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# *In vitro* antitumour activities of a novel 2:3 condensation product of salicylaldoxime with di-n-butyltin(IV) oxide

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**The antitumor activities of three novel condensation products of salicylaldoxime with di-n-butyltin(IV) oxide (compound 1), di-t-butyltin oxide (compound 2) and diphenyltin oxide (compound 3) are presented. Against MCF-7, a human mammary tumor cell line, compounds 1 and 2 are characterized by inhibition doses $ID_{50}$ *in vitro* of 67 and 49 ng $cm^{-3}$ respectively, whereas *cis*-platin, an antitumor drug used clinically, has an $ID_{50}$ of 850 ng $cm^{-3}$. Against WiDr, a colon carcinoma, they also score better than *cis*-platin: 215 and 121 ng $cm^{-3}$ versus 624 ng $cm^{-3}$. In contrast, the diphenyltin compound, 3, is inactive against both tumor cell lines.**

**The results of a pre-screening performed on compound 1 by the National Cancer Institute (NCI) on a panel of 60 human tumor cell lines show that two of the selectivity parameters calculated by the NCI for that compound are statistically significant, namely $D_{GI50}$ (51.9 > 50) and $MGD_H$ (80.1 > 75). One is almost satisfactory ($D_H$ = 72.4 = *ca* 75). The other two, $D_{TGI}$ (40.0 < 50) and $D_{LC50}$ (16.7 ≤ 50) are not. (Abbreviations are explained in the text and in Gielen, M. and Willem, R. *Anticancer Res.*, 1992, in press)**

**Keywords: Organotin, antitumor, salicylaldoxime, butyltin, phenyltin**

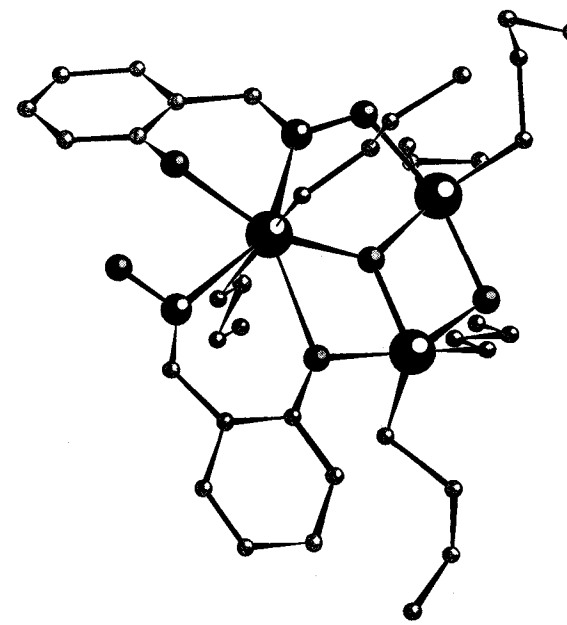

**Figure 1** Crystalline molecular structure of the 2:3 condensation product of salicylaldoxime with tri-n-butyltin oxide, compound **1**.

## INTRODUCTION

During the last two years, we have synthesized and characterized several series of diorganotin compounds.[1] They were tested *in vitro* against various human cancer cell lines. The results obtained with diorganotin carboxylates are quite representative.[2]

When carboxylic acids (RCOOH) react with diorganotin oxides, e.g. di-n-butyltin oxide, two types of condensation products can be obtained, depending on the molar ratio RCOOH:$Bu_2SnO$. When a 1:1 molar ratio is used, dimeric bis(carboxylatodi-n-butyltin) oxides are formed (see Eqn [1]).

*1:1 ratio:*

$$4RCOOH + Bu_2SnO \rightarrow ([Bu_2(RCOO)Sn]_2O)_2 + 2H_2O \quad [1]$$

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When a 2:1 ratio is used, di-n-butyltin dicarboxylates are obtained (see Eqn [2]).

*2:1 ratio:*

$$2RCOOH + Bu_2SnO \rightarrow Bu_2(RCOO)_2Sn + H_2O \quad [2]$$

Many bis(carboxylatodi-n-butyltin) oxides were tested against two human tumor cell lines, MCF-7, a mammary tumor, and WiDr, a colon *carcinoma.*[3] The inhibition doses, $ID_{50}$, obtained for selected compounds of that type are presented in Table 1. The same pre-screening on di-n-butyltin dicarboxylates[3] provided the $ID_{50}$ values listed in Table 2.

From Tables 1 and 2, it is clear that many compounds of both series are characterized by $ID_{50}$ values of *ca* 50 ng cm$^{-3}$ and have even lower values against MCF-7. Abbreviations are explained in the Materials and methods section. For comparison, *cis*-platin, an antitumor drug used clinically, is characterized by an $ID_{50}$ of 850 ng cm$^{-3}$ against MCF-7. The same holds for the cytotoxicity of these di-n-butyltin compounds against WiDr since many of them are characterized by $ID_{50}$ values of *ca* 300 ng cm$^{-3}$ or even less (e.g. di-n-butyltin bis(3-methoxy-4-hydroxybenzoate; see Table 2), whereas the $ID_{50}$ value for *cis*-platin is 624 ng cm$^{-3}$. We examined whether diorganotin oxides can be condensed analogously with salicylaldoxime and whether these condensation products have antitumor properties comparable to those of the diorganotin carboxylates.

## MATERIALS AND METHODS

### Synthesis of condensation products of diorganotin oxides with salicylaldoxime

The synthesis and characterization of the new condensation product of salicylaldoxime with di-n-butyltin(IV) oxide, compound **1**, are now described.

#### Synthesis of compound 1

Di-n-butyltin oxide (0.03 mol) and salicylaldoxime (0.02 mol) were refluxed in 100 cm$^3$ ethanol and 400 cm$^3$ toluene. The ternary azeotrope, water/ethanol/toluene, was distilled off with a Dean–Stark funnel. After 6 h the solvent was evaporated. The solid obtained was recrystallized from n-hexane (yield 91%; m.p. 92–94 °C). Elemental analysis, performed at the Università degli Studi di Bari by Professor Giovanni Natile, gave: H, 6.95; C, 45.8; N, 2.57. Calcd for $C_{38}H_{66}O_6N_2Sn_3$: H, 6.63; C, 45.5; N, 2.79%. Compound **1** is characterized by elemental analysis and X-ray diffraction[4] giving results compatible with $[C_6H_4(OH)CH{=}NO]_2SnBu_2$ $(Bu_2SnO)_2$ and Fig. 1. The compound probably remains unchanged in $CDCl_3$ as suggested by $^{119}$Sn NMR.

The same compound was obtained by use of 2:1, 1:2 and 2:3 molar ratios of reagents; the preparation reaction may be represented by Eqn [3],

$$2C_6H_4(OH)CH{=}NOH + 3SnR_2O \rightarrow [C_6H_4(OH)CH{=}NO]_2SnR_2(R_2SnO)_2 + H_2O \quad [3]$$

The compounds **2** and **3** were prepared analogously.

### *In vitro* screening

These three compounds were tested *in vitro* against two human tumor cell lines: MCF-7 mammary carcinoma (ITRI-TNO) and WiDr colon carcinoma.[5] The cell lines were maintained in a continuous logarithmic culture in Dulbecco's medium supplemented with 10% fetal calf serum, penicillin (100 IU cm$^{-3}$) and streptomycin (100 μg cm$^{-3}$). The cells were mildly trypsinized for passage and for use in experiments.

Furthermore, compound **1** was screened at the National Cancer Institute (NCI) using the standard protocols developed there according to its new investigational *in vitro*, disease-oriented, primary antitumor screen procedures. The cell panel consists of 60 lines against which the compounds have been tested at five concentrations differing by 10-fold dilutions from $10^{-4}$ to $10^{-8}$ mol dm$^{-3}$. A 48 h continuous drug exposure protocol was used. A sulforhodamine B (SRB) protein assay allowed the estimation of cell viability or growth.[6]

### Definitions of abbreviations

$ID_{50}$: dose of the drug [expressed for instance in g litre$^{-1}$ (g dm$^{-3}$), more often in ng ml$^{-1}$ (ng cm$^{-3}$)] at which the growth of the tumor cells is inhibited by 50%.

$ID_{t=0}$: optical density at time $t = 0$ (proportional to the number of cells).

$OD_{ctrl}$: optical density determined 48 h later on the control cell culture.

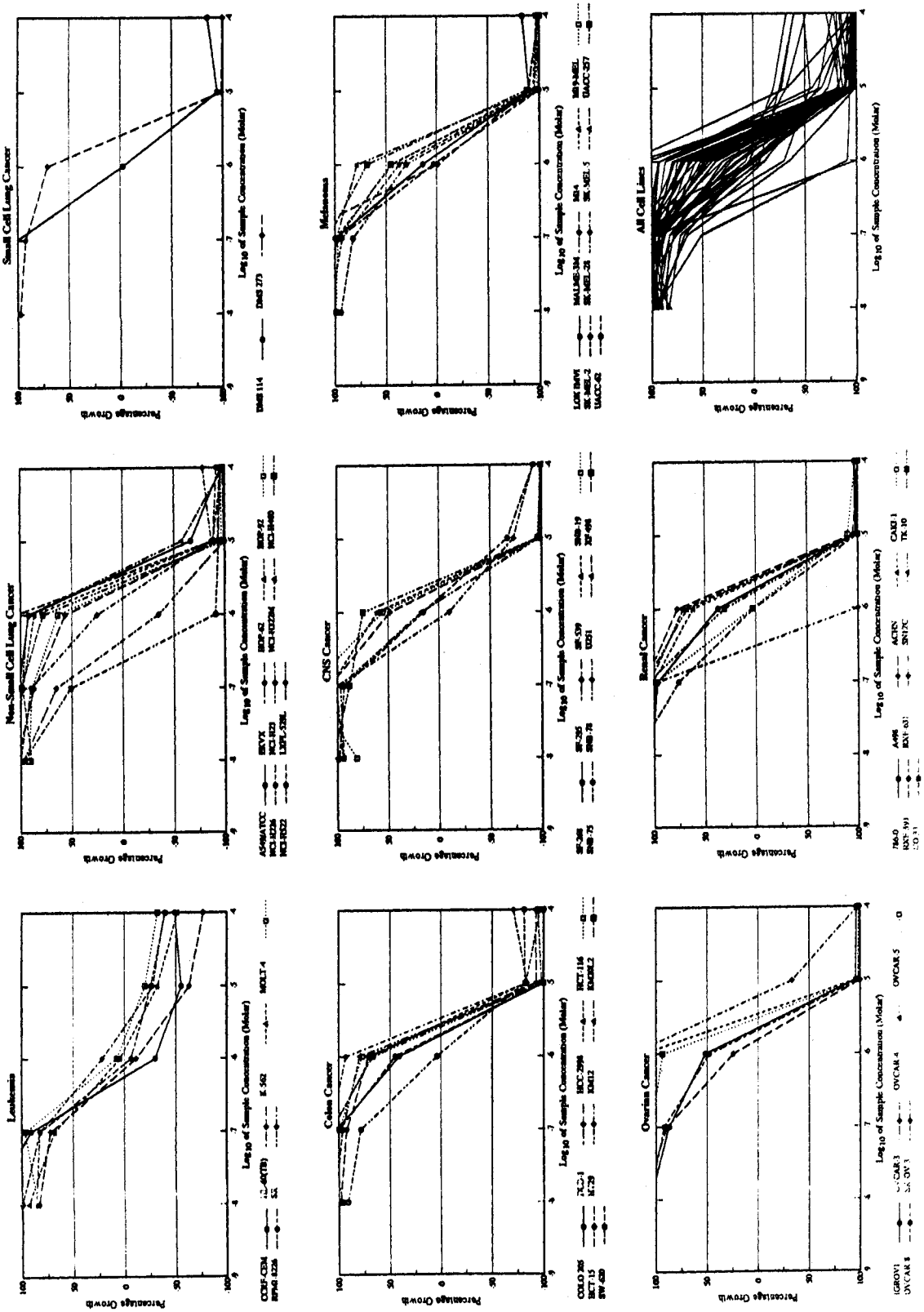


**Figure 2** Dose–response curves obtained by the National Cancer Institute for compound **1**.

**Table 1** $ID_{50}$ values of selected diorganotin(IV) derivatives of substituted salicylic acids $[YC_6H_3(OH)COOSnBu_2]_2O$ against MCF-7 and WiDr

| | $ID_{50}$ (ng cm$^{-3}$) against: | |
|---|---|---|
| Y | MCF-7 | WiDr |
| 3-$CH_3$ | 44 | 330 |
| 4-$CH_3$ | 51 | 316 |
| 5-$CH_3$ | 90 | 337 |
| 3-$CH_3O$ | 45 | 323 |
| 4-$CH_3O$ | 190 | 1 794 |
| 5-$CH_3O$ | 29 | 122 |
| 4-$NH_2$ | 42 | 330 |
| 5-$NH_2$ | 38 | 316 |
| 5-COOH | 41 | 190 |
| 5-F | 46 | 256 |
| 5-Cl | 31 | 280 |
| 5-$SO_3H$ | 47 | 107 |
| Doxorubicin | 63 | 31 |
| *Cis*-platin | 850 | 624 |
| Etoposide | 187 | 624 |
| Mitomycin C | 3 | 17 |

$OD_{test}$: optical densities obtained after 48 h when respectively $10^{-8}$, $10^{-7}$, $10^{-6}$, $10^{-5}$ and $10^{-4}$ mol dm$^{-3}$ drug is added to the culture medium.

PG: percentage growth calculated for these five concentrations respectively, using either

$$PG = \frac{100(\text{Mean } OD_{test} - \text{mean } OD_{t=0})}{\text{Mean } OD_{ctrl} - \text{mean } OD_{t=0}}$$

when $OD_{test} > OD_{t=0}$, or

$$PG = \frac{100\,(\text{Mean } OD_{test} - \text{mean } OD_{t=0})}{\text{Mean } OD_{t=0}}$$

when $OD_{test} < OD_{t=0}$.

GI50: concentration [often named $IC_{50}$, which is the value calculated from $ID_{50}$ and expressed in mol litre$^{-1}$ (mol dm$^{-3}$)] at which the growth of the cells is inhibited by 50%.

TGI: concentration of the drug at which the number of cells after 48 h is identical to the initial number of cells at $t=0$ (corresponds to PG = 0).

**Table 2** $ID_{50}$ values of a series of di-n-butyltin(IV) dicarboxylates (X, Y, Z-$C_6H_2COO)_2SnRR'$ against MCF-7 and WiDr

| | | | | $ID_{50}$ (ng cm$^{-3}$) against: | |
|---|---|---|---|---|---|
| RR' | X | Y | Z | MCF-7 | WiDr |
| n-$Bu_2$ | H | H | 2-$OCOCH_3$ | 283 | 2 495 |
| n-$Bu_2$ | H | H | 2-$NH_2$ | 60 | 259 |
| n-$Bu_2$ | H | H | 2-$NHCH_3$ | 125 | 507 |
| n-$Bu_2$ | H | H | 3-$N(CH_3)_2$ | 174 | 1 959 |
| n-$Bu_2$ | H | H | 2-NHPh | 138 | 819 |
| n-$Bu_2$ | H | H | 2-$NHCOCH_3$ | 125 | 787 |
| n-$Bu_2$ | H | H | 2-F | 74 | 242 |
| n-$Bu_2$ | H | H | 3-F | 63 | 197 |
| n-$Bu_2$ | H | H | 4-F | 90 | 309 |
| n-$Bu_2$ | 2-OH | H | H | 541 | 2 974 |
| n-$Bu_2$ | 2-OH | H | 3-$CH_3O$ | 105 | 474 |
| n-$Bu_2$ | 2-OH | H | 4-$CH_3O$ | 131 | 1 182 |
| n-$Bu_2$ | 2-OH | H | 5-$CH_3O$ | 54 | 611 |
| n-$Bu_2$ | 2-OH | H | 4-$NH_2$ | 106 | 394 |
| n-$Bu_2$ | 2-OH | H | 5-Cl | 89 | 319 |
| n-$Bu_2$ | 4-OH | H | 3-$CH_3O$ | 44 | 82 |
| n-$Bu_2$ | 2-$CF_3$ | H | 5-$CF_3$ | 48 | 176 |
| n-$Bu_2$ | 3-$NH_2$ | 4-$CH_3$ | H | 98 | 349 |
| n-$Bu_2$ | 2-OH | 3-$CH_3$ | 6-i-Pr | 57 | 280 |
| n-$Bu_2$ | 3-$OCH_3$ | 4-$OCH_3$ | 5-$OCH_3$ | 84 | 356 |
| n-$Bu_2$ | 2-$OCH_3$ | 3-$OCH_3$ | 4-$OCH_3$ | 93 | 398 |
| n-$Bu_2$ | 2-$OCH_3$ | 4-$OCH_3$ | 5-$OCH_3$ | 132 | 368 |
| *Cis*-platin | | | | 850 | 624 |

**Table 3** $ID_{50}$ values obtained for compounds **1–3** against MCF-7 and WiDr

| Compound | $ID_{50}$ (ng cm$^{-3}$) against MCF-7 | WiDr |
|---|---|---|
| Salicylaldoxime/n-$Bu_2SnO$, **1** | 67 | 215 |
| Salicylaldoxime/t-$Bu_2SnO$, **2** | 49 | 121 |
| Salicylaldoxime/$Ph_2SnO$, **3** | 1 643 | 4 565 |
| *Cis*-platin | 850 | 624 |

LC50: concentration at which the number of cells after 48 h is 50% of its initial number at $t=0$.

MG-MID: mean value of GI50, TGI or LC50 for all the cell lines tested.

$D_{GI50}$, $D_{TGI}$ and $D_{LC50}$: selectivity parameters associated with PG = 50, 0 and −50% calculated by the NCI following a rather complicated procedure.[7]

$D_H$ and $MGD_H$ are other selectivity parameters calculated by the NCI following another rather complicated procedure.[7]

## RESULTS AND DISCUSSION

The results of the *in vitro* screening of compounds **1**, **2** and **3** are reported in Table 3. They show that the two dialkyltin compounds, **1** and **2**, score similarly as compared with the di-n-butyltin compounds of Tables 1 and 2. The diphenyltin compound, **3**, is much less active than *cis*-platin. Analogous observations, namely that diphenyltin compounds, which were found to be more active than the corresponding di-n-butyltin analogs when tested *in vivo* against P388 leukemia in mice,[8,9] scored much worse than the di-n-butyltin analogs *in vitro* against human tumor cell lines were reported.[2]

Compound **1** was tested *in vitro* by the NCI against a panel of 60 human cancer cell lines. The results are shown in Table 4. The first column gives the 60 cell lines grouped in eight subpanels, (viz. leukemia, non-small-cell lung cancer, small-cell lung cancer, colon cancer, CNS cancer, melanoma, ovarian cancer and renal cancer). The second column of Table 4 gives the optical density at time $t=0$ ($OD_{t=0}$), which is proportional to the number of cells. The third column gives the optical densities determined 48 h later on the control cell culture ($OD_{ctrl}$). The next five columns give the optical densities obtained after 48 h ($OD_{test}$) when $10^{-8}$, $10^{-7}$, $10^{-6}$, $10^{-5}$ and $10^{-4}$ mol dm$^{-3}$ compound **1** was administered, respectively. The next five columns give the percentage growth (PG) calculated for these five concentrations respectively, using either $PG = 100 \times (\text{mean } OD_{test} - \text{mean } OD_{t=0})$ (mean $OD_{ctrl}$ − mean $OD_{t=0}$) when $OD_{test} > OD_{t=0}$, or $PG = 100 \times (\text{mean } OD_{test} - \text{mean } OD_{t=0})$ mean $OD_{t=0}$ when $OD_{test} < OD_{t=0}$.

Figure 3 gives the response curves and shows how PG changes in function of the drug concentration for each of the cell lines, again grouped in the eight subpanels. The intersections of the experimental curve of Fig. 2 with the horizontal lines PG = 50, 0 and −50% give the corresponding GI50, TGI and LC50 values, respectively. GI50 is nothing else than the inhibition concentration $IC_{50}$. TGI describes the concentration of compound **1** for which the number of cells after 48 h is identical to the initial number of cells at $t=0$ PG = 0) and LC50, the concentration for which the number of cells has been decreased by 50% as compared with the initial number at $t=0$.

The same GI50, TGI and LC50 values are again shown in the mean graph depicted in Fig. 3: the experimental concentrations are compared in that figure with the mean value MG-MID for each of the three situations (PG = 50, 0 and −50%). This figure visualizes very clearly the selectivity of the drug (bars extending to the right show higher activities than the mean one on a logarithmic scale, and bars extending to the left, lower activities): the longer the bars, the better the selectivity. From these experimental data, the NCI calculated sensitivity and selectivity parameters using a procedure that has been reported earlier,[7] namely $D_{GI50}$, $D_{TGI}$ and $D_{LC50}$ for the three cases respectively (PG = 50, 0 and −50%). Computer simulations performed by the NCI show that these D-values are statistically significant if they exceed 50. In the case of compound **1**, only $D_{GI50}$ is statistically significant (51.9 > 50), which should be considered as unsatisfactory. The NCI also calculated the $D_H$ and $MGD_H$ selectivity parameters according to a procedure described previously.[7] They represent statistically significant selectivities if they are larger than 75. In the case of compound **1**, $MGD_H$ is statistically significant (80.1 > 75) and $D_H$ almost is (72.4 ≃ 75). This shows that compound **1** exhibits only a marginal antitumor selectivity which prevented it from being selected by the NCI for further testing.

**Table 4** National Cancer Institute Development therapeutics program *in vitro* testing results
NSC: 633498-S/1. Experiment ID: 9010MD20. Test type: 8. Units: Molar. Report date: 25 November 1990. Test date: 30 October 1990. QNS: 8. Stain reagent: PRO.

| | | | Mean optical densities | | | | | Percentage growth | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Panel/Cell line | Time zero | Ctrl | −8.0 | −7.0 | −6.0 | −5.0 | −4.0 | −8.0 | −7.0 | −6.0 | −5.0 | −4.0 | GI50 | TGI | LC50 |
| Leukemia | | | | | | | | | | | | | | | |
| CCRF-CEM | 0.41 | 1.13 | 1.36 | 1.07 | 0.28 | 0.18 | 0.21 | 130.6 | 91.0 | −30.1 | −55.3 | −49.3 | 2.18E-07 | 5.64E-07 | — |
| HL-60 (TB) | 0.34 | 1.50 | 1.31 | 1.17 | 0.30 | 0.12 | 0.08 | 83.4 | 71.9 | −11.6 | −63.2 | −76.9 | 1.83E-07 | 7.26E-07 | 5.54E-06 |
| K-562 | 0.27 | 1.29 | 1.22 | 0.96 | 0.32 | 0.19 | 0.13 | 93.3 | 68.0 | 4.5 | −32.4 | −51.5 | 1.92E-07 | 1.33E-06 | 8.38E-05 |
| MOLT-4 | 0.69 | 1.79 | 1.62 | 1.75 | 0.77 | 0.55 | 0.47 | 84.7 | 96.9 | 7.7 | −19.9 | −32.4 | 3.35E-07 | 1.90E-06 | >1.00E-04 |
| RPMI-8226 | 0.75 | 1.80 | 1.80 | 1.61 | 0.70 | 0.56 | 0.45 | 99.6 | 82.1 | −6.3 | −25.7 | −39.9 | 2.31E-07 | 8.48E-07 | >1.00E-04 |
| SR | 0.66 | 1.75 | 1.60 | 1.56 | 0.90 | 0.48 | 0.40 | 85.9 | 82.4 | 21.7 | −27.8 | −39.4 | 3.42E-07 | 2.75E-06 | >1.00E-04 |
| Non-small-cell lung | | | | | | | | | | | | | | | |
| A549/ATCC | 0.21 | 0.92 | 0.96 | 0.94 | 0.87 | 0.07 | 0.01 | 105.8 | 101.8 | 92.0 | −66.6 | −96.3 | 1.84E-06 | 3.80E-06 | 7.86E-06 |
| EKVX | 0.72 | 1.29 | 1.31 | 1.21 | 1.04 | 0.05 | 0.04 | 103.8 | 86.6 | 56.5 | −92.9 | −94.7 | 1.11E-06 | 2.39E-06 | 5.16E-06 |
| HOP-62 | 0.67 | 1.29 | 1.22 | 1.27 | 1.20 | 0.08 | 0.02 | 89.2 | 97.8 | 86.5 | −88.5 | −96.7 | 1.62E-06 | 3.12E-06 | 6.03E-06 |
| HOP-92 | 0.66 | 0.97 | 0.95 | 0.94 | 0.86 | 0.02 | 0.03 | 91.7 | 88.8 | 63.7 | −96.7 | −96.1 | 1.22E-06 | 2.49E-06 | 5.11E-06 |
| NCI-H226 | 0.54 | 0.90 | 0.91 | 0.91 | 0.92 | 0.06 | 0.05 | 104.0 | 104.1 | 105.2 | −88.6 | −91.7 | 1.93E-06 | 3.49E-06 | 6.32E-06 |
| NCI-H23 | 0.25 | 0.66 | 0.66 | 0.62 | 0.36 | 0.03 | 0.06 | 100.1 | 89.7 | 25.3 | −86.9 | −78.4 | 4.13E-07 | 1.68E-06 | 4.69E-06 |
| NCI-H322M | 0.57 | 1.52 | 1.55 | 1.50 | 1.45 | 0.24 | 0.01 | 103.8 | 98.4 | 92.6 | −57.7 | −98.6 | 1.92E-06 | 4.13E-06 | 8.89E-06 |
| NCI-H460 | 0.21 | 1.20 | 1.23 | 1.19 | 0.98 | 0.00 | 0.00 | 103.0 | 99.2 | 78.1 | −99.0 | −98.1 | 1.44E-06 | 2.76E-06 | 5.29E-06 |
| NCI-H522 | 0.34 | 0.69 | 0.67 | 0.52 | 0.03 | 0.02 | 0.01 | 96.7 | 51.1 | −91.1 | −93.6 | −96.1 | 1.02E-07 | 2.29E-07 | 5.14E-07 |
| LXFL-529L | 0.58 | 1.52 | 1.49 | 1.19 | 0.38 | 0.00 | 0.01 | 97.4 | 65.2 | −35.1 | −99.7 | −97.6 | 1.42E-07 | 4.47E-07 | 1.70E-06 |
| Small-cell lung cancer | | | | | | | | | | | | | | | |
| DMS 114 | 0.31 | 0.83 | 0.85 | 0.83 | 0.30 | 0.02 | 0.05 | 103.2 | 100.6 | −2.8 | −94.6 | −85.1 | 3.09E-07 | 9.40E-07 | 3.27E-06 |
| DMS 273 | 0.21 | 0.86 | 0.84 | 0.81 | 0.67 | 0.00 | −0.01 | 97.5 | 92.1 | 70.5 | −98.6 | −100 | 1.32E-06 | 2.61E-06 | 5.16E-06 |
| Colon cancer | | | | | | | | | | | | | | | |
| COLO 205 | 0.24 | 0.97 | 0.98 | 0.99 | 0.54 | 0.00 | −0.00 | 100.3 | 102.4 | 41.0 | −99.2 | −100 | 7.13E-07 | 1.96E-06 | 4.46E-06 |
| DLD-1 | 0.12 | 0.65 | 0.64 | 0.61 | 0.50 | 0.01 | 0.01 | 98.2 | 92.1 | 71.4 | −92.6 | −92.2 | 1.35E-06 | 2.72E-06 | 5.50E-06 |
| HCC-2998 | 0.14 | 0.47 | 0.50 | 0.49 | 0.37 | 0.02 | 0.01 | 107.6 | 106.0 | 68.4 | −82.9 | −96.4 | 1.32E-06 | 2.83E-06 | 6.06E-06 |
| HCT-116 | 0.13 | 0.66 | 0.69 | 0.66 | 0.54 | −0.03 | −0.01 | 105.3 | 99.4 | 77.3 | −100 | −100 | 1.43E-06 | 2.73E-06 | 5.22E-06 |
| HCT-15 | 0.30 | 0.89 | 0.96 | 0.89 | 0.57 | −0.01 | −0.00 | 111.6 | 99.6 | 44.9 | −100 | −100 | 8.08E-07 | 2.04E-06 | 4.52E-06 |
| HT29 | 0.12 | 0.50 | 0.51 | 0.53 | 0.48 | 0.02 | 0.03 | 102.7 | 107.4 | 93.1 | −83.8 | −70.9 | 1.75E-06 | 3.36E-06 | 6.44E-06 |
| KM12 | 0.21 | 1.30 | 1.33 | 1.26 | 1.08 | −0.01 | −0.00 | 103.4 | 96.1 | 79.8 | −100 | −100 | 1.47E-06 | 2.78E-06 | 5.27E-06 |
| KM20L2 | 0.38 | 1.18 | 1.15 | 1.24 | 0.91 | 0.01 | 0.02 | 96.4 | 107.5 | 66.8 | −97.8 | −94.5 | 1.26E-06 | 2.54E-06 | 5.12E-06 |
| SW-620 | 0.20 | 0.89 | 0.83 | 0.74 | 0.23 | 0.04 | 0.04 | 91.1 | 78.6 | 3.9 | −81.8 | −81.3 | 2.41E-07 | 1.11E-06 | 4.26E-06 |

| | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| CNS cancer | | | | | | | | | | | | | | | |
| SF-268 | 0.12 | — | 0.30 | 0.29 | 0.11 | 0.01 | 0.00 | — | — | — | — | — | — | — | — |
| SF-295 | 0.27 | 0.91 | 0.92 | 0.95 | 0.58 | 0.00 | 0.00 | 102.2 | 107.4 | 48.1 | −98.7 | −98.7 | 9.30E-07 | 2.13E-06 | 4.66E-06 |
| SF-539 | 0.46 | 1.15 | 1.14 | 1.19 | 0.88 | 0.02 | 0.00 | 99.6 | 106.7 | 60.7 | −96.6 | −99.4 | 1.17E-06 | 2.43E-06 | 5.06E-06 |
| SNB-19 | 0.68 | 1.33 | 1.21 | 1.50 | 1.04 | 0.03 | 0.01 | 81.0 | 126.3 | 55.5 | −95.8 | −99.3 | 1.09E-06 | 2.33E-06 | 4.98E-06 |
| SNB-75 | 0.33 | 0.63 | 0.63 | 0.61 | 0.38 | 0.11 | 0.03 | 98.3 | 93.3 | 15.3 | −66.8 | −92.1 | 3.59E-07 | 1.54E-06 | 6.25E-06 |
| SNB-78 | 0.72 | 0.96 | 0.95 | 0.96 | 0.64 | 0.20 | 0.06 | 94.9 | 100.6 | −10.1 | −72.8 | −91.9 | 2.87E-07 | 8.11E-07 | 4.33E-06 |
| U251 | 0.28 | 1.08 | 1.03 | 1.06 | 0.42 | 0.01 | 0.01 | 93.7 | 96.9 | 17.1 | −97.3 | −98.2 | 3.87E-07 | 1.41E-06 | 3.86E-06 |
| XF 498 | 0.46 | 0.57 | 0.58 | 0.56 | 0.54 | 0.01 | 0.01 | 104.3 | 88.1 | 74.7 | −97.2 | −99.0 | 1.39E-06 | 2.72E-06 | 5.31E-06 |
| Melanoma | | | | | | | | | | | | | | | |
| LOX IMVI | 0.22 | 1.14 | 1.15 | 1.14 | 0.34 | 0.02 | 0.04 | 100.5 | 99.6 | 13.6 | −89.7 | −83.5 | 3.77E-07 | 1.35E-06 | 4.13E-06 |
| MALME-3M | 0.83 | 1.12 | 1.19 | 1.23 | 0.82 | 0.09 | 0.01 | 125.7 | 142.5 | −1.4 | −89.7 | −98.7 | 4.39E-07 | 9.78E-07 | 3.55E-06 |
| M14 | 0.44 | 1.07 | 1.12 | 1.07 | 0.72 | 0.03 | 0.01 | 106.9 | 99.2 | 44.1 | −93.8 | −97.1 | 7.80E-07 | 2.09E-06 | 4.81E-06 |
| M19-MEL | 0.26 | 1.11 | 1.10 | 1.08 | 0.65 | 0.01 | 0.01 | 99.0 | 96.9 | 45.4 | −97.5 | −96.8 | 8.15E-07 | 2.08E-06 | 4.65E-06 |
| SK-MEL-2 | 0.61 | 0.96 | 1.00 | 0.95 | 0.62 | 0.01 | −0.01 | 111.7 | 97.1 | 3.0 | −99.3 | −100 | 3.17E-07 | 1.07E-06 | 3.30E-06 |
| SK-MEL-28 | 0.38 | 0.85 | 0.88 | 0.82 | 0.55 | 0.00 | 0.00 | 105.3 | 92.7 | 36.7 | −98.8 | −100 | 5.80E-07 | 1.87E-06 | 4.36E-06 |
| SK-MEL-5 | 0.42 | 1.33 | 1.37 | 1.32 | 1.14 | 0.02 | 0.01 | 103.5 | 98.4 | 78.4 | −95.2 | −98.4 | 1.46E-06 | 2.83E-06 | 5.49E-06 |
| UACC-257 | 0.47 | 1.26 | 1.31 | 1.32 | 1.01 | 0.06 | −0.00 | 106.6 | 107.2 | 68.5 | −88.0 | −100 | 1.31E-06 | 2.74E-06 | 5.72E-06 |
| UACC-62 | 0.54 | 1.32 | 1.27 | 1.18 | 0.77 | 0.00 | 0.02 | 94.2 | 82.4 | 29.8 | −99.7 | −97.1 | 4.13E-07 | 1.70E-06 | 4.13E-06 |
| Ovarian cancer | | | | | | | | | | | | | | | |
| IGROV1 | 0.37 | 0.91 | 0.94 | 0.84 | 0.65 | 0.02 | 0.01 | 105.3 | 87.2 | 51.8 | −95.4 | −96.5 | 1.03E-06 | 2.25E-06 | 4.91E-06 |
| OVCAR-3 | 0.71 | 1.19 | 1.24 | 1.14 | 0.83 | −0.00 | 0.00 | 111.8 | 89.3 | 24.2 | −100 | −99.6 | 4.02E-07 | 1.57E-06 | 3.96E-06 |
| OVCAR-4 | 0.30 | 0.66 | 0.77 | 0.81 | 0.71 | 0.01 | 0.01 | 130.7 | 141.6 | 114.2 | −95.3 | −95.8 | 2.03E-06 | 3.51E-06 | 6.08E-06 |
| OVCAR-5 | 1.02 | 1.26 | 1.28 | 1.27 | 1.24 | 0.02 | 0.02 | 111.6 | 104.2 | 93.3 | −97.8 | −98.3 | 1.69E-06 | 3.08E-06 | 5.62E-06 |
| OVCAR-8 | 0.33 | 1.01 | 1.06 | 0.96 | 0.66 | 0.01 | 0.00 | 106.2 | 92.1 | 47.8 | −98.2 | −99.4 | 8.90E-07 | 2.12E-06 | 4.68E-06 |
| SK-OV-3 | 0.36 | 0.63 | 0.67 | 0.71 | 0.70 | 0.24 | 0.01 | 116.4 | 129.4 | 124.2 | −33.2 | −97.7 | 2.96E-06 | 6.15E-06 | 1.82E-05 |
| Renal cancer | | | | | | | | | | | | | | | |
| 786-0 | 0.24 | 0.90 | 0.92 | 0.88 | 0.49 | 0.01 | 0.01 | 102.2 | 96.5 | 37.2 | −97.7 | −96.7 | 6.08E-07 | 1.89E-06 | 4.43E-06 |
| A498 | 0.78 | 1.22 | 1.26 | 1.27 | 1.12 | 0.04 | −0.01 | 107.5 | 109.1 | 77.0 | −95.2 | −100 | 1.43E-06 | 2.80E-06 | 5.46E-06 |
| ACHN | 0.29 | 0.91 | 0.92 | 0.91 | 0.67 | 0.00 | 0.01 | 101.5 | 101.2 | 61.6 | −98.4 | −97.7 | 1.18E-06 | 2.43E-06 | 4.98E-06 |
| CAKI-1 | 0.62 | 1.10 | 1.10 | 1.09 | 0.63 | 0.06 | 0.01 | 100.6 | 98.2 | 3.3 | −90.0 | −98.0 | 3.22E-07 | 1.09E-06 | 3.73E-06 |
| RXF-393 | 0.37 | 0.60 | 0.64 | 0.55 | 0.38 | −0.01 | 0.01 | 119.1 | 75.8 | 2.2 | −100 | −97.7 | 2.24E-07 | 1.05E-06 | 3.24E-06 |
| RXF-631 | 0.37 | 0.80 | 0.82 | 0.79 | −0.00 | 0.00 | 0.01 | 104.5 | 98.2 | −100 | −99.9 | −96.1 | 1.75E-07 | 3.13E-07 | 5.59E-07 |
| SN12C | 0.30 | 0.83 | 0.89 | 0.88 | 0.66 | 0.00 | 0.00 | 110.0 | 108.9 | 67.3 | −99.2 | −99.8 | 1.27E-06 | 2.54E-06 | 5.07E-06 |
| TK-10 | 0.47 | 1.07 | 1.13 | 1.11 | 0.66 | 0.00 | −0.01 | 109.4 | 106.5 | 30.6 | −98.8 | −100 | 5.55E-07 | 1.72E-06 | 4.15E-06 |
| GC-31 | 0.51 | 1.12 | 1.13 | 1.15 | 0.95 | 0.01 | 0.00 | 101.8 | 104.3 | 70.9 | −99.1 | −99.3 | 1.33E-06 | 2.61E-06 | 5.14E-06 |

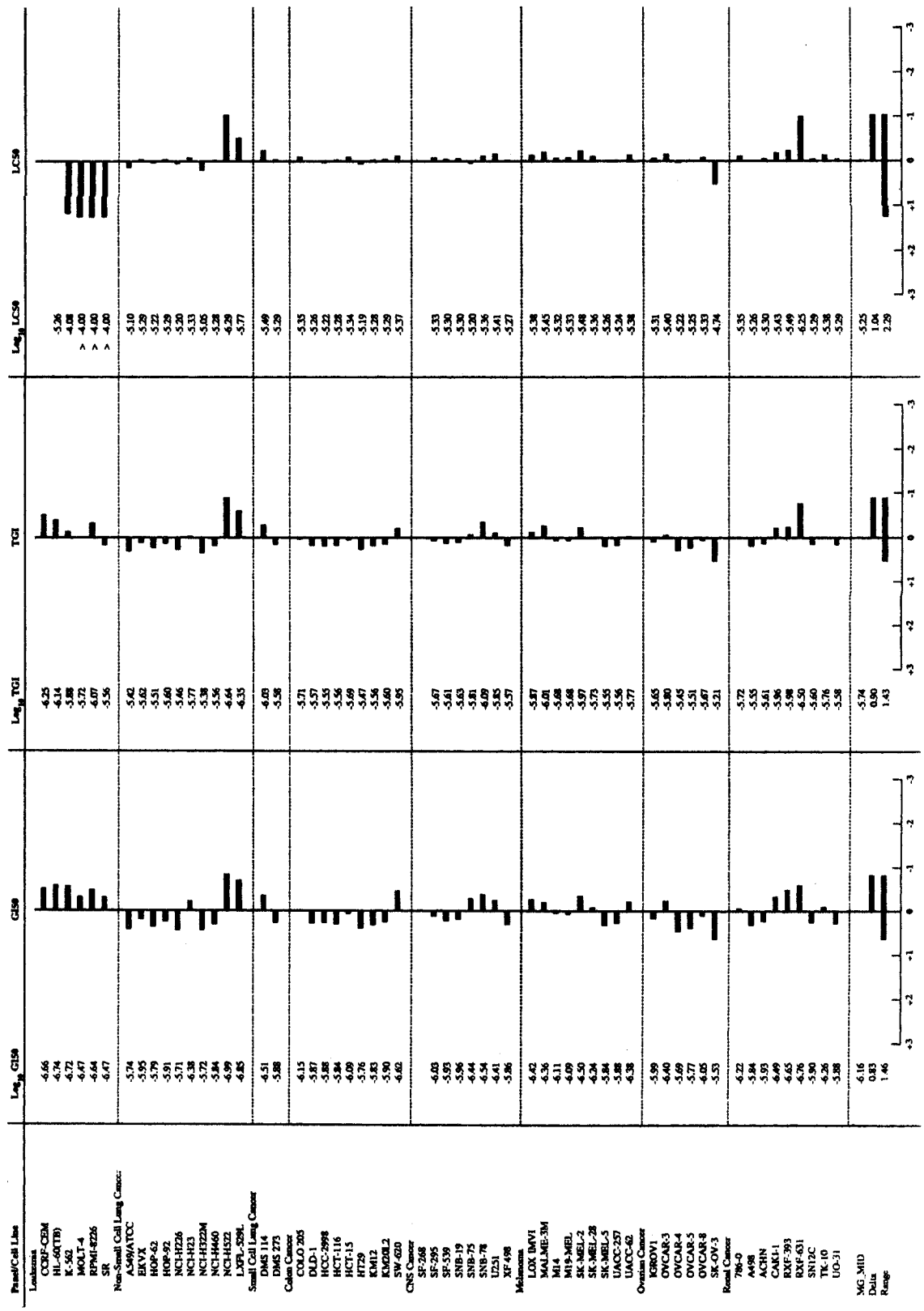


**Figure 3** Mean graphs obtained by the National Cancer Institute for compound 1.

However, it exhibits interesting *in vitro* antitumor properties at the G150 level, scoring for the leukemia subpanel as well as for the MCF-7 and WiDr cell lines. It should be mentioned however that the NCI tests provided satisfactorily better results for some di-n-butyltin carboxylates[7] and related compounds.[10]

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