```
data one;
  do trt='stroph1','stroph2','ouabain';
    ni=7; if trt='ouabain' then ni=9;
  do rep=1 to ni;
    dum1=(trt='stroph1'); dum2=(trt='stroph2');
    input tols @@; tols=tols/10; logtols=log(tols); drop rep; output;
  end; end; datalines;
155 158 171 144 124 189 234 242 185 200 227 170 147 220
523 991 476 651 668 576 493 458 669
;
***********  only comparing Strophanthus 2 with Ouabain now ***********;
data one; set one; if trt='stroph1' then delete;
proc nlin hougaard data=one;
  parms th1=20 th2=1;
  model tols=th1*dum2+th1*th2*(1-dum2);
  output out=two r=r p=p;
run;
```

The NLIN Procedure
Dependent Variable tols
Method: Gauss-Newton
Iterative Phase

Iter	th1	th2	Sum of Squares
0	20.0000	1.0000	17491.9
1	19.8714	3.0648	2240.1
2	19.8714	3.0781	2239.5

NOTE: Convergence criterion met.

Estimation Summary

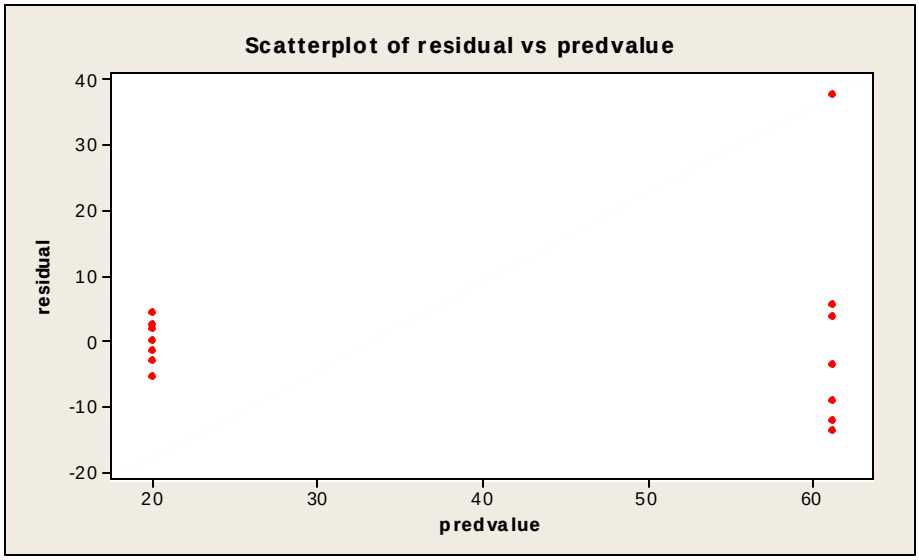
Method	Gauss-Newton
Iterations	2
R	0
PPC	0
RPC(th2)	0.004359
Object	0.000283
Objective	2239.514
Observations Read	16
Observations Used	16
Observations Missing	0

Source	DF	Sum of Squares	Mean Square	F Value	Approx Pr > F
Model	1	6714.6	6714.6	41.98	<.0001
Error	14	2239.5	160.0		
Corrected Total	15	8954.1			

Parameter	Estimate	Approx Std Error	Approximate 95% Confidence Limits		Skewness
th1	19.8714	4.7804	9.6185	30.1243	-157E-18
th2	3.0781	0.7703	1.4260	4.7302	1.3876

Approximate Correlation Matrix

	th1	th2
th1	1.0000000	-0.9613212
th2	-0.9613212	1.0000000




```
proc nlmixed data=one;
  parms th1=20 th2=1 sig=15;
  mean=th1*dum2+th1*th2*(1-dum2);
  var=sig*sig*(dum2+th2*th2*(1-dum2));
  model tols~normal(mean,var);
run;
```

The NLMIXED Procedure

Specifications

Data Set	WORK.ONE
Dependent Variable	tols
Distribution for Dependent Variable	Normal
Optimization Technique	Dual Quasi-Newton
Integration Method	None

Dimensions

Observations Used	16
Observations Not Used	0
Total Observations	16
Parameters	3

Parameters

th1	th2	sig	NegLogLike
20	1	15	96.9026642

Iteration History

Iter	Calls	NegLogLike	Diff	MaxGrad	Slope
1	2	72.5970223	24.30564	19.37577	-507.827
2	4	68.1053188	4.491703	4.574078	-2.32329
3	6	67.2351444	0.870174	0.79893	-0.68407
4	8	67.0991129	0.136031	1.016443	-0.07806
5	11	65.5912049	1.507908	4.613051	-0.07998
6	12	63.7545742	1.836631	1.578168	-1.82374
7	15	59.407569	4.347005	4.438401	-3.51229
8	18	58.381766	1.025803	5.212151	-24.7037
9	20	57.9457613	0.436005	0.808497	-2.25305
10	22	57.9193164	0.026445	0.681404	-0.06901
11	24	57.7956232	0.123693	0.978052	-0.08105

```
                  12        26     56.7993382    0.996285    1.249764    -0.18279
                  13        29     56.2484918    0.550846    1.810055    -0.91634
                  14        31     56.1550605    0.093431    0.813316    -0.21916
                  15        33     56.1393852    0.015675    0.019057    -0.03707
                  16        35     56.1387074    0.000678    0.016339     -0.0019
                  17        37     56.1386143    0.000093    0.001652    -0.00019
                  18        39      56.138614    2.673E-7     0.00003    -5.56E-7
NOTE: GCONV convergence criterion satisfied.

                                    Fit Statistics
                           -2 Log Likelihood                 112.3
                           AIC (smaller is better)           118.3
                           AICC (smaller is better)          120.3
                           BIC (smaller is better)           120.6

                                 Parameter Estimates
                        Standard
Parameter  Estimate      Error    DF  t Value  Pr > |t|   Alpha     Lower     Upper  Gradient
th1         19.4708     1.5365    16    12.67    <.0001    0.05   16.2135   22.7280   0.00003
th2          3.1926     0.3318    16     9.62    <.0001    0.05    2.4891    3.8960  0.000025
sig          4.2070     0.7833    16     5.37    <.0001    0.05    2.5465    5.8676  -0.00001
```

```
proc iml;
  start neg2ll(th) global(yy,zz,n1,n2,nn);
    th1=th[1]; th2=th[2]; sig=th[3]; sig2=sig*sig;
    ym=yy-th1*j(n1,1); zm=zz-th1*th2*j(n2,1);
    brac=th2*th2*t(ym)*ym+t(zm)*zm;
    thingy=nn*log(sig2)+2*n2*log(th2)+brac/(th2*th2*sig2);
    return(thingy);
  finish;

  n1=7; n2=9; nn=n1+n2;
  yy={24.2,18.5,20.0,22.7,17.0,14.7,22.0};
  zz={52.3,99.1,47.6,65.1,66.8,57.6,49.3,45.8,66.9};
  th0={16 3 12}; opt={.,0};
  con={.001 .001 .001,
         .    .    . };
  call nlptr(rc,theta,"neg2ll",th0,opt,con);
  minn2ll=neg2ll(theta); print theta minn2ll; ans=j(50,5);
  do jj=1 to 50;
    ans[jj,3]=minn2ll+2.71;
    ans[jj,4]=minn2ll+3.84;
    ans[jj,5]=minn2ll+6.63;
    star=2.2; fini=4.5; th2=star+(fini-star)*(jj-1)/49; ans[jj,1]=th2;
    th0=theta; opt={.,0};
    con2={.001 .001 .001,
            .    .    . };
    th0[2]=th2; con2[1,2]=th2; con2[2,2]=th2;
    call nlptr(rc,thtil,"neg2ll",th0,opt,con2);
    ans[jj,2]=neg2ll(thtil);
  end;
  create dset from ans[colname={theta2 neg2ll cut90 cut95 cut99}];
  append from ans;
quit;
data final; set dset;
  y=neg2ll;  zz=1; output;
  y=cut90;  zz=2; output;
  y=cut95;  zz=3; output;
  y=cut99;  zz=4; output;

axis1 w=2 minor=none label=(a=90 font=swiss 'Profile Likelihood');
axis2 w=2 minor=none label=(font=swiss 'relative potency');
symbol1 i=join w=5 l=1 c=blue;
```

```
symbol2 i=join w=3 l=2 c=blue;
symbol3 i=join w=3 l=3 c=blue;
symbol4 i=join w=3 l=4 c=blue;
proc gplot data=final;
  plot y*theta2=zz / fr vaxis=axis1 nolegend haxis=axis2;
run;
```

THETA			MINN2LL
19.47071	3.1925748	4.2070397	82.871195