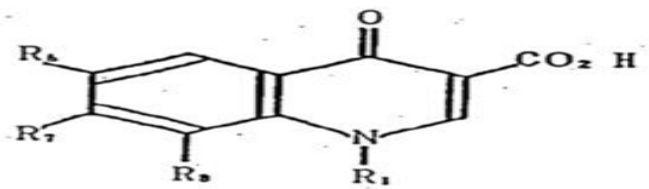
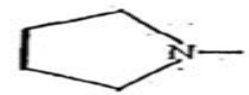
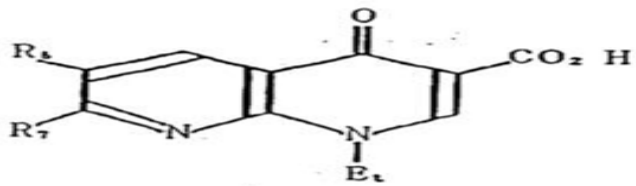
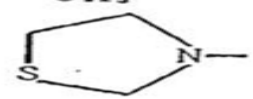
PYRIDONE CARBONIC ACID DERIVATIVES ANTIBACTERIAL ACTIVITY

John M.Domagara, Lori Doyle Hanna, Carl L.Heifetz, Marland P.Hutt, Thomas F.Mich, Joseph P.Sanchez, and Marjorie Solomon, Journal of Medicinal Chemistry, 29, 394 (1986).



R6	R7
F	H
NO_2	H
F	
H	$H_2NCH_2CH_2NH-$



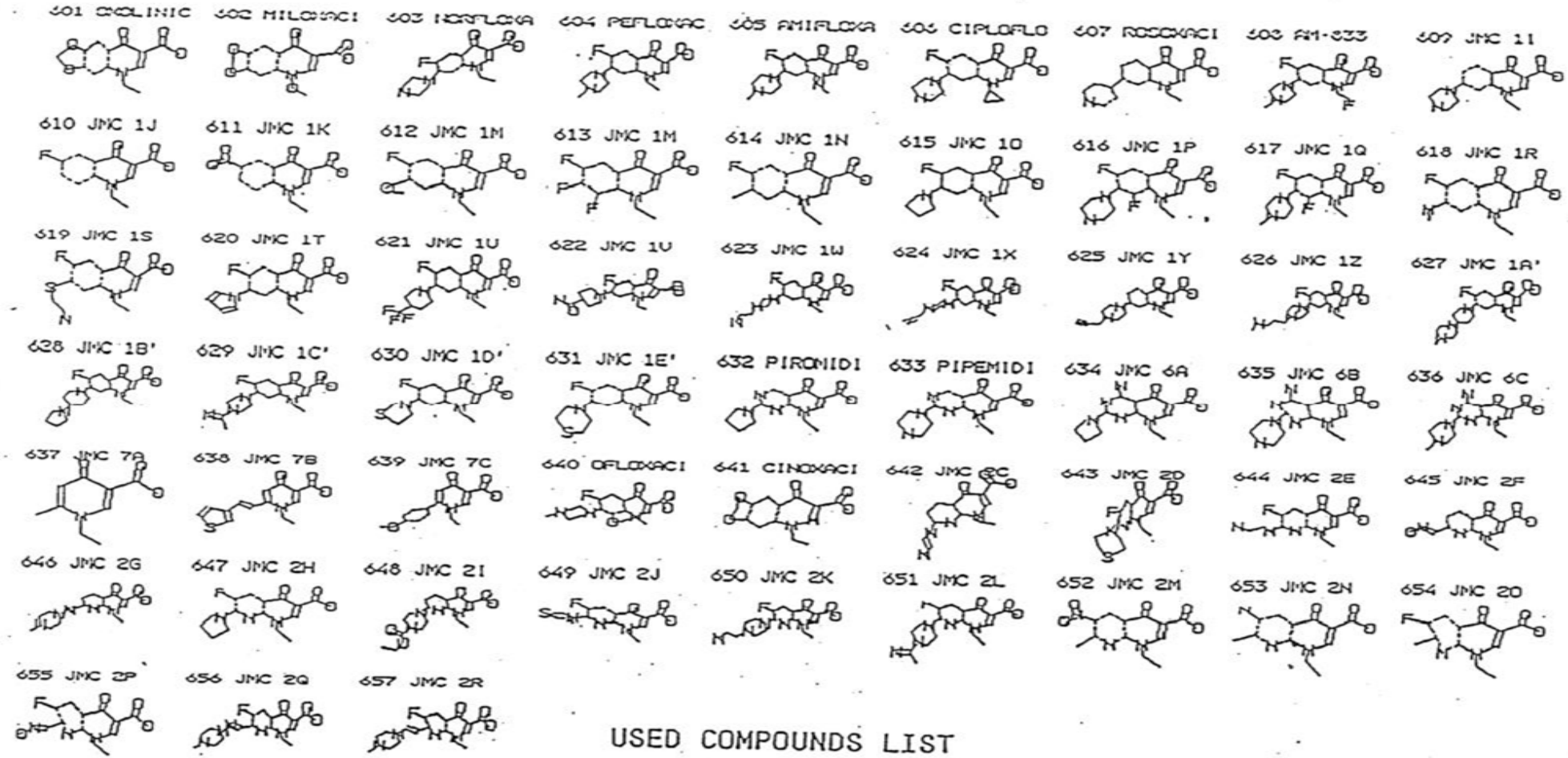
R6	R7
F	HON=CH−
NH_2	CH_3
F	

BASIC STRUCTURES OF USED COMPOUNDS

ANTIBACTERIAL ACTIVITY

E. coli H560 MIC 0.1 ～ > 100.0 μg/mL

- ☐ ACTIVE CLASS
  MIC 0.1～ 6.3 μg/mL 27 COMPOUNDS
- ☐ INACTIVE CLASS
  MIC 12.5～100.0 μg/mL 30 COMPOUNDS



USED COMPOUNDS LIST

USED DESCRIPTOR SET IN ORDER TO CHOOSE LEAD CANDIDATES FROM THE GENERATED COMPOUNDS

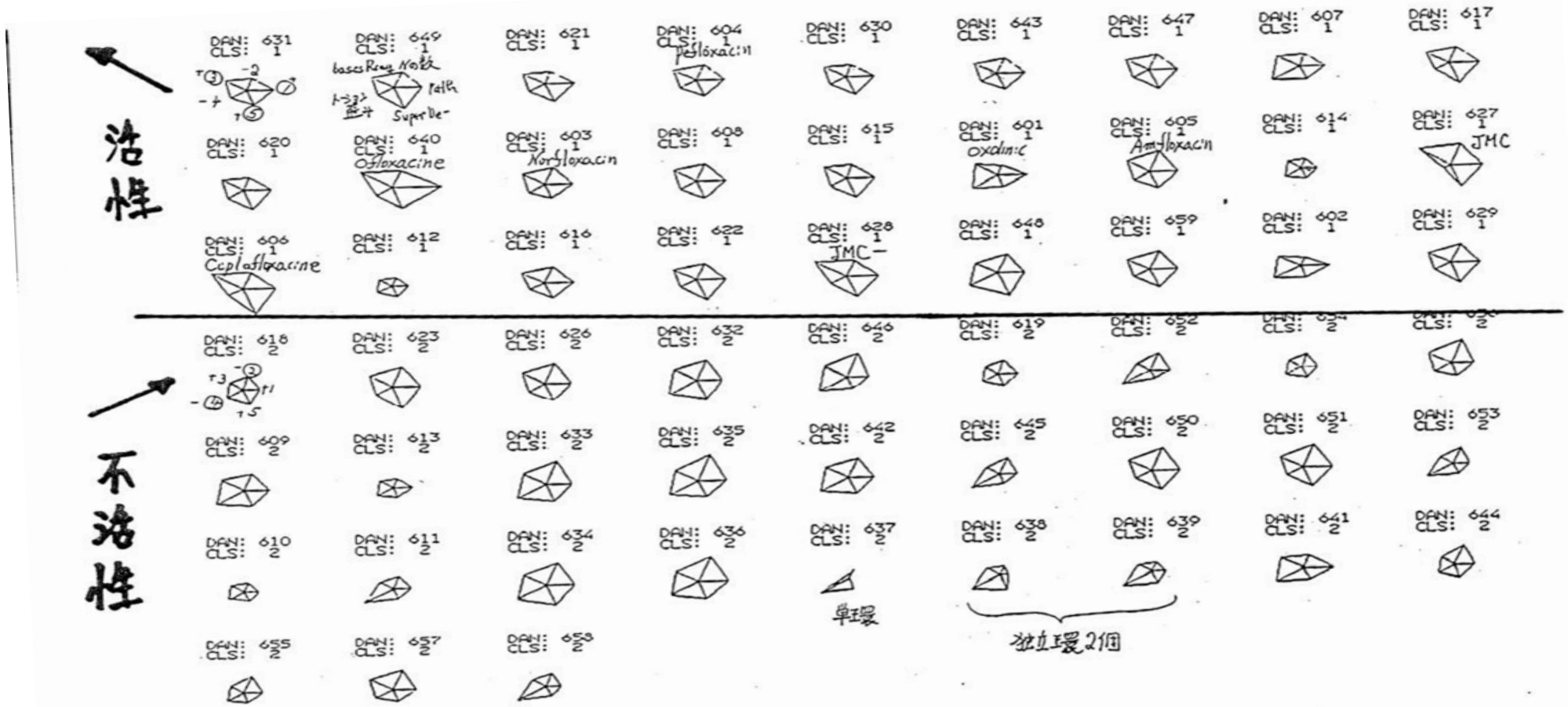
(DOESN' T INCLUDE SBSTRUCTURE DESCRIPTORS)

+ 1. TOTAL NUMBER OF PATHS/NUMBER OF ATOMS
— 2. NUMBER OF NITROGEN ATOMS IN STRUCTURE
+ 3, NUMBER OF BASIS RINGS IN STRUCTURE
— 4. MINIMUM NUCLEOPHILIC SUPERDELOCALIZABILITY
+ 5. TORSIONAL STRAIN ENERGY OF MOLECULE

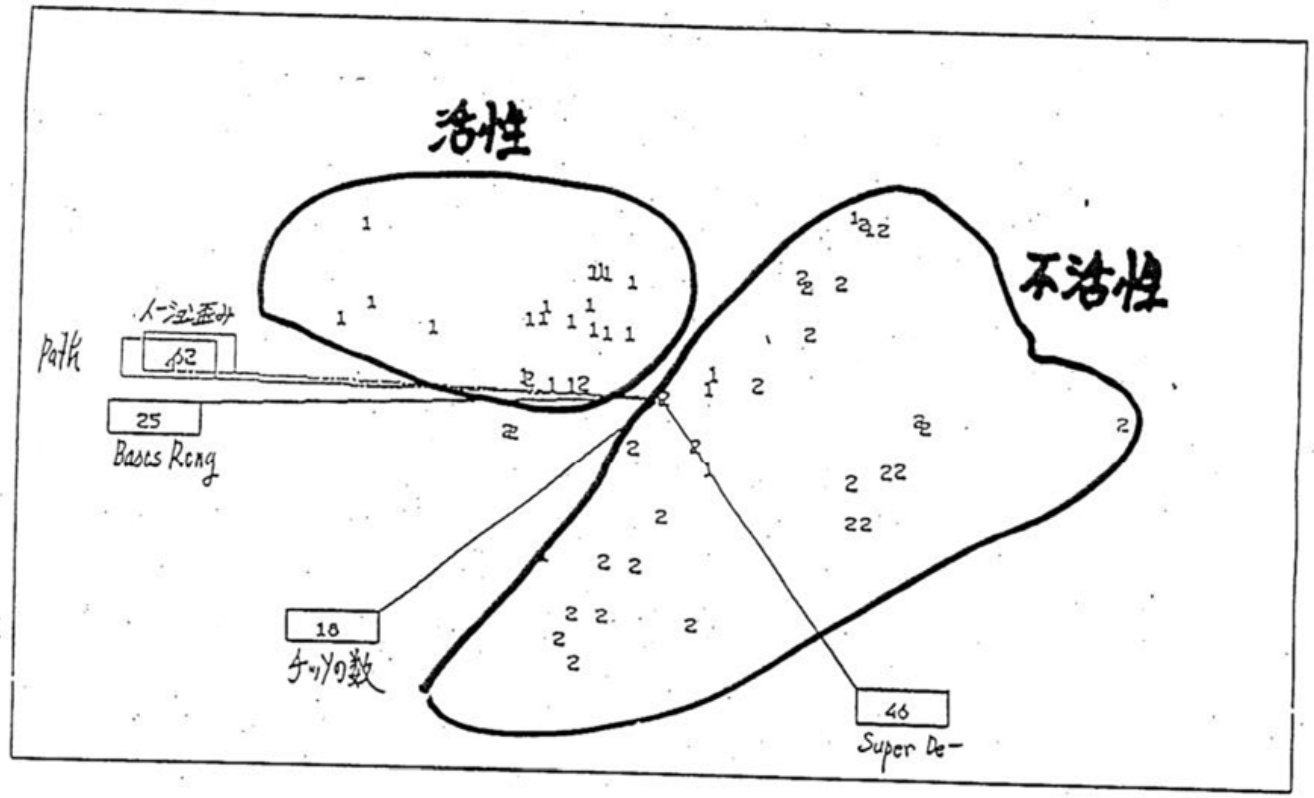
DATA SET CONDITION

CLASS 1 (ACTIVE CLASS)	27 COMPOUNDS	
CLASS 2 (INACTIVE CLASS)	29 COMPOUNDS	TOTAL=56

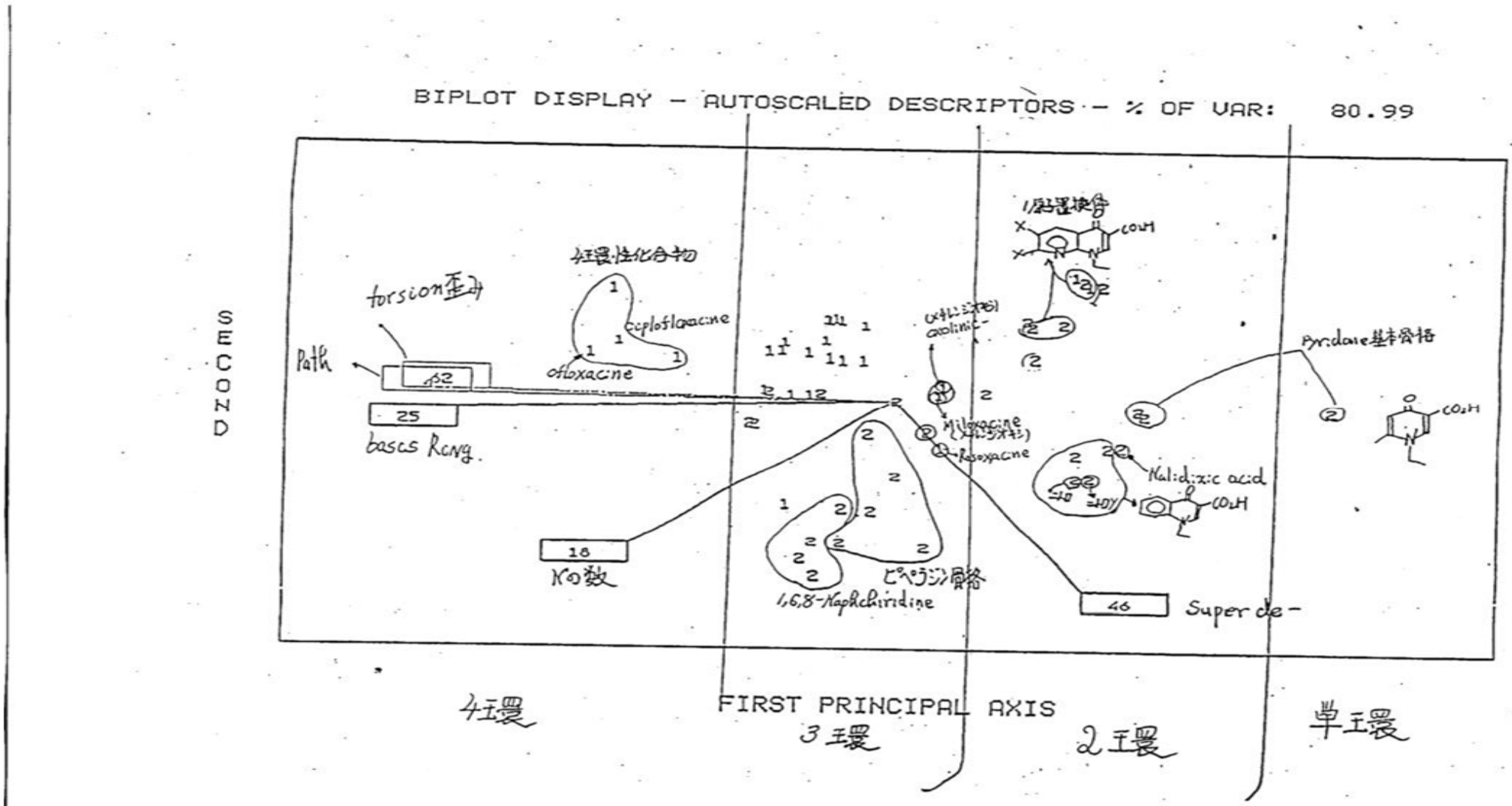
* ONE COMPOUND WAS DELETED FROM THE ORIGINAL DATA SET TO KEEP DICHOTOMIZATION


浩性
不浩性
DAN: 631 CLS: 1
DAN: 649 CLS: 1
DAN: 621 CLS: 1
DAN: 604 CLS: 1
Pefloxacin
DAN: 630 CLS: 1
DAN: 643 CLS: 1
DAN: 647 CLS: 1
DAN: 607 CLS: 1
DAN: 617 CLS: 1
DAN: 620 CLS: 1
DAN: 640 CLS: 1
Ofloxacine
DAN: 603 CLS: 1
Norfloxacin
DAN: 608 CLS: 1
DAN: 615 CLS: 1
DAN: 601 CLS: 1
Oxalinic
DAN: 605 CLS: 1
Amifloxacin
DAN: 614 CLS: 1
DAN: 627 CLS: 1
JMC
DAN: 606 CLS: 1
Ciprofloxacine
DAN: 612 CLS: 1
DAN: 616 CLS: 1
DAN: 622 CLS: 1
DAN: 628 CLS: 1
JMC−
DAN: 648 CLS: 1
DAN: 659 CLS: 1
DAN: 602 CLS: 1
DAN: 629 CLS: 1
DAN: 618 CLS: 2
DAN: 623 CLS: 2
DAN: 626 CLS: 2
DAN: 632 CLS: 2
DAN: 646 CLS: 2
DAN: 619 CLS: 2
DAN: 652 CLS: 2
DAN: 609 CLS: 2
DAN: 613 CLS: 2
DAN: 633 CLS: 2
DAN: 635 CLS: 2
DAN: 642 CLS: 2
DAN: 645 CLS: 2
DAN: 650 CLS: 2
DAN: 651 CLS: 2
DAN: 653 CLS: 2
DAN: 610 CLS: 2
DAN: 611 CLS: 2
DAN: 634 CLS: 2
DAN: 636 CLS: 2
DAN: 637 CLS: 2
単環
DAN: 638 CLS: 2
DAN: 639 CLS: 2
DAN: 641 CLS: 2
DAN: 644 CLS: 2
独立環2個
DAN: 655 CLS: 2
DAN: 657 CLS: 2
DAN: 658 CLS: 2

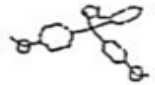
BIPLOT DISPLAY - AUTOSCALED DESCRIPTORS -- % OF VAR: 80.99



FIRST PRINCIPAL AXIS


BIPLOT DISPLAY – AUTOSCALED DESCRIPTORS – % OF VAR: 80.99
SECOND
torsion歪み
Path
52
25
basis Rcvg.
4環性化合物
ciprofloxacine
ofloxacine
Milloxacine
Rosoxacine
Nalidixic acid
Pyridone基本骨格
18
Nの数
1,6,8-Naphthiridine
ピペラジン骨格
46
Super de-
FIRST PRINCIPAL AXIS
4環
3環
2環
単環

701 4,4PR-DI



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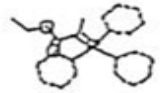

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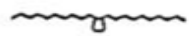

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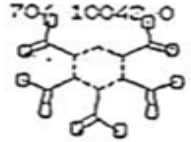

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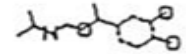

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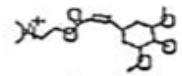

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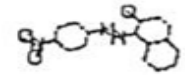

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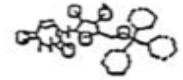

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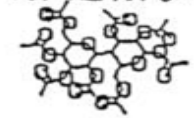

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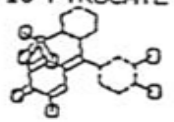

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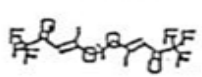

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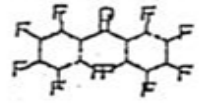

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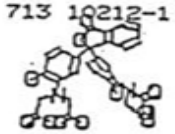

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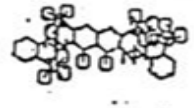

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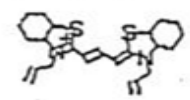

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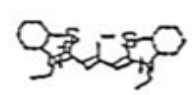

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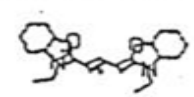

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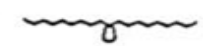

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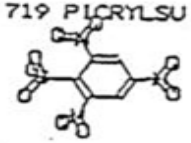

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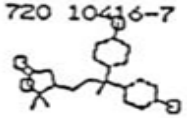

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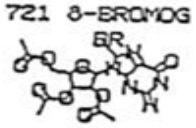

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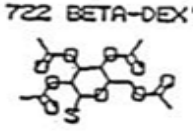

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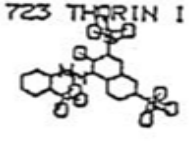

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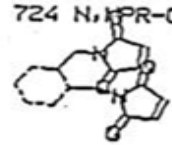

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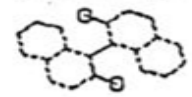

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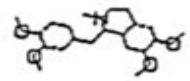

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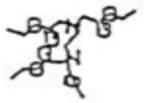

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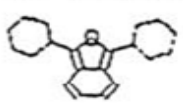

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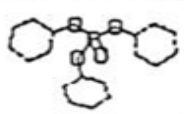

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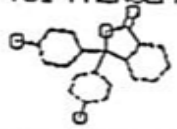

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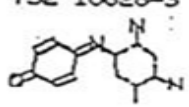

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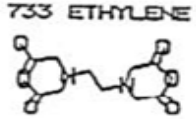

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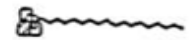

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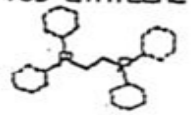

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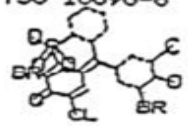

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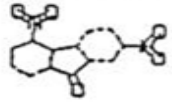

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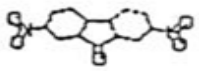

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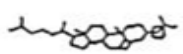

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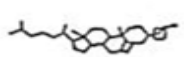

741 DEOXYCHO

742 TRIPENTA

743 ARSENAZO

744 10806-5

745 2-TERT.-

746 OXOTREMO

747 PARA-TRI

748 10977-0

749 11039-6

750 11066-8

751 D-(PLUS)

752 11287-9

753 11341-7

754 BIS-(TRI

755 11391-3

756 ALIZARIN

757 2,4,5,7-

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759 12803-1

760 TRIBENZY

761 PARA-ANI

762 (MERRYL:

763 TRIS-(BU

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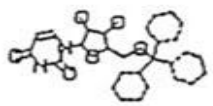

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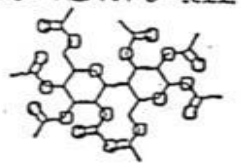

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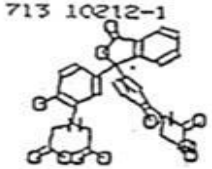

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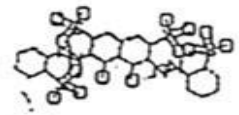

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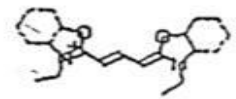

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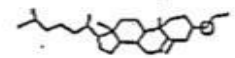

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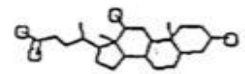

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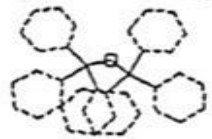

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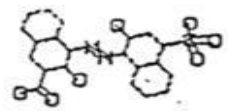

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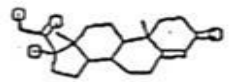

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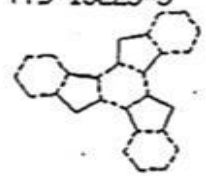

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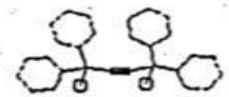

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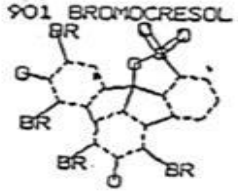

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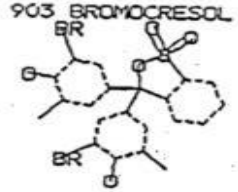

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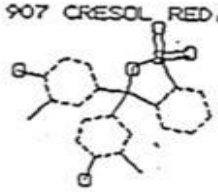

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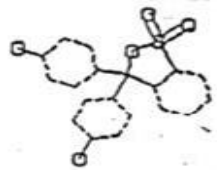

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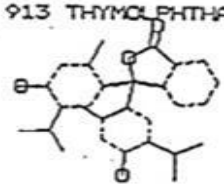

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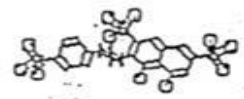

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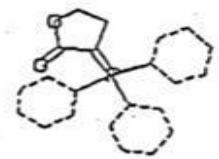

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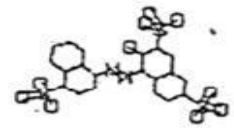

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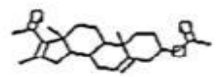

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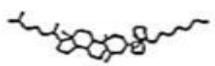

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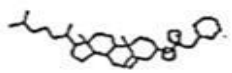

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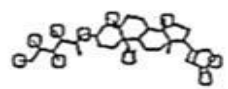

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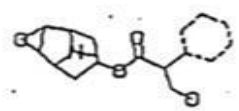

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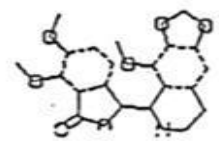

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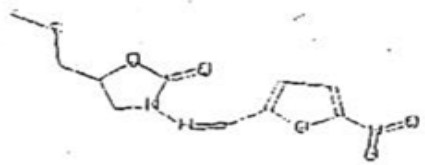

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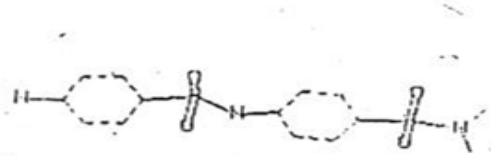

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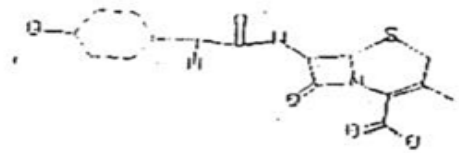

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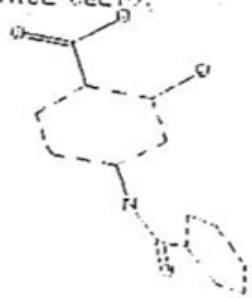

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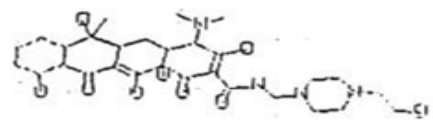

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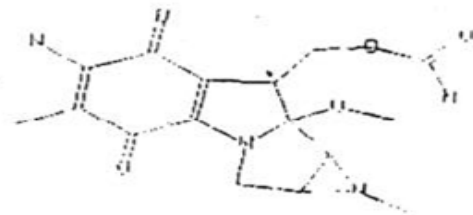

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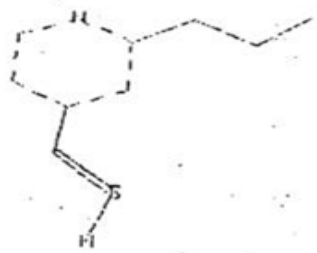

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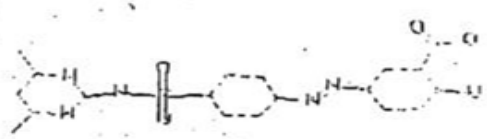

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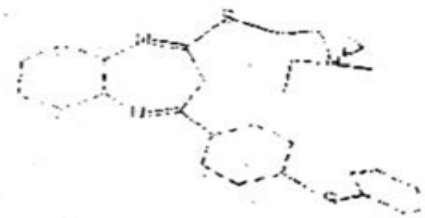

CONCLUSION AND REMARKS

- ☐ EASY TO FIND OUT SOME LEAD CANDIDATES FROM COMPOUND DATA BASE
- ☐ FIND OUT LEAD CANDIDATES, EVEN IF THE DIFFERENCES OF STRUCTURE ARE GREAT
- ☐ THIS METHOD CAN HANDLE A LARGE NUMBER OF COMPOUNDS WITHIN A SHORT TERM
- ☐ THIS METHOD CAN CHECK VARIOUS KINDS OF ACTIVITIES AT A TIME
- ☐ PRACTICAL USE OF COMPOUND PROPERTY