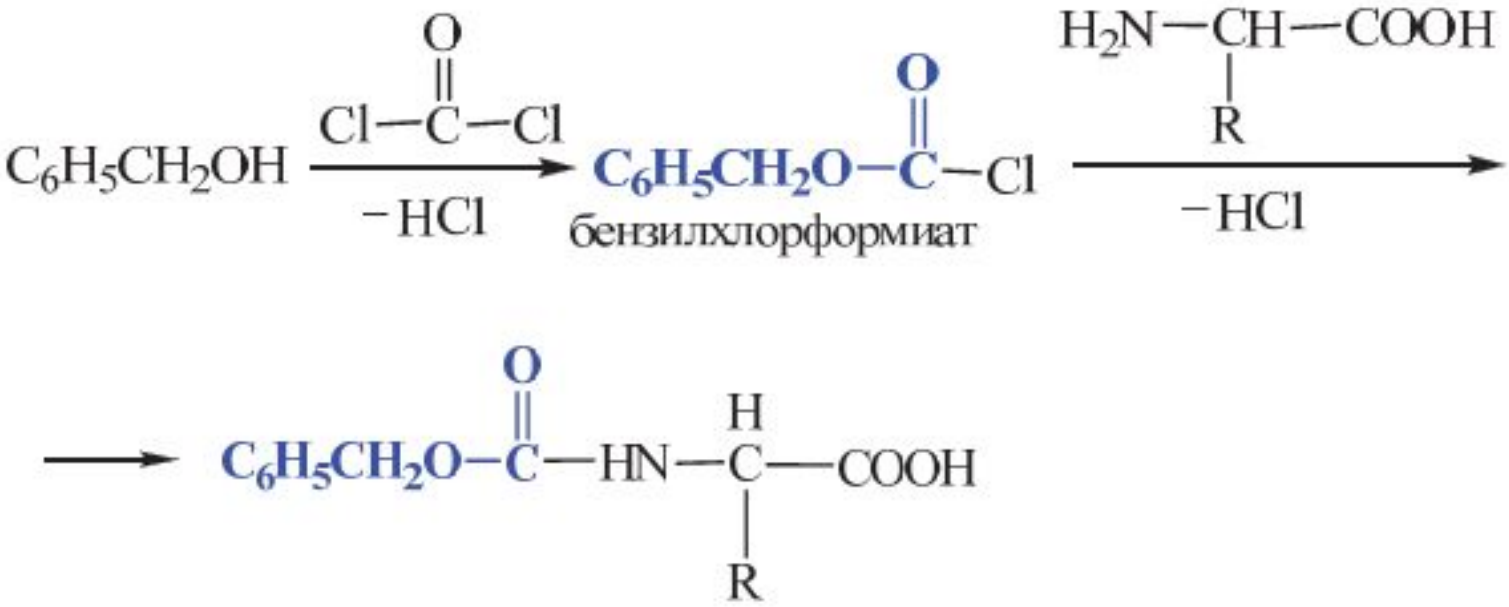


гидрохлорид смешанного ангидрида этилового эфира угольной кислоты и аминокислоты

ЦЕФАЗОЛИН

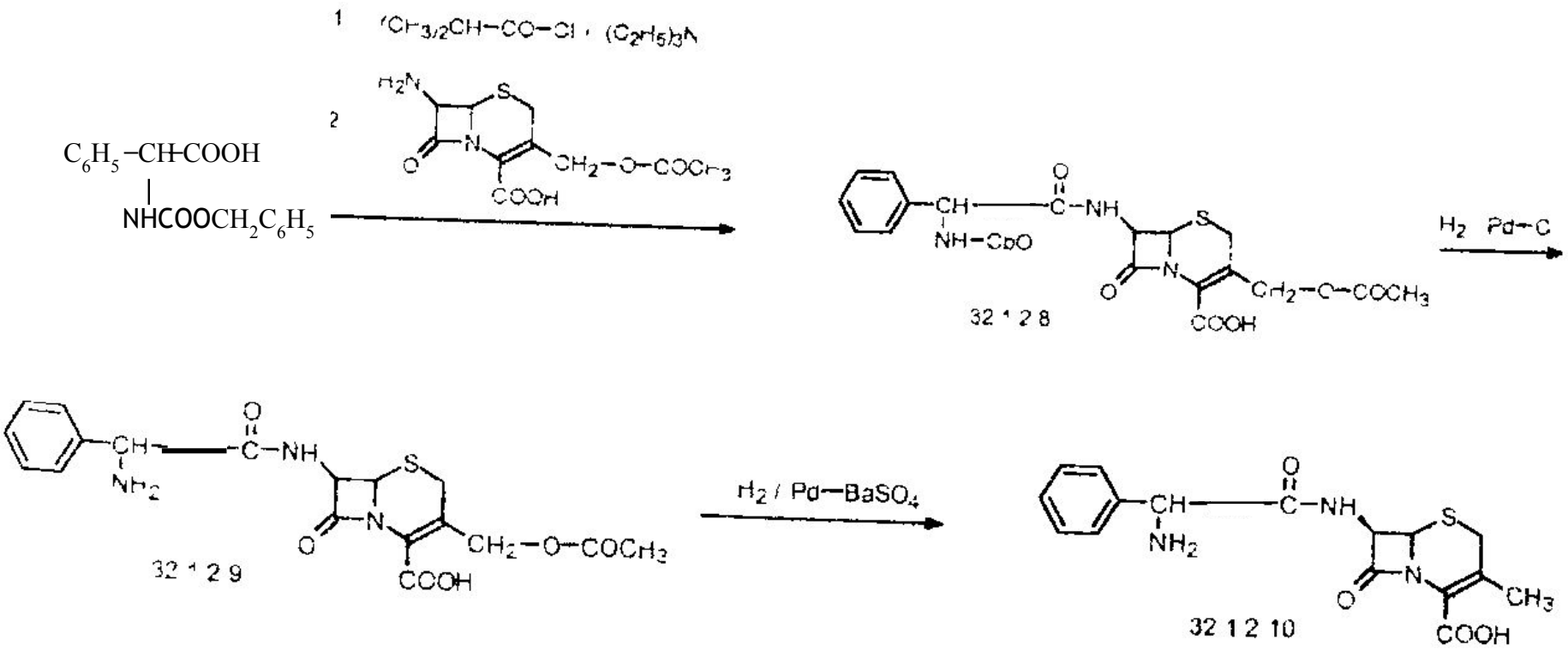

(CH3)3C–CO–Cl
(C2H5)3N
H2N
S
N
CH2–O–COCH3
COOH
N=N
N–CH2–COOH
N–CH2–C–NH
O
HS
CH3
CH2–S
CH3

а) *карбобензоксизащита* – осуществляется путем взаимодействия аминокислот с бензилхлорформиатом, получаемым реакцией бензилового спирта с $COCl_2$:

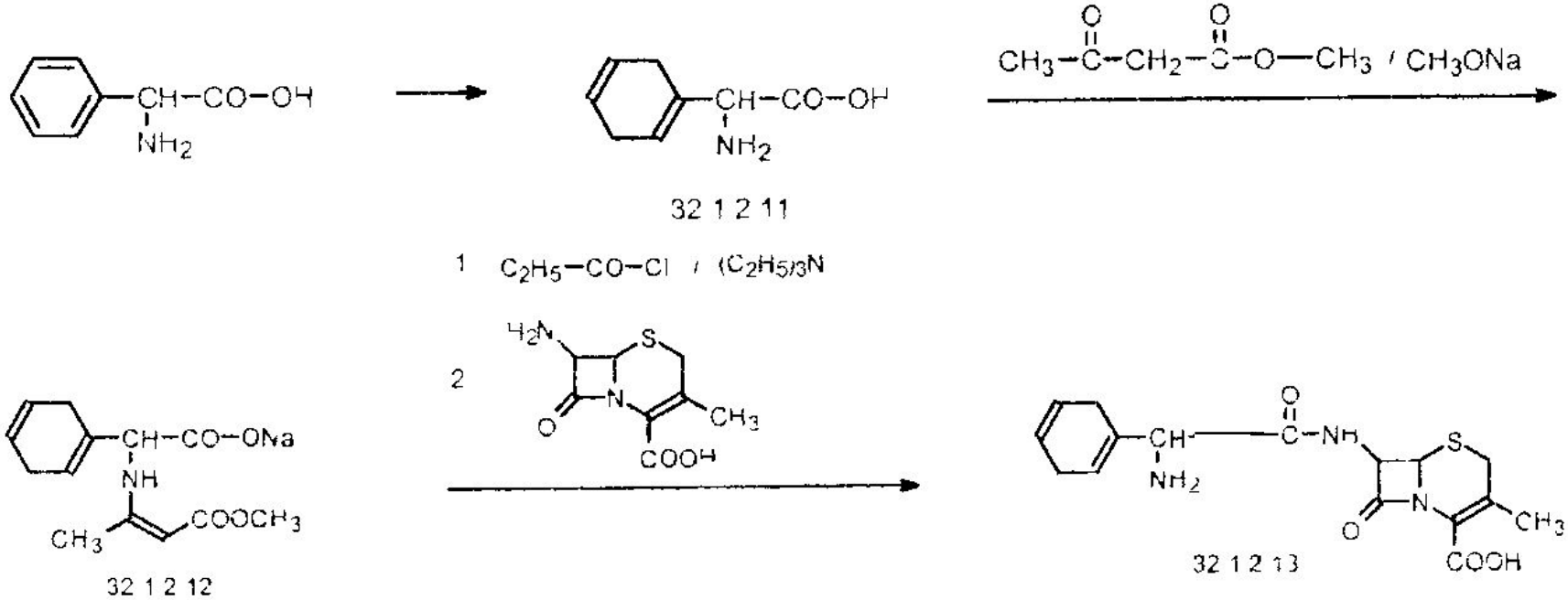


Защитная карбобензоксигруппа легко удаляется действием H_2/Pd при комнатной температуре либо действием трифторуксусной и бромоводородной кислоты без нагревания

ЦЕФАЛЕКСИН

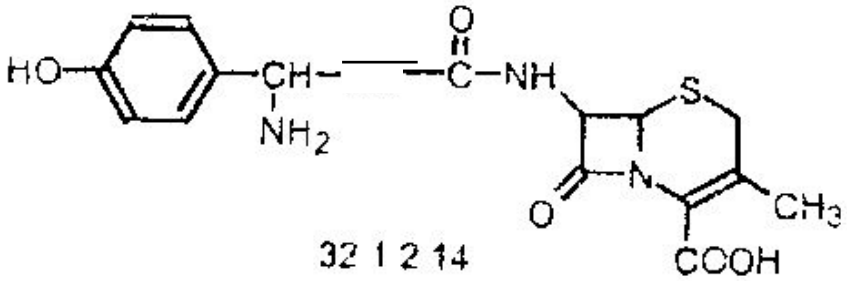

1 (CH3)2CH–CO–Cl , (C2H5)3N
2
C6H5–CH–COOH
NHCOOCH2C6H5
H2N
S
N
O
CH2–O–COCH3
COOH
CH
NH–CbO
C–NH
32 1 2 8
H2 Pd–C
CH2–C–COCH3
32 1 2 9
NH2
CH2–O–COCH3
H2 / Pd–BaSO4
32 1 2 10
CH3

ЦЕФРАДИН


CH–CO–OH
NH2
32 1 2 11
CH3–C–CH2–C–O–CH3 / CH3ONa
1 C2H5–CO–Cl / (C2H5)3N
2
H2N
S
N
O
CH3
COOH
CH–CO–ONa
NH
CH3
COOCH3
32 1 2 12
CH
NH2
C–NH
32 1 2 13

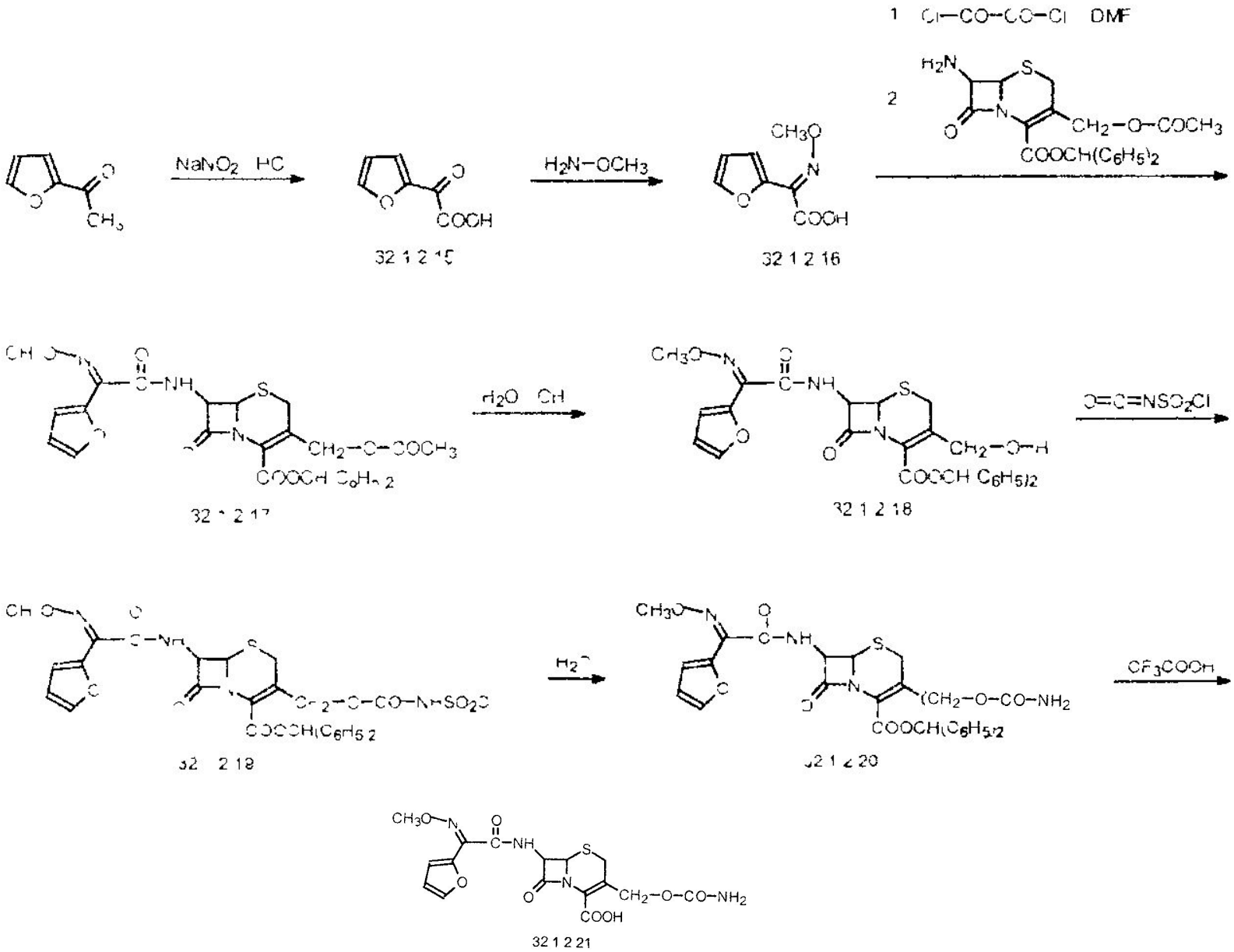
ЦЕФАДРОКСИЛ

- Получают по аналогичной схеме цефрадина.
- Отличается от цефалекисна, наличием гидросильной группы в 4 положении фенильного радикала.

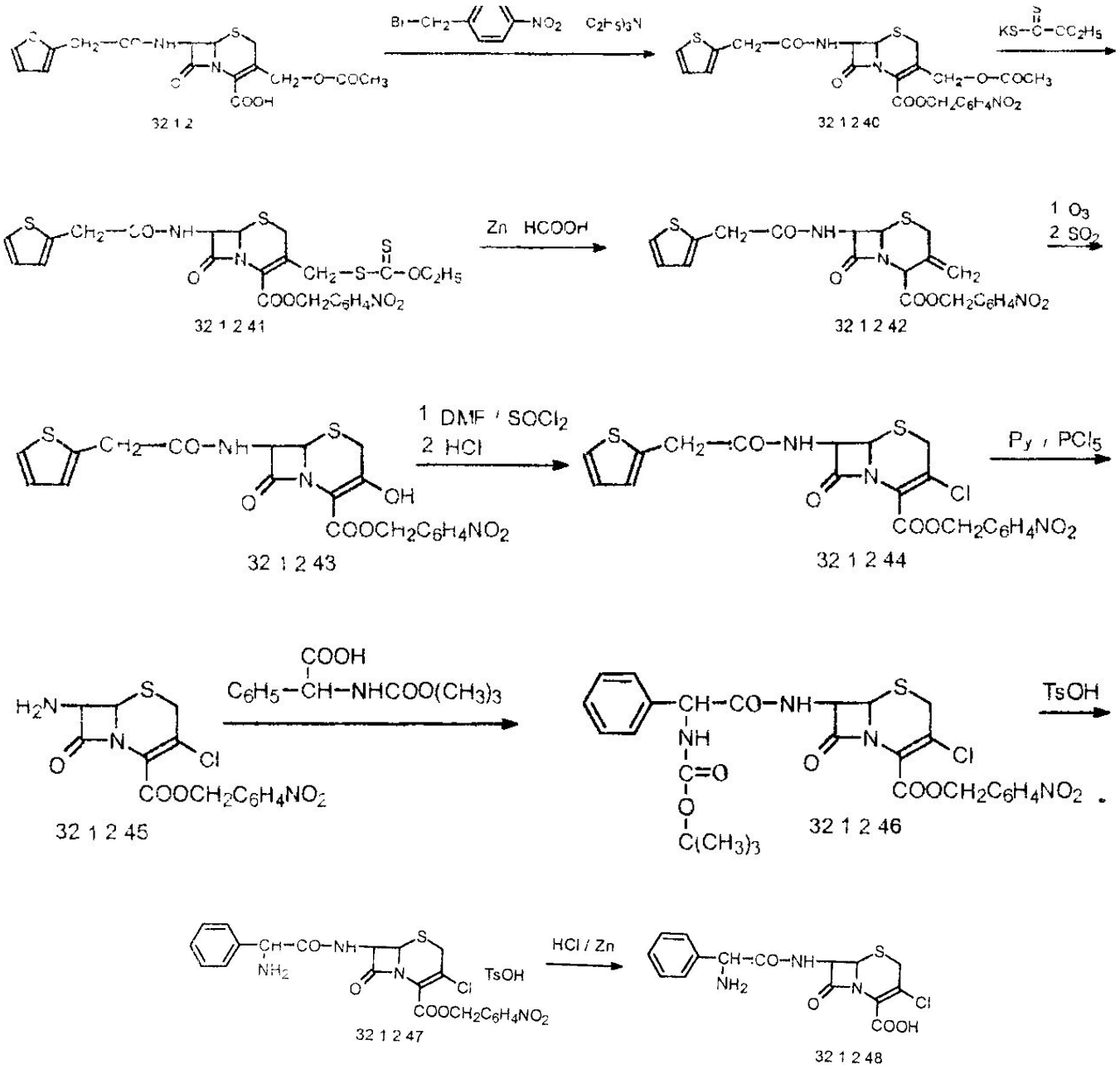


ЦЕФАЛОСПОРИНЫ II ПОКОЛОЕНИЯ

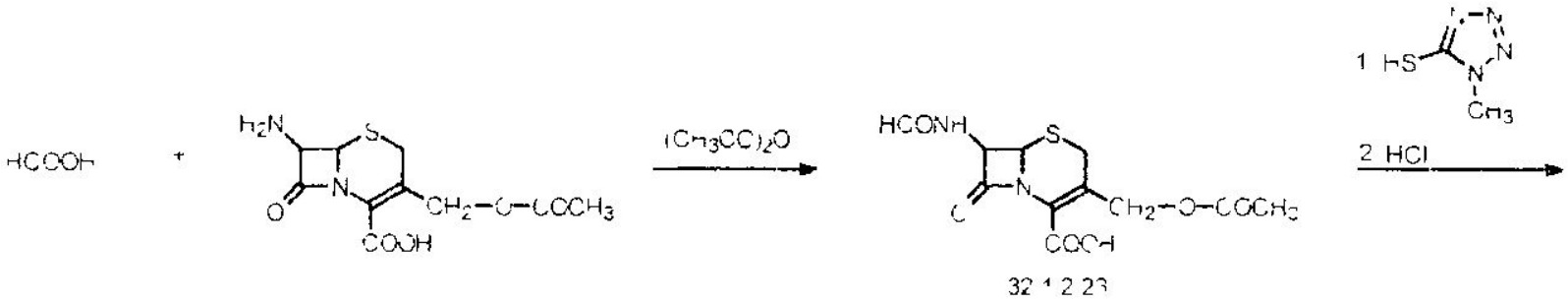
ЦЕФУРОКСИМ


1 Cl—CO—CO—Cl DMF
2
NaNO2 HC
H2N—OCH3
CH3O
COOH
CH2—O—COCH3
COOCH(C6H5)2
H2O OH
O=C=NSO2Cl
CF3COOH
CH2—O—CO—NH2
32 1 2 16
32 1 2 18
32 1 2 21

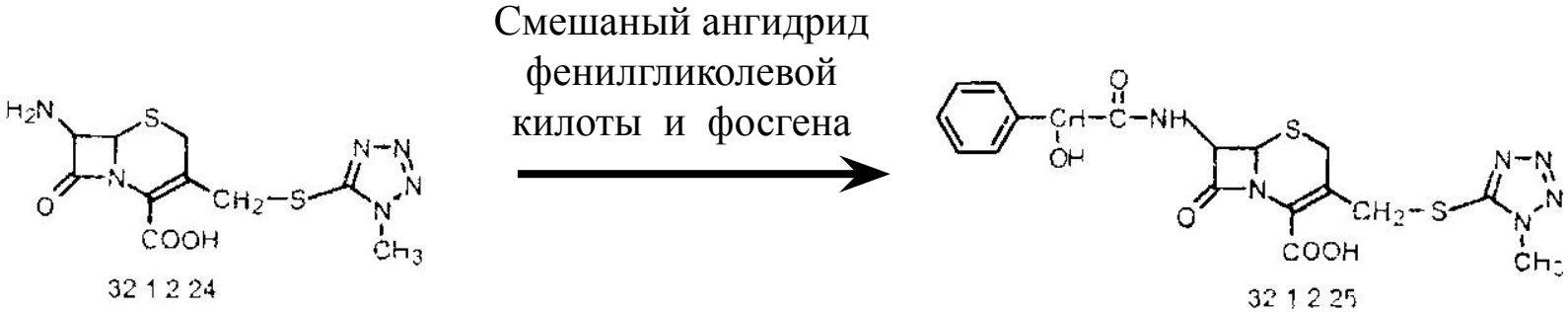
ЦЕФАКЛОР


32 1 2
32 1 2 40
32 1 2 41
32 1 2 42
32 1 2 43
32 1 2 44
32 1 2 45
32 1 2 46
32 1 2 47
32 1 2 48
Zn HCOOH
1 O3
2 SO2
1 DMF / SOCl2
2 HCl
Py / PCl5
TsOH
HCl / Zn

ЦЕФАМАНДОЛ



32 1 2 23

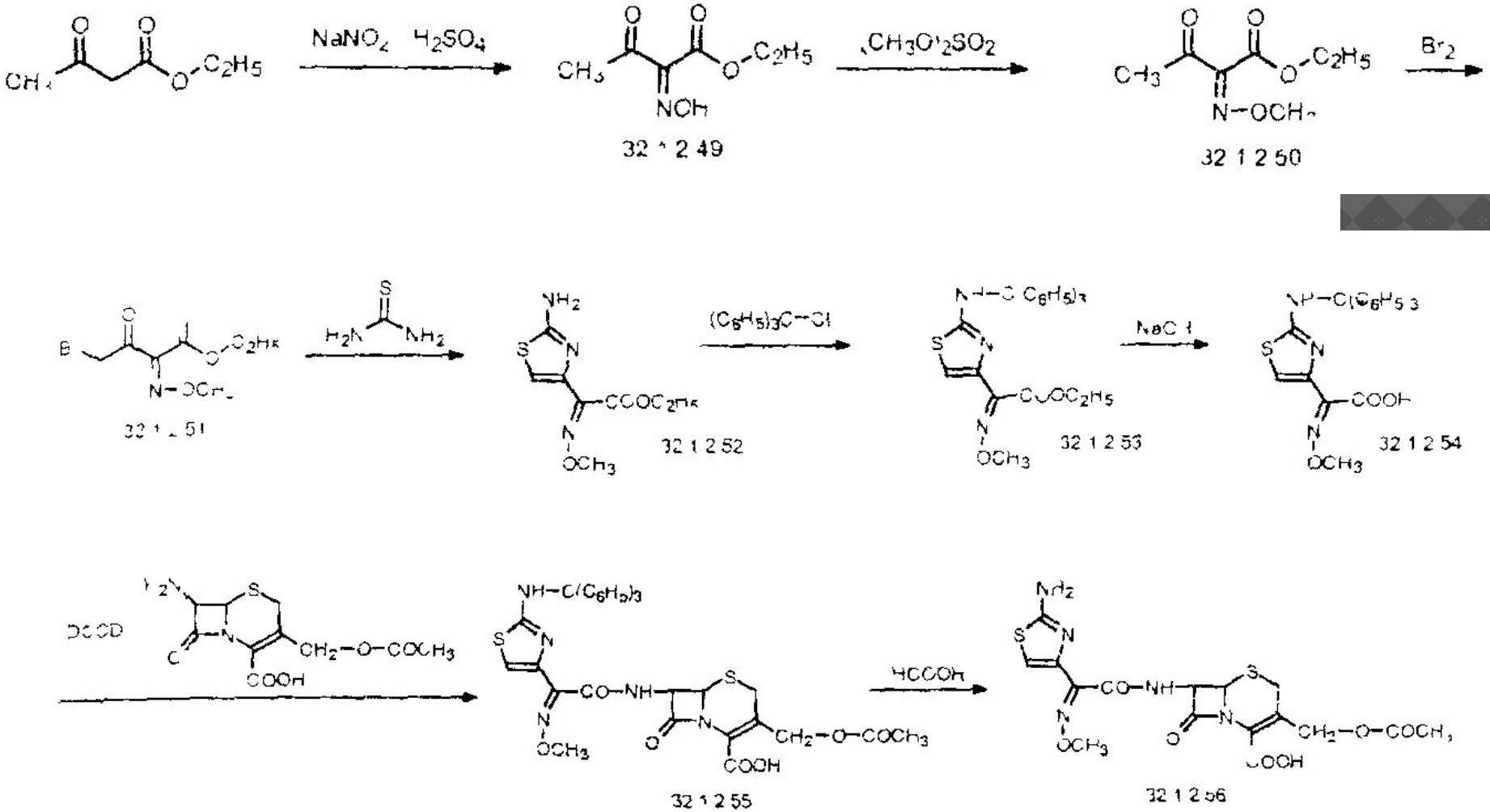


32 1 2 24

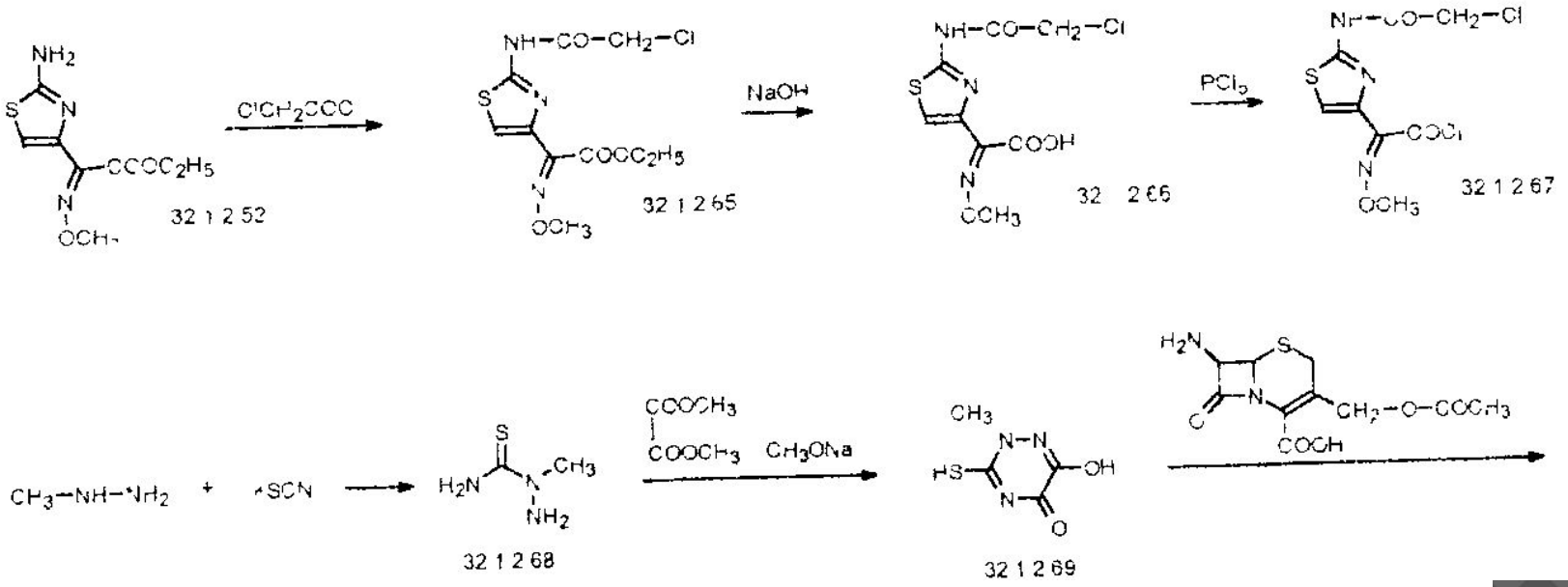
32 1 2 25

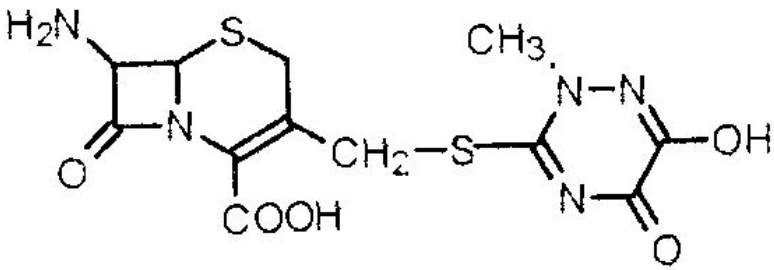
ЦЕФАЛОСПОРИНЫ III ПОКОЛОЕНИЯ

ЦЕФОТАКСИМ

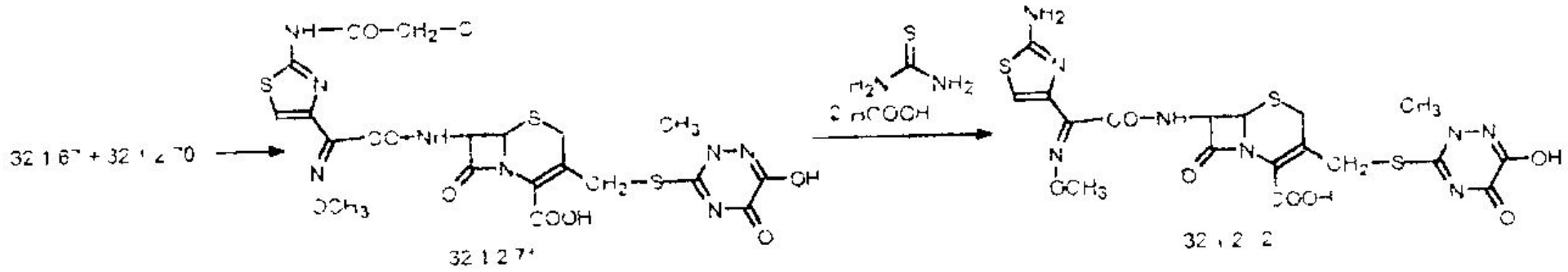

NaNO2 H2SO4
(CH3O)2SO2
Br2
32 1 2 49
32 1 2 50
32 1 2 51
32 1 2 52
(C6H5)3C–Cl
32 1 2 53
NaCl
32 1 2 54
DCCD
32 1 2 55
HCOOH
32 1 2 56

ЦЕФТРИАКСОН

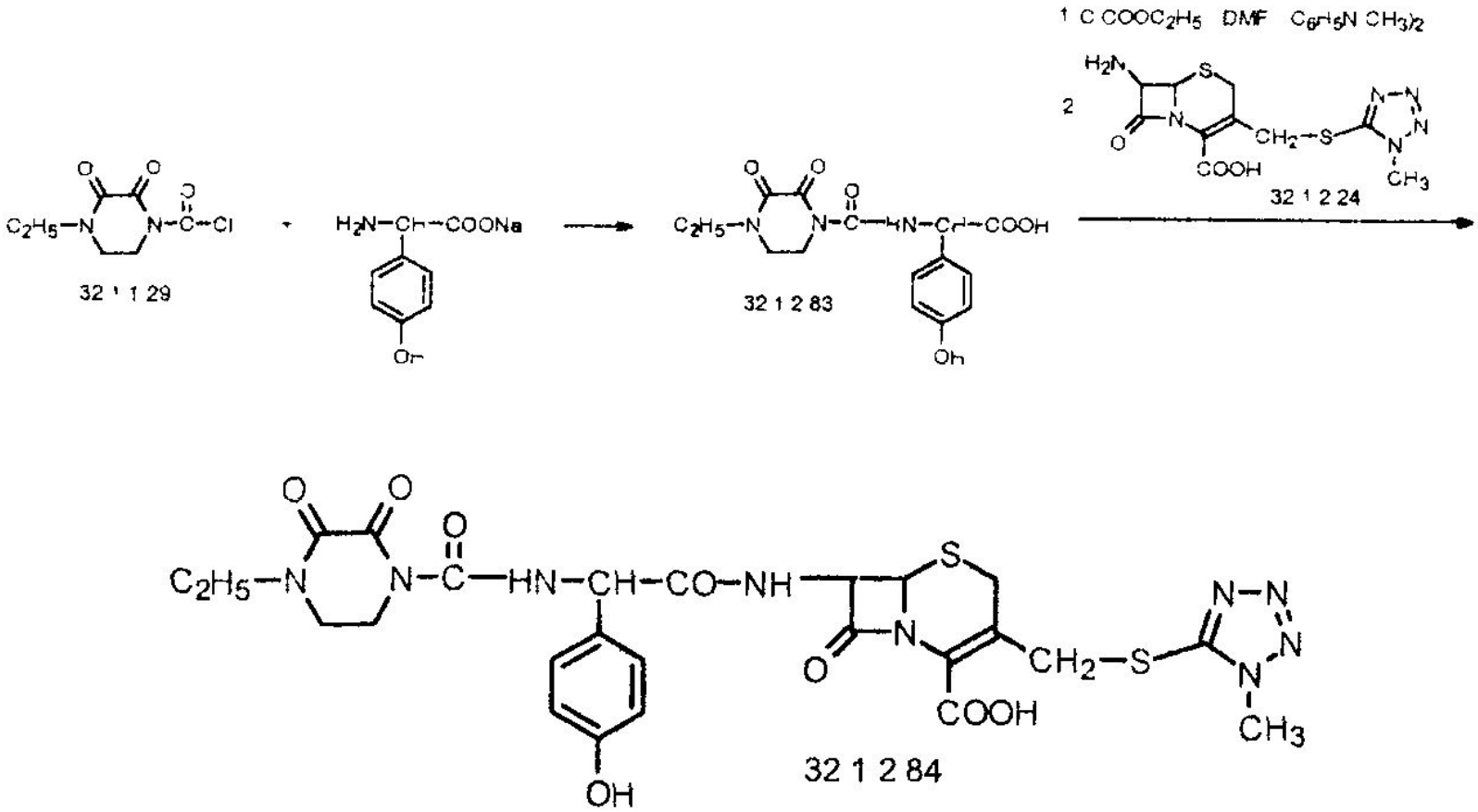




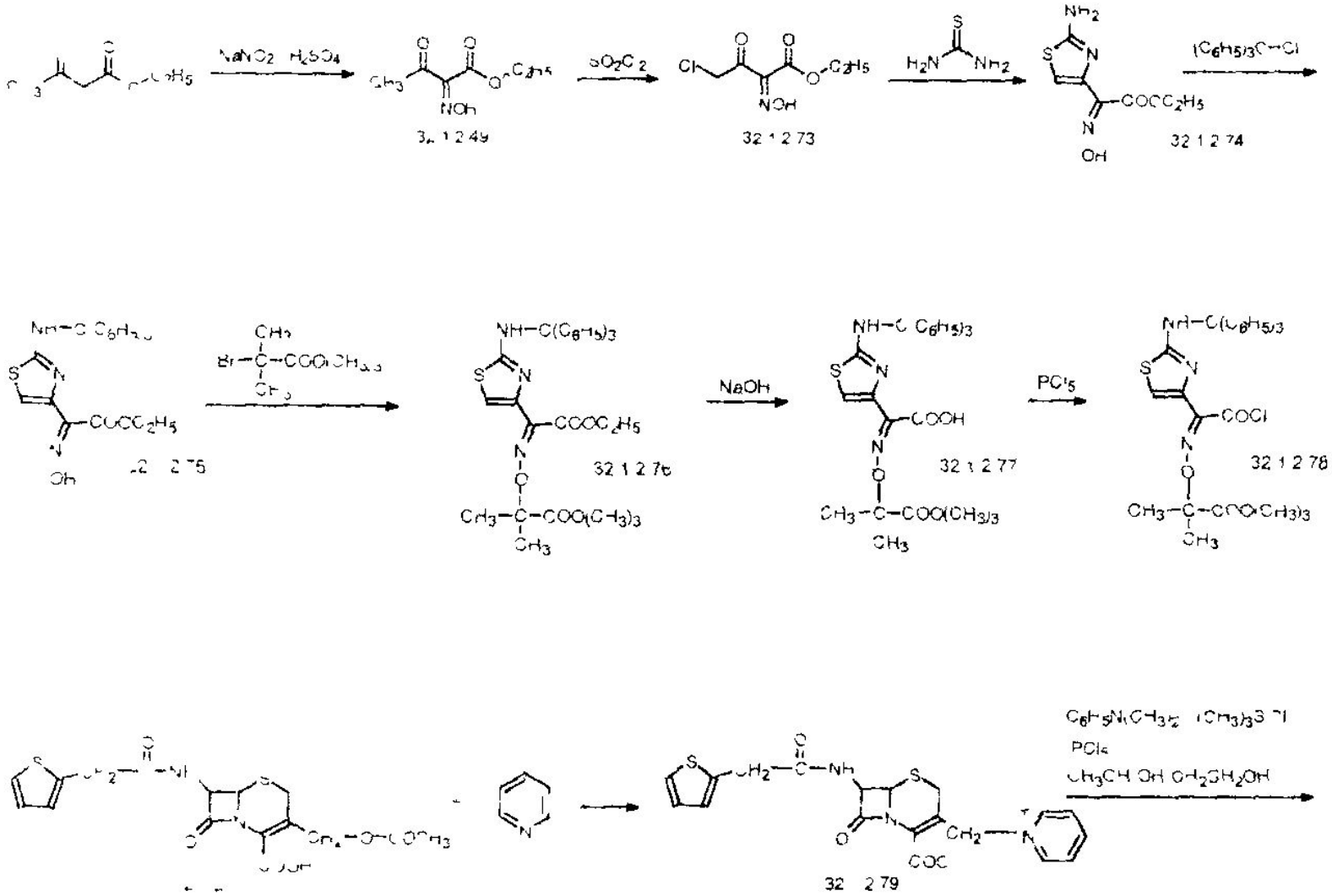
32 1 2 70

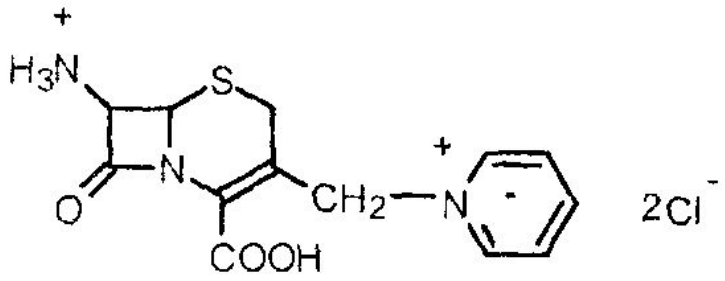


ЦЕФОПЕРАЗОН

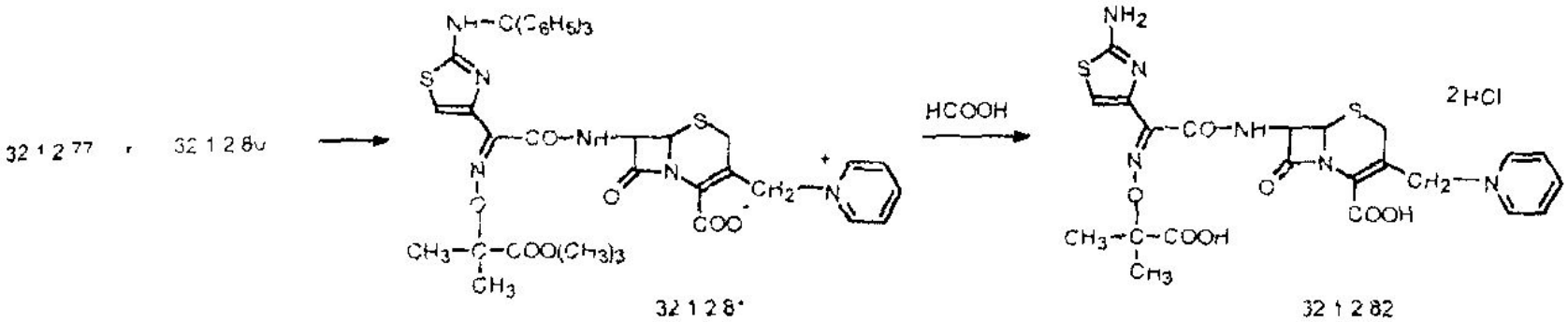


ЦЕФТАЗИДИМ



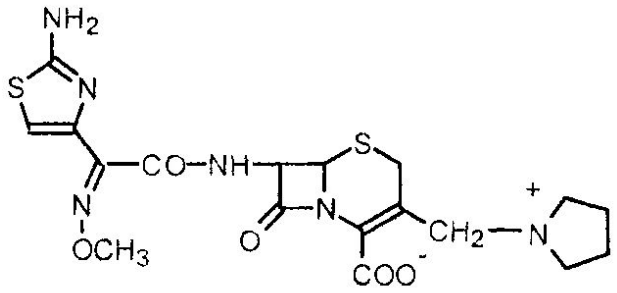

H3N
S
N
O
CH2
N
COOH
2Cl-

32 1 2 80

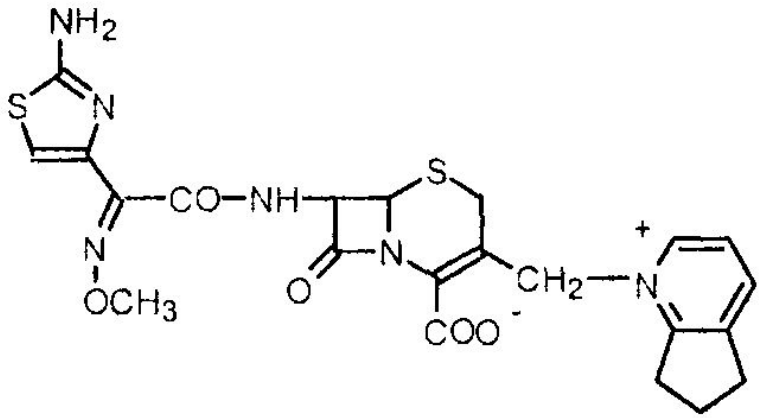

32 1 2 77
32 1 2 80
NH-C(C6H5)3
CO-NH
CH2
N
COO-
CH3-C-COO(CH3)3
CH3
32 1 2 8
HCOOH
NH2
2HCl
CO-NH
CH2
N
COOH
CH3-C-COOH
CH3
32 1 2 82

ЦЕФАЛОСПОРИНЫ IV ПОКОЛОЕНИЯ

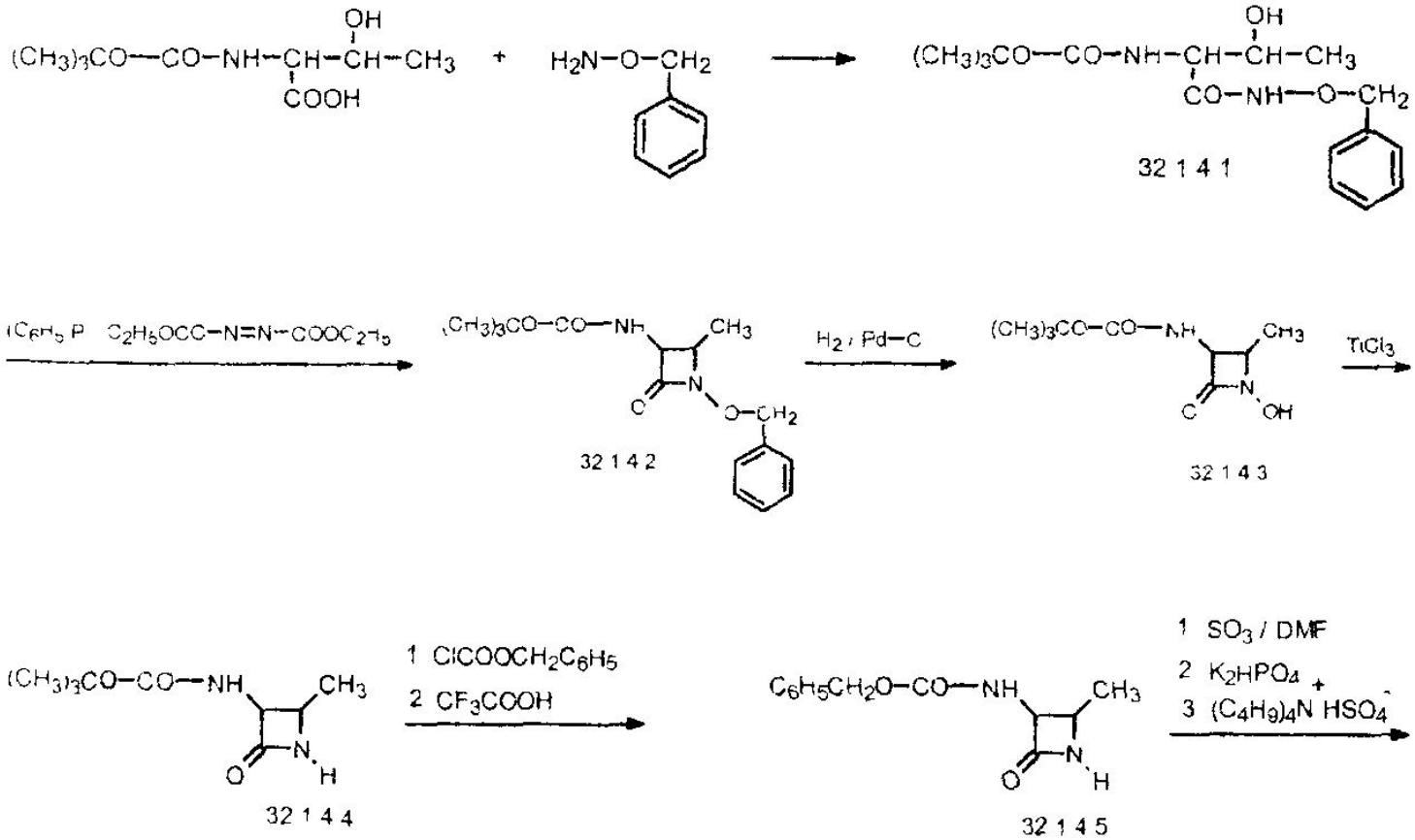
ЦЕФЕПИМ

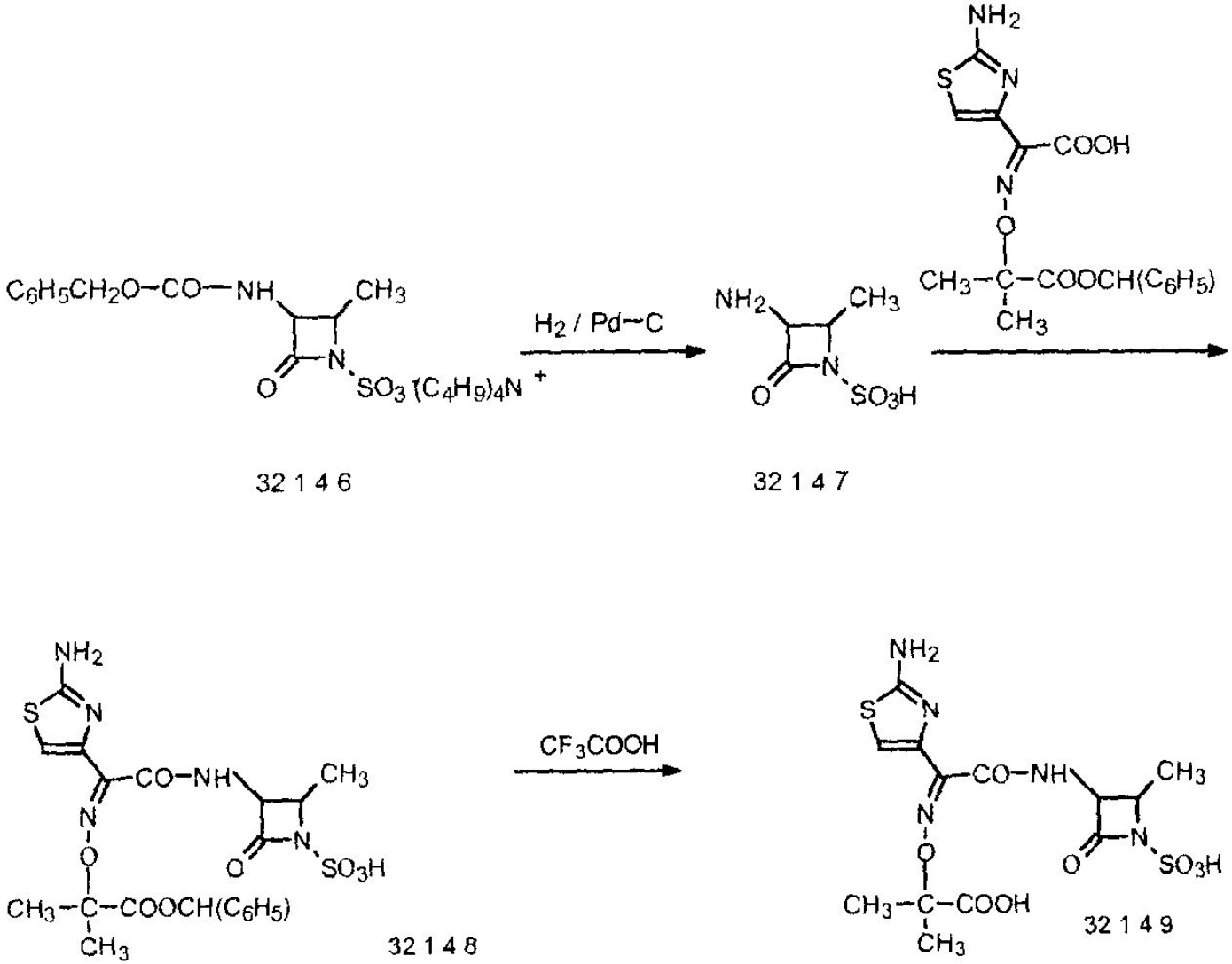


ЦЕФЕПИРОМ

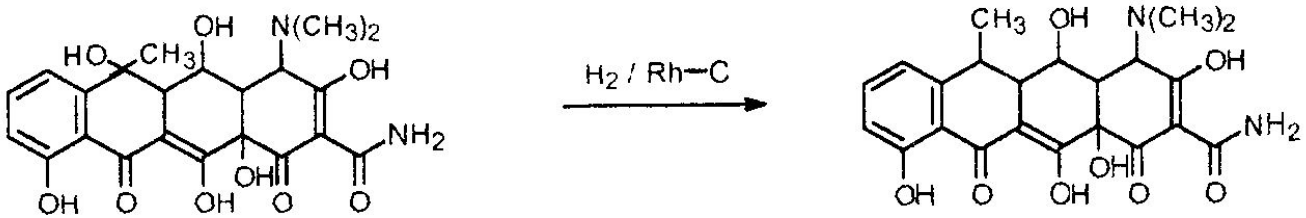


АЗТРЕОНАМ

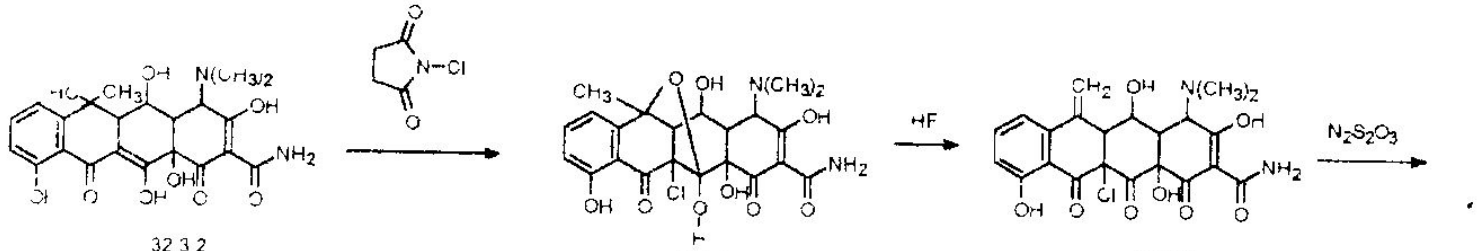

(CH3)3CO—CO—NH—CH—CH—CH3
OH
COOH
H2N—O—CH2
(CH3)3CO—CO—NH—CH—CH—CH3
CO—NH—O—CH2
32 1 4 1
(C6H5)3P C2H5OCC—N=N—COOC2H5
(CH3)3CO—CO—NH
CH3
O—CH2
32 1 4 2
H2 / Pd—C
OH
32 1 4 3
TiCl3
32 1 4 4
1 ClCOOCH2C6H5
2 CF3COOH
C6H5CH2O—CO—NH
32 1 4 5
1 SO3 / DMF
2 K2HPO4 +
3 (C4H9)4N HSO4-


C6H5CH2O–CO–NH
CH3
N
O
SO3 (C4H9)4N +
32 1 4 6
H2 / Pd–C
NH2
CH3
N
O
SO3H
32 1 4 7
NH2
S
N
COOH
N
O
CH3–C–COOCH(C6H5)
CH3
NH2
S
N
CO–NH
CH3
N
O
N
O
SO3H
CH3–C–COOCH(C6H5)
CH3
32 1 4 8
CF3COOH
NH2
S
N
CO–NH
CH3
N
O
N
O
SO3H
CH3–C–COOH
CH3
32 1 4 9

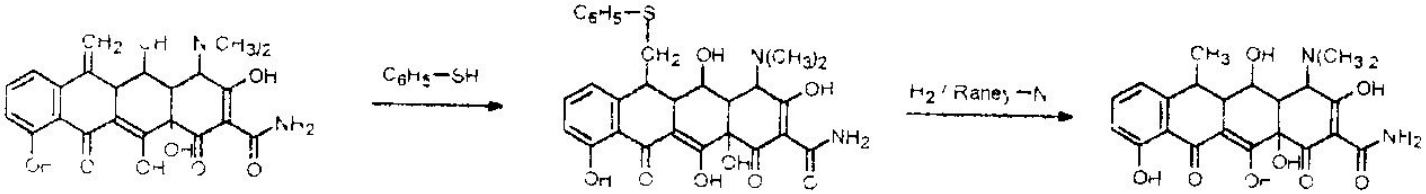
ДОКСИЦИКЛИН



32 3 2 32.3 7

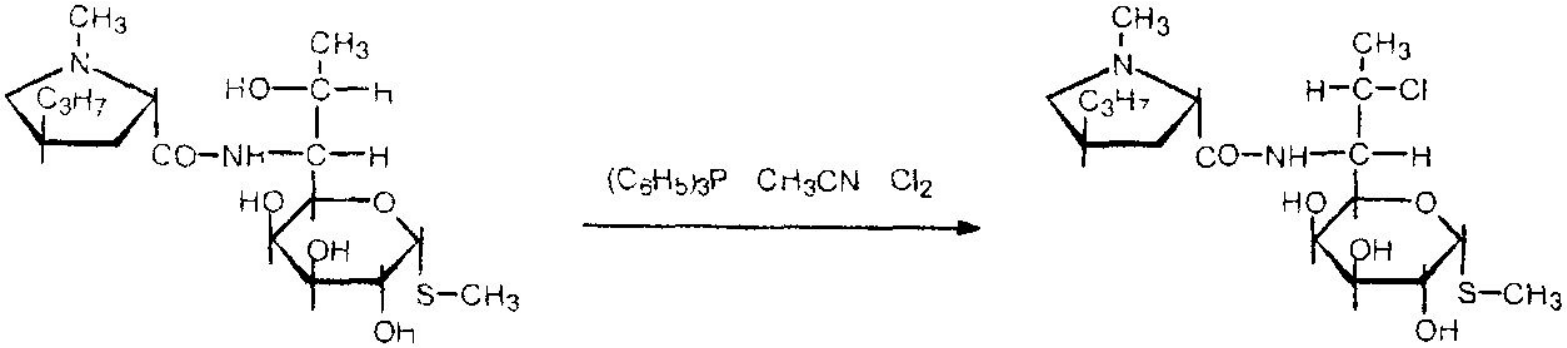


32 3 2 32 3 8 32 3 9



32 3 8 32 3 10 32 3 7

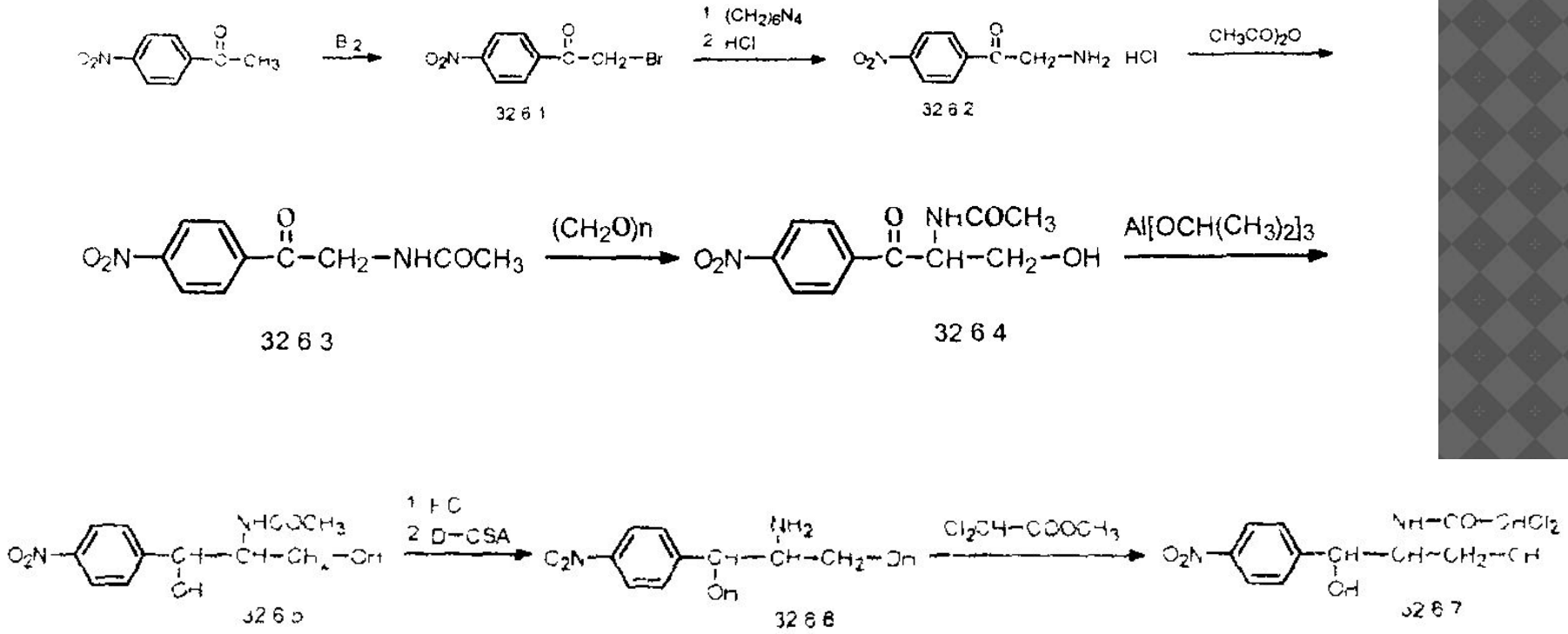
КЛИНДАМИЦИН

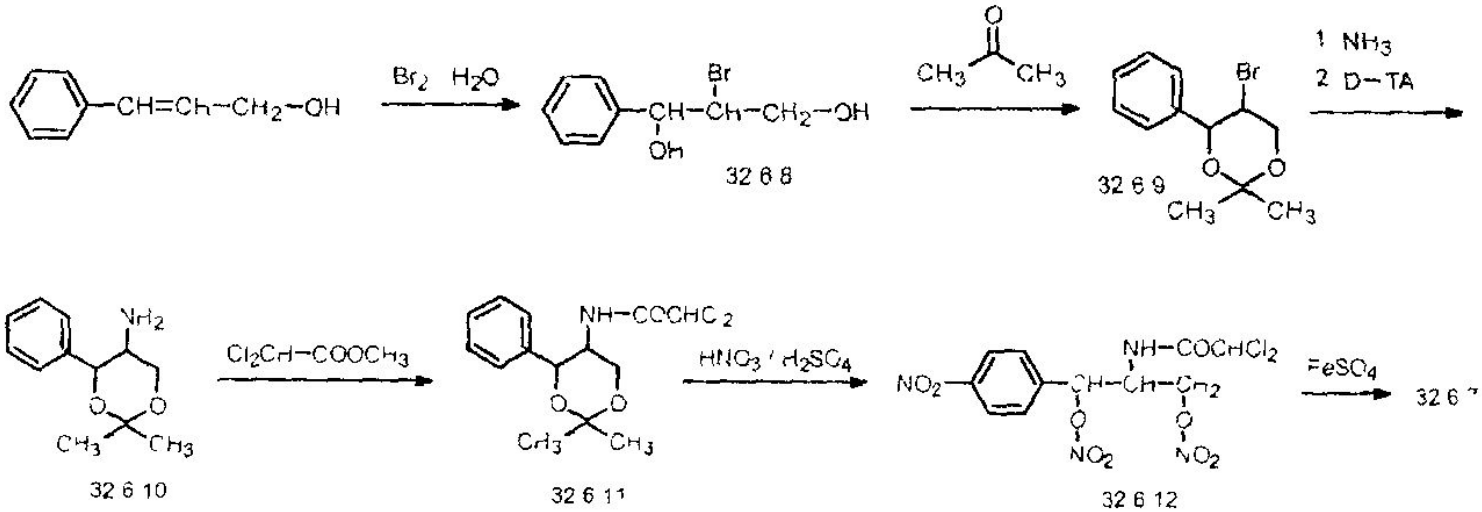


32 5 1

32 5 2

ХЛОРАМФЕНИКОЛ (ЛЕВОМИЦЕТИН)




CH=CH–CH2–OH
Br2 H2O
Br
CH–CH–CH2–OH
OH
32 6 8
CH3 CH3
Br
O O
CH3 CH3
32 6 9
1 NH3
2 D–TA
NH2
O O
CH3 CH3
32 6 10
Cl2CH–COOCH3
NH–COCHCl2
O O
CH3 CH3
32 6 11
HNO3 / H2SO4
NO2
NH–COCHCl2
CH–CH–CH2
O NO2
O NO2
32 6 12
FeSO4