Five-Membered Ring Peroxide Selectively Initiates Ferroptosis in Cancer Cells

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Supplementary Information

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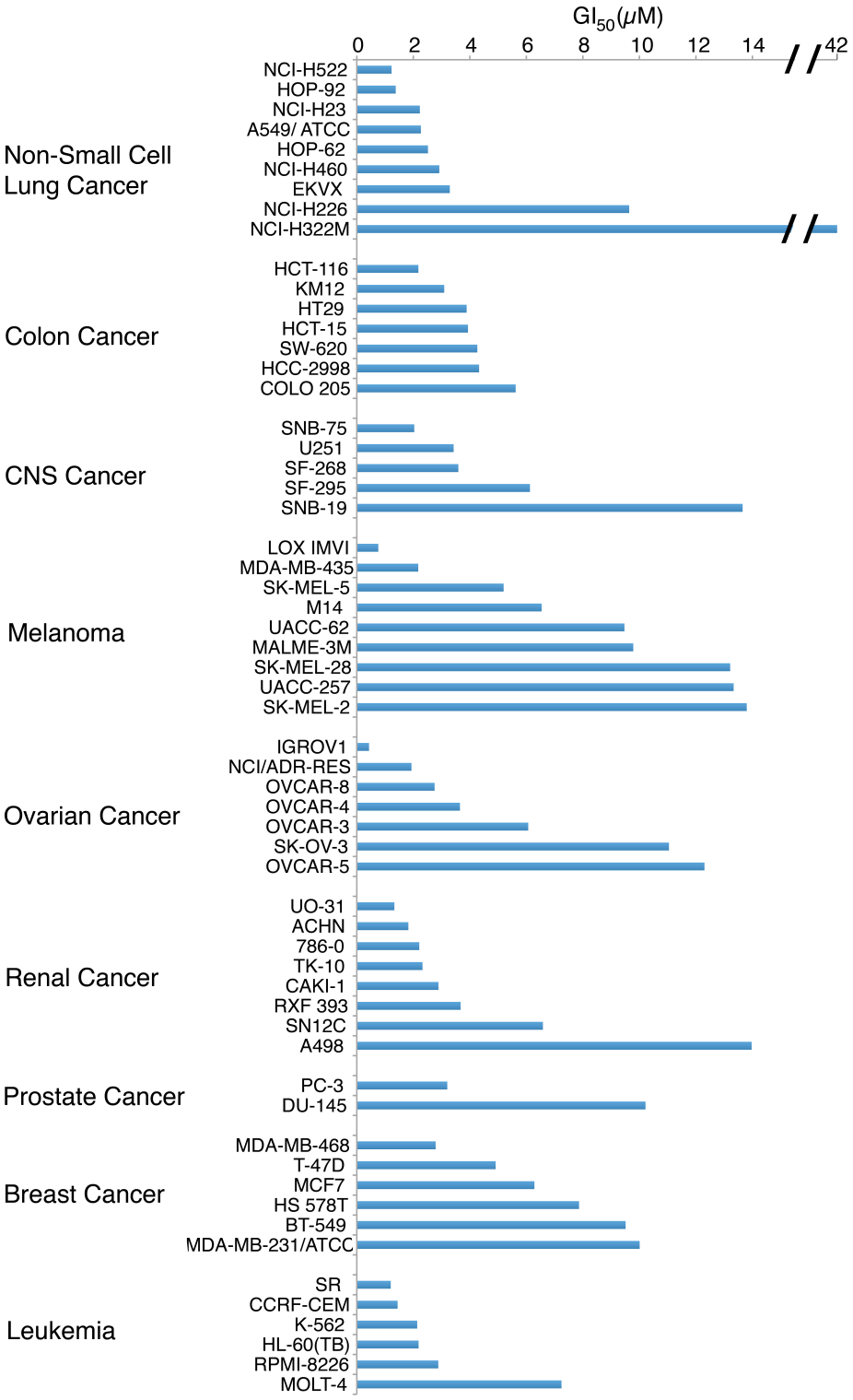
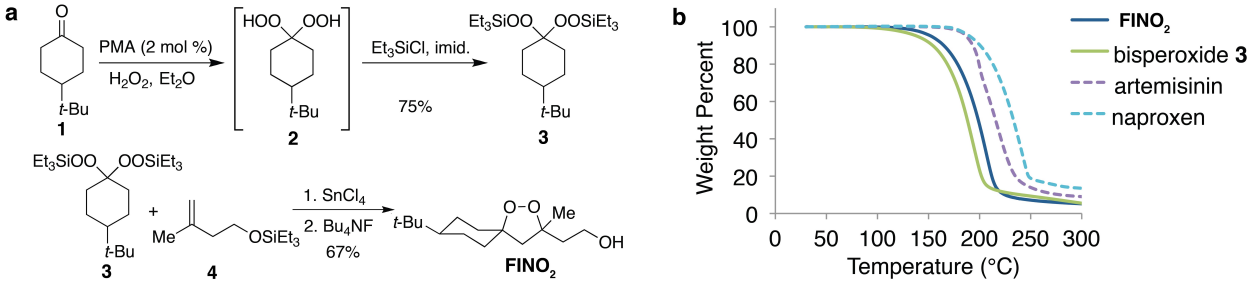
Supplementary Figures

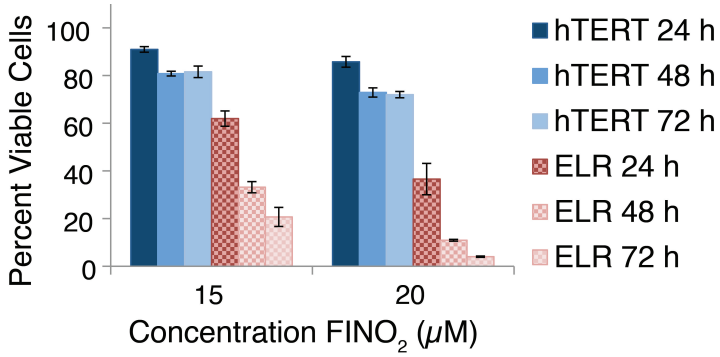


Supplementary Figure 1. The concentrations at which 50% of cell growth was inhibited (GI_{50}) grouped by tissue of origin to illustrate that $FINO_2$ is both active and inactive in a range of cell

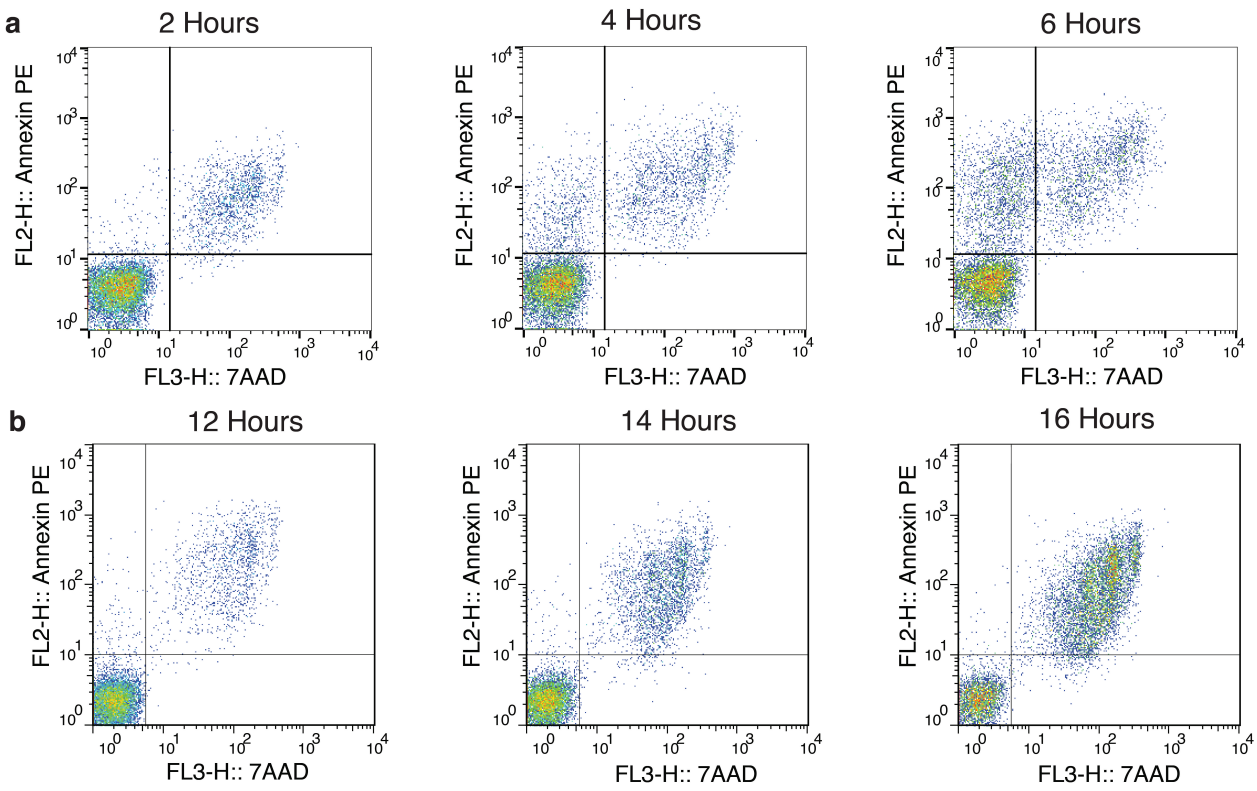
lines from different tissues. Data obtained by the Developmental Therapeutic Program of the National Cancer Institute.



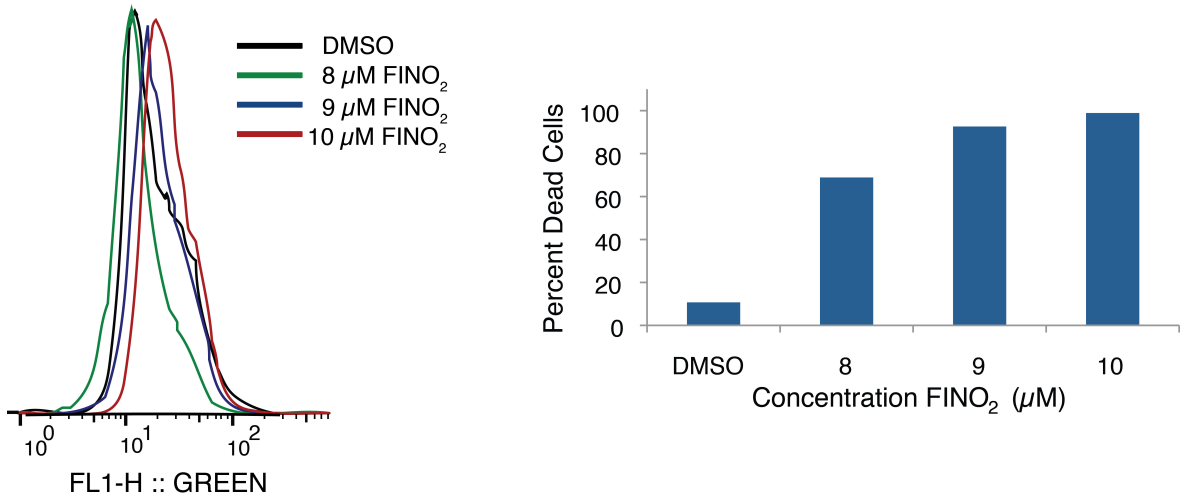
Supplementary Figure 2. Synthesis and stability. (a) Synthesis of $FINO_2$; Phosphomolybdic acid (PMA), imidazole (imid.). (b) Thermogravimetric analysis. The thermal stability of $FINO_2$ was corroborated by NMR analysis of a sample that had been heated to 150 °C.



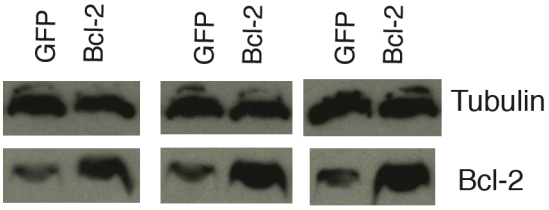
Supplementary Figure 3. Selectivity of $FINO_2$ measured by Promega CellTiter–Glo® Luminescence Assay. Cell viability decreases for cancerous cells (ELR), but not non-canceous cells (hTERT) over time, resulting in the best selectivity being observed after 72 hours of treatment with $FINO_2$.



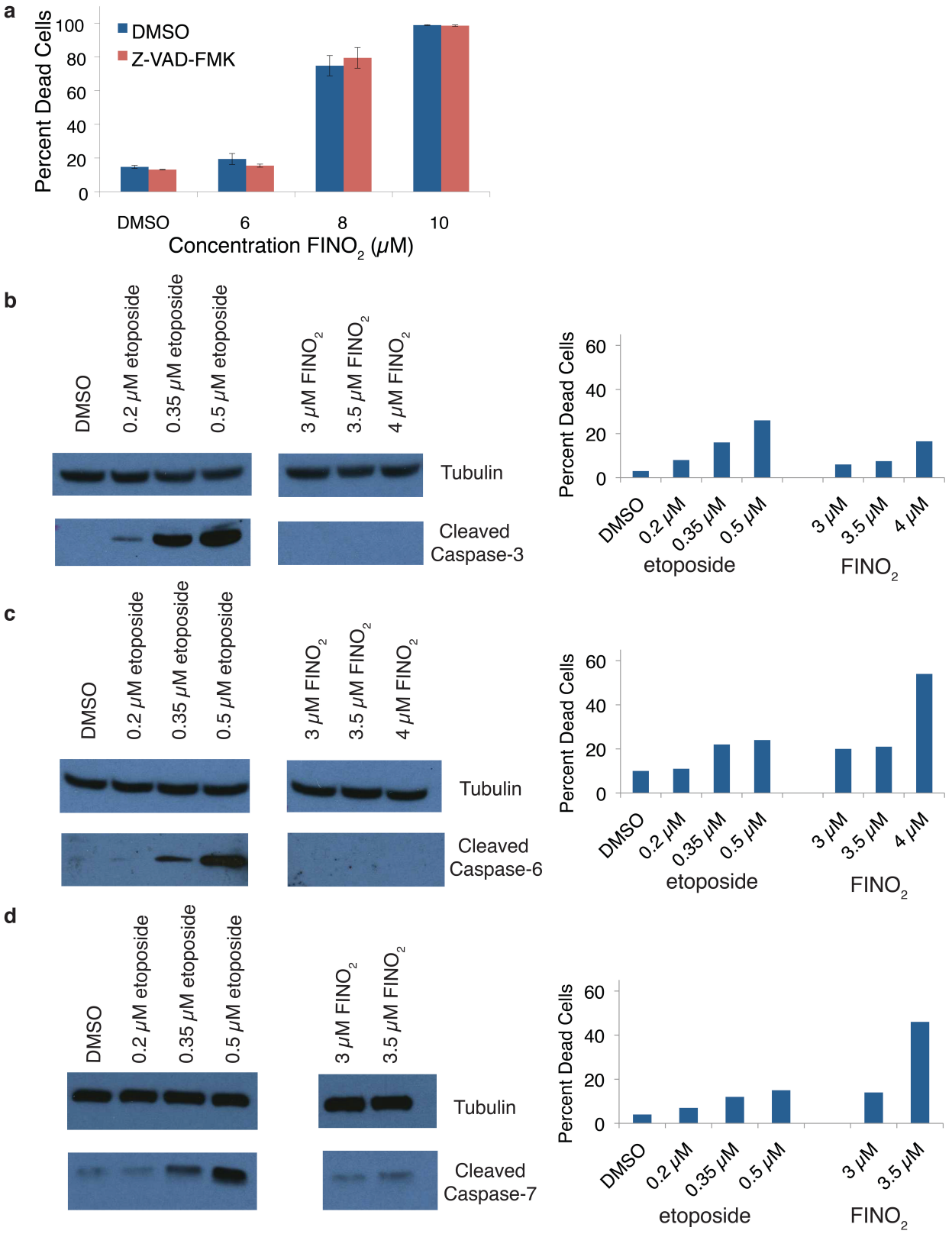
Supplementary Figure 4. Annexin V-PE and 7AAD apoptosis assay. a) Annexin V-PE staining is observed prior to 7AAD with 50 μM of etoposide treatment at indicated time points. b) Annexin V-PE staining is not observed prior to 7AAD incorporation with 6 μM of $FINO_2$ treatment at indicated time points.



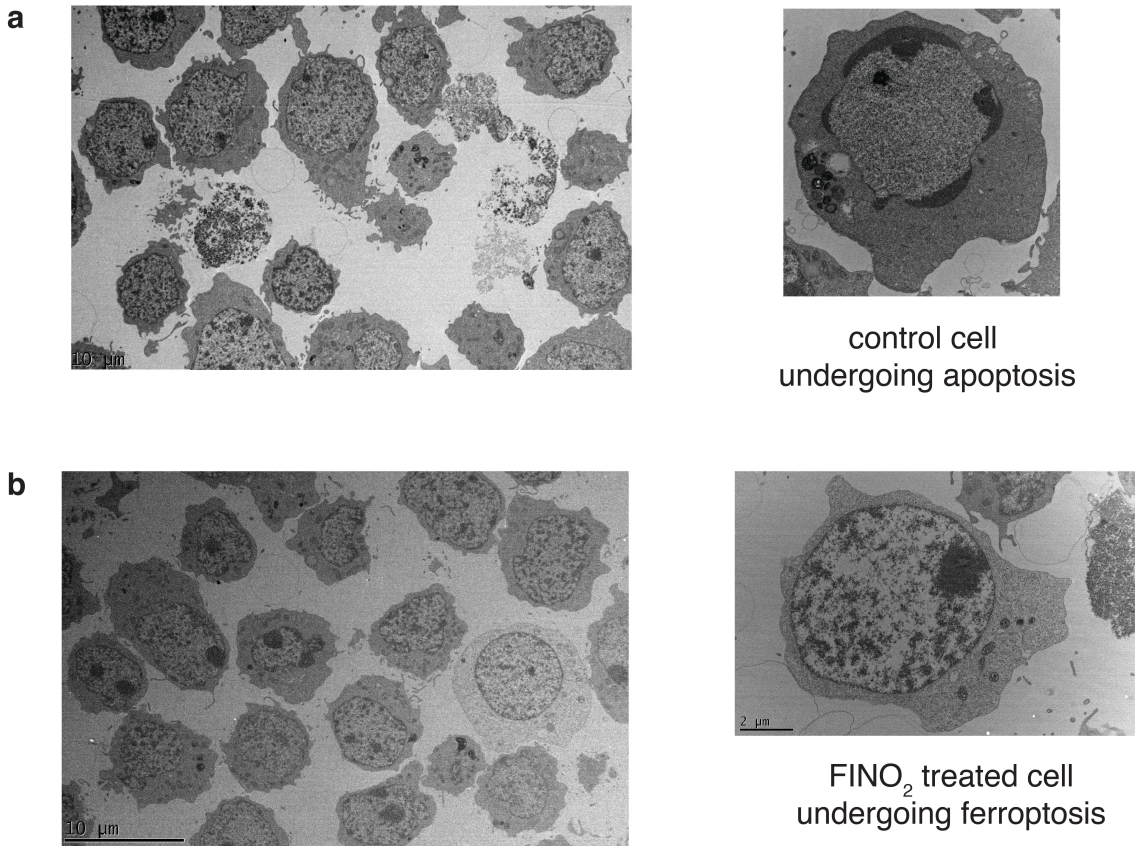
Supplementary Figure 5. The BioVision MitoCapture™ Mitochondrial Apoptosis Detection Kit showed a shift in green fluorescence. The shift in fluorescence was not observed until after the majority of the cells were dead, as indicated by Trypan Blue staining.



Supplementary Figure 6. Western blot showing overexpression of the bcl-2 protein in cells collected the day of experiment plating.

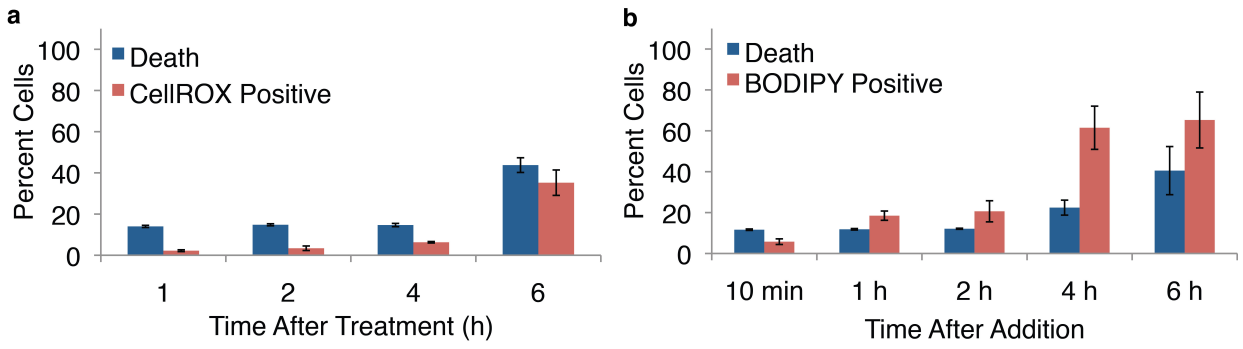

a
Percent Dead Cells
100
80
60
40
20
0
DMSO
Z-VAD-FMK
DMSO
6
8
10
Concentration FINO2 (μM)
b
DMSO
0.2 μM etoposide
0.35 μM etoposide
0.5 μM etoposide
3 μM FINO2
3.5 μM FINO2
4 μM FINO2
Tubulin
Cleaved Caspase-3
Percent Dead Cells
60
40
20
0
DMSO
0.2 μM
0.35 μM
0.5 μM
3 μM
3.5 μM
4 μM
etoposide
FINO2
c
DMSO
0.2 μM etoposide
0.35 μM etoposide
0.5 μM etoposide
3 μM FINO2
3.5 μM FINO2
4 μM FINO2
Tubulin
Cleaved Caspase-6
Percent Dead Cells
60
40
20
0
DMSO
0.2 μM
0.35 μM
0.5 μM
3 μM
3.5 μM
4 μM
etoposide
FINO2
d
DMSO
0.2 μM etoposide
0.35 μM etoposide
0.5 μM etoposide
3 μM FINO2
3.5 μM FINO2
Tubulin
Cleaved Caspase-7
Percent Dead Cells
60
40
20
0
DMSO
0.2 μM
0.35 μM
0.5 μM
3 μM
3.5 μM
etoposide
FINO2

Supplementary Figure 7. Caspase activation is not involved in cell death induced by $FINO_2$. (a) Pretreatment with 2.4 μM of a pan-caspase inhibitor (Z-VAD-FMK) does not inhibit cell death. Percent dead cells indicate the Annexin V and 7AAD positive cell population. (b) Activation of executioner caspase-3, -6, or -7 was not observed by the detection of cleaved proteins by Western blot. Similar quantities of cell death induced by chemotherapeutic agents, such as etoposide, result in activation of executioner caspases. All caspase antibodies were used at 1:500 dilutions and incubated overnight. Tubulin was used at a 1:5000 dilution and incubated overnight. Trypan Blue staining was used to indicate cell death.

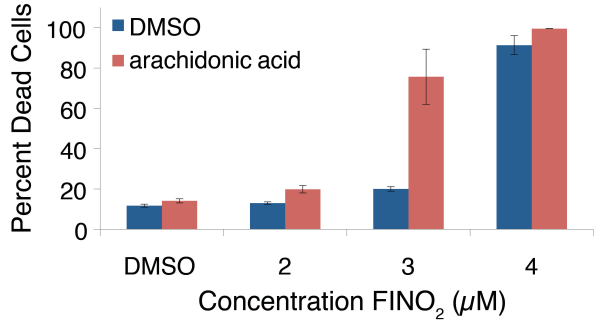


Supplementary Figure 8. Electron microscopy images of RS4;11 cells. a) Cells treated with vehicle only (DMSO) and example of RS4;11 cell undergoing apoptosis. b) Cells treated with

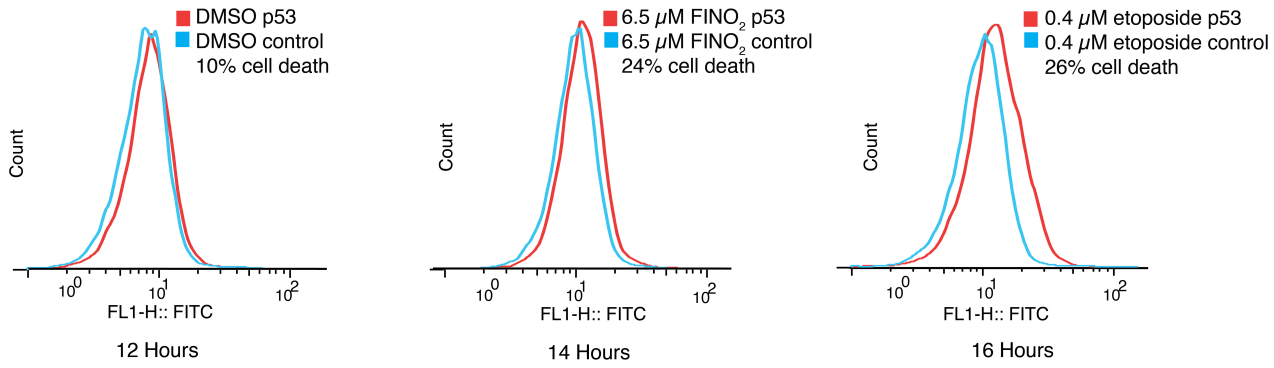
$FINO_2$ lacking hallmarks of apoptosis, necrosis, and autophagy (performed by the Microscopy Core at New York University Langone Medical Center).



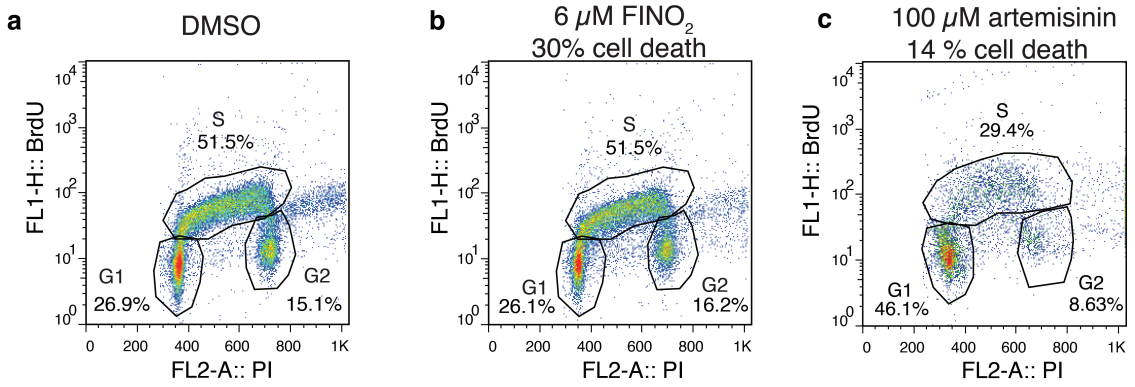
Supplementary Figure 9. A time-course experiment indicated $FINO_2$ does not react directly with oxidation probes. a) Cells were treated with 7 µM of $FINO_2$ for indicated times and then the CellROX was added for 20 min following the appropriate protocol. b) Cells were treated with 6 µM of $FINO_2$ and then the C11-BODIPY was added for 20 min following the appropriate protocol. These experiments verify there is no direct interaction between the redox probes and $FINO_2$ because at each time point $FINO_2$ was in contact with the probe for the same amount of time (20 min).



Supplementary Figure 10. Pretreatment of RS4;11 cells with 10 µM of arachidonic acid for 2 hours caused increased cell death in response to $FINO_2$. Percent dead cells indicate the Annexin V and 7AAD positive cell population.



Supplementary Figure 11. In contrast to etoposide, $FINO_2$ did not increase p53 protein expression even in cells expressing wild type p53 (RS4;11). (a) Expression of p53 is not increased by $FINO_2$ treatment (middle) as it does with etoposide (right). A representative figure from at least three independent experiments is shown. Trypan Blue staining was used to indicate cell death.



Supplementary Figure 12. Cell cycle analysis revealed no change in distribution upon treatment with $FINO_2$. Cell cycle distribution was observed by monitoring bromodeoxyuridine (BrdU) incorporation and propidium iodide (PI) staining[1]. Trypan Blue staining was used to indicate cell death. A representative figure from at least three independent experiments is shown.

Supplementary Discussion

The previously reported synthesis[2] was optimized starting with one gram of ketone **1**, which provided the protected bisperoxide **3** in 75% yield.[3] Carrying forward one gram of protected bisperoxide **3**, $FINO_2$ was obtained in 67% yield.[2] This synthesis involves four linear steps (five total) from commercially available starting material, only two of which required purification, with an overall yield of pure $FINO_2$ of about 50%. This route provided quantities surpassing the amount needed for biological testing and allows for the production of gram quantities of $FINO_2$.

To address potential stability concerns on the use of organic peroxides as drugs, $FINO_2$ was subjected to thermogravimetric analysis. This method measures weight loss of a compound as a function of increasing temperature, and therefore gives information about a compound's stability.[4] The precursor, bisperoxide **3**, and $FINO_2$ are both stable to over 150 ºC, suggesting that these compounds are more stable than might be anticipated for peroxide-containing structures. These temperatures are higher than would be required for the therapeutic use of these compounds and differ little in stability from artemisinin ($C_{15}H_{22}O_5$) and naproxen ($C_{14}H_{14}O_3$), which were chosen for comparison because they have similar numbers of carbon and oxygen atoms to $FINO_2$ ($C_{15}H_{28}O_3$). The thermal stability of $FINO_2$ was corroborated by NMR analysis of a sample that had been heated to 150 °C.

Materials and Methods

Cell Culture

RS4;11 cells [5] obtained from the American Type Culture Collection (ATCC) were grown in RPMI-1640 medium supplemented with 10% fetal bovine serum (FBS) and 1% penicillin-streptomycin under 5% CO_2 at 37 °C. BJ-5ta (BJ-hTERT) [6,7] cells and 293T [8] cells obtained from the American Type Culture Collection (ATCC) were grown in DMEM medium supplemented with 10% fetal bovine serum (FBS) and 1% penicillin-streptomycin under 5% CO_2 at 37 °C. BJ-ELR [9] cells were generously donated by the laboratory of William Hahn at the Dana-Farber Cancer Institute and maintained under the same conditions as the BJ-5ta cells.

Chemical Compounds

The synthesis of $FINO_2$ is described below. $FINO_2$ was prepared as a 10 mM stock solution in DMSO, aliquoted in single use portions, and frozen at –20 °C until the day of use. Serial dilutions of the 10 mM stock into water were performed for use at the indicated concentrations. All other compounds were obtained from Sigma-Aldrich unless otherwise indicated. Etoposide was prepared as a 4 mM stock solution in DMSO and serially diluted into water for use at the indicated concentrations.

Thermogravimetric Analysis (TGA)

The PerkinElmer Pyris™ 1 TGA instrument and software were used to measure the thermal stability of various compounds under an atmosphere of nitrogen. A sample of 1–3 mg was heated from 30 to 300 °C at a rate of 10 °C/ minute for solid compounds and 1 °C/ minute for oils. The weight was measured at one-second intervals. All data points were plotted and a line of best fit is

displayed. All compounds were measured in at least two independent experiments with little variability observed between readings.

Cell Viability Assay

BJ-hTERT and BJ-ELR cells were plated at 33,000 cells per mL in a white 96-well plate and the plate was returned to the cell culture incubator for 24 h. Either vehicle (DMSO in water) or indicated compound was added to achieve a 10-fold dilution by addition of 10 µL of stock solution to 100 µL of cells in media and the plate was returned to the cell culture incubator for the indicated times. The Promega CellTiter–Glo® Luminescence Assay was used as indicated in the manual, and luminescence was read on a FlexStation 3 Multi-Mode Microplate Reader. All percent viabilities reported are normalized to vehicle-treated cells. All experiments were performed in triplicate, and error bars reflect the standard deviation of one experiment. A representative graph of at least three independent experiments is shown.

Expression Level of p53

RS4;11 cells were plated at 666,000 cells per mL. Either vehicle (DMSO in water) or indicated compound was added to achieve a 10-fold dilution by addition of 100 µL of stock solution to 1 mL of cells in media and the plate was returned to the cell culture incubator for 24 h. Trypan Blue staining and counting using a hemocytometer determined the percentage of cell death in each sample. The cells were fixed and permeablized using the BD Cytofix/Cytoperm™ Fixation Permeabilization kit (554714). A fluorescein isothiocyanate (FITC)-conjugated p53 antibody or control antibody (FITC Mouse Anti-p53 Antibody Set, BD Pharmingen™) was incubated with the cells at a 1:50 dilution for 30 minutes on ice and in the dark. The samples were processed by

flow cytometry on the BD FACSCalibur cell analyzer. Analysis was conducted using FlowJo (Tree Star, Inc.). Representative results of at least three independent experiments are shown.

Annexin V-PE and 7-Aminoactinomycin D (7AAD) Apoptosis Assay

RS4;11 cells were plated at 666,000 cells per mL. Either vehicle (DMSO in water) or indicated compound was added to achieve a 10-fold dilution by addition of 50 µL of stock solution to 500 µL of cells in media and the plate was returned to the cell culture incubator for the indicated times. The BD Pharmagen™ PE Annexin V Apoptosis Detection Kit protocol was followed. The cells were pelleted and washed with phosphate-buffered saline (PBS) prior to staining with annexin V-PE and 7AAD for 20 minutes in the dark. The samples were transferred to flow cytometry tubes and were processed on the BD FACSCalibur cell analyzer. Analysis was conducted using FlowJo (Tree Star, Inc.). All experiments were performed in triplicate, and error bars reflect the standard deviation of one experiment. A representative graph of at least three independent experiments is shown.

Bcl-2 Overexpression

pCDH-puro-Bcl2 was a gift from Jialiang Wang at Vanderbilt University Medical Center (Addgene plasmid #46971) [10]. plenti-neo-GFP was a gift from the laboratory of Mark Phillips at New York University Langone Medical Center. The cDNA constructs were transfected into 293T cells along with helper plasmids using the calcium phosphate method [11,12] to produce replication-defective virus. The supernatant was collected 48 h after transfection and used to transduce RS4;11 cells supplemented with 8 mg/mL of Polybrene®. The virus-containing medium was replaced after 24 h. The Bcl-2 overexpressing cells and the GFP control cells were then selected for by treatment with 2 µg/mL of puromycin and 600 µg/mL of G418, respectively.

Overexpression of Bcl-2 was confirmed by Western blot at the time of plating each experiment (Fig. S6). About one million cells were lysed in 100 µL of 0.5% NP-40 lysis buffer also containing 50 mM of Tris-HCl, 150 mM of NaCl, 1 mM of PMSF, 1 mM of NaF, and protease inhibitor (GE Healthcare). The samples were incubated on ice for 15 min. The lysates were centrifuged at 12,000 rpm for 10 min at 4 °C. The protein was quantified, then subjected to electrophoresis on 12% SDS-Tris acrylamide gels and transferred to PVDF membranes. The membranes were incubated with 4% milk in PBST (0.1% tween) for 1 h followed by incubation with a 1:750 dilution of mouse monoclonal antibody to Bcl-2 (Santa Cruz, sc-7382) or a 1:5000 dilution of rabbit polyclonal antibody to β-Tubulin (Abcam, ab6046) for 2 h at room temperature. The membranes were washed with PBST then incubated with a 1:10,000 dilution of horseradish peroxidase (HRP)-conjugated secondary antibody to mouse or rabbit (GE Healthcare) for 1 h and developed using enhanced chemiluminescence (ECL; GE Healthcare). The response of GFP and Bcl-2 overexpressing cells to treatment with either etoposide or $FINO_2$ for 24 h was detected using the BD Pharmagen™ PE Annexin V Apoptosis Detection Kit, as described above.

Modulation of Cell Death with Chemical Compounds

RS4;11 cells were plated at 666,000 cells per mL. Either vehicle or indicated compound was added to achieve the final desired concentration (listed below) and the plate was returned to the cell culture incubator for at least 2 h. Either vehicle, $FINO_2$, or etoposide (as a control) were then added to the give the indicated concentration and the plate was returned to the cell culture incubator for 24 h. Cell death was detected using the BD Pharmagen™ PE Annexin V Apoptosis Detection Kit, as described above. Representative results of at least three independent experiments are shown. Compound concentrations: 2.4 µM of caspase inhibitor z-VAD-FMK

(BioVision); 20 μM of deferoxamine (DFO); 38 μM of ferric ammonium citrate (FAC); 500 nM of Ferrostatin; 200 nM of Liproxstatin (ChemDiv); 5 μM of nordihydroguaiaretic acid (NDGA); 100 μM of indomethacin; 10 μM of arachidonic acid

Cell Cycle Analysis

RS4;11 cells were plated at 666,000 cells per mL. Either vehicle (DMSO in water) or indicated compound was added to achieve a 100-fold dilution by addition of 30 μL of stock solution to 3 mL of cells in media and the plate was returned to the cell culture incubator for 24 h. Trypan Blue staining and counting using a hemocytometer determined the percentage of cell death in each sample. The cells were treated with 5 μg/mL of bromodeoxyuridine (BrdU) and the plate was returned to the cell culture incubator for 30 min. The cells were then fixed using 1 mL of cold 70% ethanol/ water solution and incubated overnight at 4 °C. After washing with PBS, the cells were resuspended in 200 μL of 0.4 mg/mL pepsin in 0.1 M HCl (aq) and incubated at room temperature for 20 min. The cells were centrifuged and resuspended in 0.5 mL of 2 M HCl and incubated at 37 °C for 10 min. The cells were centrifuged and resuspended in 1.5 mL of 0.05 M of sodium borate (pH 8.5) and incubated for 5 min at room temperature. After washing twice with 0.1% bovine serum albumin (BSA) in PBS, the cells were resuspended in 50 μL of a 1:50 dilution FITC-anti-BrdU (Rouche, 11202693001) in the dark at room temperature for 45 min. After washing with 0.1% BSA in PBS, the cells were resuspended in a solution containing 200 μL of 0.1% BSA in PBS, 2 μL of 100 mg/mL RNAse A, and 10 μL of 1 mg/mL propidium iodide (PI) and incubated for 1 h at 37 °C in the dark. After centrifugation, the cells were resuspended in 400 μL of 0.1% BSA in PBS and transferred to flow cytometry tubes. The samples were processed on the BD FACSCalibur cell analyzer. Analysis was conducted using

FlowJo (Tree Star, Inc.). Representative results of at least three independent experiments are shown.

CellROX® Green Reagent and BODIPY 581/591 C11

RS4;11 cells were plated at 666,000 cells per mL. Either vehicle (DMSO in water) or indicated compound was added to achieve a 10-fold dilution by addition of 50 µL of stock solution to 500 µL of cells in media and the plate was returned to the cell culture incubator for the indicated times. An aliquot of 1.1 µL of a 2.5 mM stock of either CellROX® Green Reagent (Life Technologies, C10444) or BODIPY 581/591 C11 dye (Life Technologies, D-3861) was added to the cells and the plate was returned to the cell culture incubator for 20 min. After washing the cells with PBS twice, the cells were transferred to flow cytometry tubes and processed on the BD FACSCalibur cell analyzer. Analysis was conducted using FlowJo (Tree Star, Inc.). Representative results of at least three independent experiments are shown.

BioVision MitoCapture™ Mitochondrial Apoptosis Detection Kit

RS4;11 cells were plated at 666,000 cells per mL. Either vehicle (DMSO in water) or indicated compound was added to achieve a 100-fold dilution by addition of 30 µL of stock solution to 3 mL of cells in media and the plate was returned to the cell culture incubator for 24 h. Trypan Blue staining and counting using a hemocytometer determined the percentage of cell death in each sample. The BioVision MitoCapture™ Mitochondrial Apoptosis Detection Kit protocol was followed using one million live cells per sample. Samples were processed on the BD FACSCalibur cell analyzer. Analysis was conducted using FlowJo (Tree Star, Inc.). Representative results of at least three independent experiments are shown.

Caspase Western Blots

Trypan Blue staining and counting using a hemocytometer determined the percentage of cell death in each sample. About one million cells were lysed in 100 µL of 0.5% NP-40 lysis buffer also containing 50 of mM Tris-HCl, 150 of mM NaCl, 1 mM of PMSF, 1 mM of NaF, and protease inhibitor (GE Healthcare). The samples were incubated on ice for 15 min. The lysates were centrifuged at 12,000 rpm for 10 min at 4 °C. The protein was quantified, then subjected to electrophoresis on 9% SDS-Tris acrylamide gels and transferred to PVDF membranes. The membranes were incubated with 4% milk in PBST (0.1% tween) for 1 h, followed by incubation with a 1:500 dilution of rabbit polyclonal antibody to cleaved caspase-7 (Cell Signaling, 9491), cleaved caspase-6 (Cell Signaling, 9761), cleaved caspase-3 (Cell Signaling, 9661), or 1:5000 dilution of rabbit polyclonal antibody to β-Tubulin (Abcam, ab6046) overnight at 4 °C. The membranes were washed with PBST then incubated with a 1:10,000 dilution of horseradish peroxidase (HRP)-conjugated secondary antibody to mouse or rabbit (GE Healthcare) for 1 h and developed using enhanced chemiluminescence (ECL; GE Healthcare). Representative blots of three independent experiments are shown (Supplementary Figure 6).

Electron Microscopy

RS4;11 cells were plated at 666,000 cells per mL. Either vehicle (DMSO in water) or $FINO_2$ was added to achieve a 10-fold dilution by addition of 800 µL of stock solution to 8 mL of cells in media and the plate was returned to the cell culture incubator for nine, ten, eleven, twelve, or thirteen hours. Trypan Blue staining and counting using a hemocytometer determined the percentage of cell death in each sample. The eleven h time point exhibiting 22% cell death was chosen for analysis. Cells were submitted to the Microscopy Core at New York University

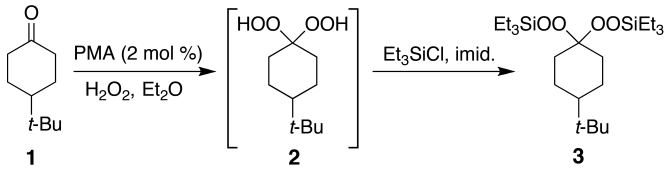
Langone Medical Center for processing and acquisition of transmission electron microscopy images.

General Synthesis Procedures

Using Bruker AV-400, AV-500, or AVIII-600 spectrometers at ambient temperature, ^{1}H NMR spectra were recorded at 400, 500, or 600 MHz, respectively and ^{13}C NMR spectra were recorded at 100, 125, or 150 MHz, respectively. Chemical shifts are reported in ppm on the δ scale, referenced to internal standard tetramethylsilane (δ 0.00) or residual solvent (^{1}H NMR: δ 7.26 for $CDCl_3$ or 7.16 for C_6D_6; ^{13}C NMR: δ 77.2 for $CDCl_3$ or 128.1 for C_6D_6).[13] Infrared (IR) spectra were obtained by a Thermo Nicolet AVATAR 360 Fourier Transform Infrared Spectrometer using attenuated total reflectance (ATR). High-resolution mass spectra (HRMS) were aquired on an Agilent 6224 Accurate-Mass time-of-flight spectrometer using peak matching. Analytical thin layer chromatography was performed with Silicycle silica gel 60 Å F_{254} plates. Flash chromatography was perfomed using the indicated solvent system on Silicycle silica gel (SiO_2)60 (230-400 mesh). Tetrahydrofuran (THF), methylene chloride (CH_2Cl_2), diethyl ether (Et_2O), ethyl acetate (EtOAc) and *N*,*N*-dimethylformamide (DMF) were dried by filtration through alumina.[14] All dry reactions were run under an atmosphere of either argon or nitrogen in flame-dried glassware.

Caution: In general, hydrogen peroxide and organic peroxides should be handled with care. Avoid exposure to strong heat, light, mechanical shock, oxidizable organic materials, and metals. All reactions should be carried out behind a blast shield.[15]

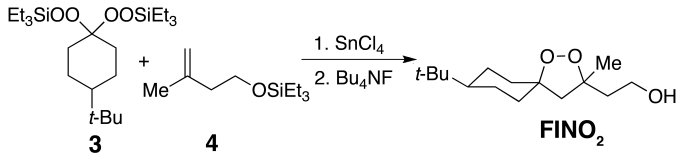
Synthesis of $FINO_2$



Silylated Peroxyketal 3. 1,1-Dihydroperoxide **2** was prepared following a literature procedure.[3] Ethereal hydrogen peroxide was prepared (behind a blast shield) by addition of sodium chloride (NaCl, until the solution becomes saturated) to H_2O_2 (30% aqueous solution, 90 mL). Diethyl ether (Et_2O, 40 mL) was placed in a separatory funnel and it was washed with the salt-saturated aqueous peroxide solution (15 mL x 6). The ethereal layer was dried over magnesium sulfate ($MgSO_4$) and filtered directly into a flame-dried round-bottom flask. Ketone **1** (1.00 g, 6.49 mmol) and phosphomolybdic acid hydrate (PMA, 0.237 g, 0.120 mmol) were added to the ethereal peroxide solution. After 3 h at ambient temperature, diethyl ether (Et_2O, 25 mL) and H_2O (50 mL) were added. The mixture was added to Et_2O (25 mL) and the layers were separated. The aqueous layer was extracted with Et_2O (3 x 40 mL). The organic layers were combined, dried over $MgSO_4$, filtered, and concentrated under a stream of nitrogen. The unpurified product **2** exhibited spectroscopic properties consistent with those reported[3]: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.51 (s, 1H), 7.70 (s, 1H), 2.32–2.28 (m, 2H), 1.73–1.71 (m, 2H), 1.48–1.41 (m, 2H), 1.29–1.21 (m, 2H), 1.09–1.03 (m, 1H), 0.87 (s, 9H).

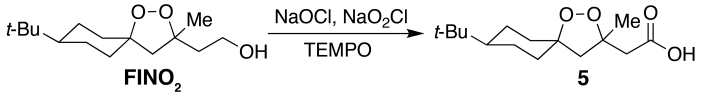
The unpurified peroxide **2** was subjected to protection conditions[2] by immediate dissolution into anhydrous THF (10 mL). Imidazole (1.33 g, 19.5 mmol) was added followed by drop-wise addition over 30 min of freshly distilled triethylchlorosilane (3.30 mL, 19.5 mmol). After 72 h at ambient temperature, a saturated aqueous solution of sodium bicarbonate (35 mL) was added to the reaction mixture. The reaction mixture was then added to hexanes (50 mL) and

H_2O (15 mL). The layers were separated and the aqueous layer was extracted with hexanes (50 mL). The organic layers were combined and washed with a saturated aqueous solution of sodium chloride (50 mL). The layers were separated and the aqueous layer was extracted with hexanes (3 x 75 mL). The organic layers were combined, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (100% hexanes) on Davisil® grade silica afforded triethylsilylperoxyketal **3** as a clear oil (2.09 g, 75%), whose spectroscopic data matched those reported[2]: ^{1}H NMR (400 MHz, C_6D_6) δ 2.61–2.59 (m, 2H), 1.57–1.56 (m, 2H), 1.40–1.38 (m, 4H), 1.15 (t, J = 8.0 Hz, 9H), 1.11 (t, J = 8.0 Hz, 9H), 0.87 (m, 1H), 0.86 (q, J = 8.0 Hz, 6H), 0.82 (s, 9H), 0.81 (q, J = 8.0 Hz, 6H); ^{13}C NMR (100 MHz, C_6D_6) δ 109.7, 47.8, 32.4, 31.1, 27.8, 24.1, 7.23, 7.22, 4.51, 4.47.



$FINO_2$. The synthesis of **$FINO_2$** followed a general procedure reported previously.[2] To a mixture of triethylsilylperoxyketal **3** (1.00 g, 2.31 mmol), triethyl(3-methylbut-3-enyloxy)silane **4** [16] (1.39 g, 6.93 mmol), and CH_2Cl_2 (14.4 mL) was added $SnCl_4$ (4.62 mL) dropwise over 30 min at –78 °C. The reaction mixture was stirred at –10 °C for 12 h, then was warmed to –2 °C. Cold H_2O (0 °C, 10 mL) was added to the reaction mixture. Potassium sodium tartrate tetrahydrate was added until the solution was saturated, and the mixture was stirred for 30 min. The reaction mixture was partitioned between Et_2O (70 mL) and a saturated aqueous solution of sodium chloride (70 mL). The layers were separated and the aqueous layer was extracted with Et_2O (3 x 75 mL). The organic layers were combined, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The unpurified products were subjected immediately to deprotection

conditions[17] by dissolution into anhydrous THF (23.0 mL) followed by addition of tetrabutylammonium fluoride (1 M solution in THF, 3.47 mL, 3 mmol). After 17 h at ambient temperature, the reaction mixture was partitioned between a saturated aqueous solution of sodium chloride (60 mL) and Et_2O (60 mL). The layers were separated and the organic layer was washed with a saturated aqueous solution of sodium chloride (60 mL). The aqueous layers were combined and extracted with Et_2O (3 x 75 mL). The organic extracts were combined, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (12–25% EtOAc in hexanes) afforded **$FINO_2$** as a white solid (0.396 g, 67%), whose spectroscopic data matched those reported[2]: mp 79–81 °C, lit 69–71 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.81–3.78 (m, 2H), 2.24–2.22 (d, J = 12.0 Hz, 1H), 2.12–2.09 (m, 3H), 2.05–2.00 (m, 2H), 1.83–1.80 (m, 1H), 1.63–1.60 (m, 2H), 1.48–1.46 (m, 1H), 1.39–1.27 (m, 3H), 1.38 (s, 3H), 0.98–0.94 (m, 1H), 0.84 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 85.5, 84.9, 59.5, 57.7, 47.2, 41.6, 36.2, 35.8, 32.5, 27.6, 24.5, 24.0, 23.8.

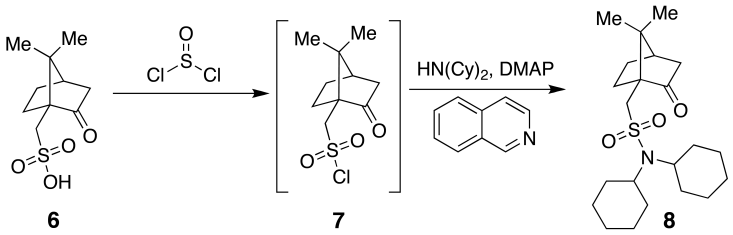


$FINO_2$ **5**

1,2-Dioxolane 5. A slightly modified literature procedure for oxidation of alcohols to carboxylic acids[18] was followed to afford **5**. A solution of **$FINO_2$** (0.18 g, 0.70 mmol), 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO, 0.0077 mg, 0.049 mmol), CH_3CN (3.5 mL), and aqueous phosphate buffer (pH 6.7, 2.6 mL) was heated to 35 °C. Sodium chlorite (2.0 M aqueous solution, 140 µL) and sodium hypochlorite (0.045 M aqueous solution, 62 µL) were added simultaneously to the reaction mixture. After 30 min, additional sodium chlorite (2.0 M aqueous solution, 560 µL) and sodium hypochlorite (0.045 M aqueous solution, 248 µL) were added. After 24 hours, more sodium chlorite (2.0 M aqueous solution, 180 µL), sodium hypochlorite (0.045 M aqueous

solution, 25 μL) and TEMPO (0.0015 mg, 9.6 μmol) were added. After an additional 24 hours, the temperature was increased to 43 °C. After 4 h at 43 °C, the reaction mixture was allowed to cool to room temperature and H_2O (10 mL) was added. The reaction mixture was added to a mixture of H_2O (20 mL), an aqueous solution of saturated sodium chloride (5 mL), and CH_2Cl_2 (30 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 30 mL). Purification by flash column chromatography (20% EtOAc/hexanes) on silica gel that had been pretreated with acetic acid (0.5% acetic acid/hexanes) afforded 1,2-dioxolane **5** as a white solid (0.17 g, 91%) whose spectroscopic data matched those reported[2]: mp 134–137 °C, lit 113–114 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.78–2.72 (dd, J = 22.8, 15.0 Hz, 2H), 2.41–2.39 (d, J = 12.6 Hz, 1H), 2.15–2.12 (m, 2H), 1.96–1.93 (m, 1H), 1.62–1.60 (m, 2H), 1.57–1.52 (td, 13.8, 4.2 Hz, 1H), 1.47 (s, 3H), 1.37–1.32 (m, 2H), 1.25–1.21 (m, 1H), 0.98–0.94 (m, 1H), 0.84 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 176.5, 84.9, 83.1, 56.5, 46.9, 44.0, 35.9, 35.6, 32.3, 27.4, 23.9, 23.7, 23.4.

Preparation of Enantiomers of $FINO_2$ Using a Chiral Auxiliary

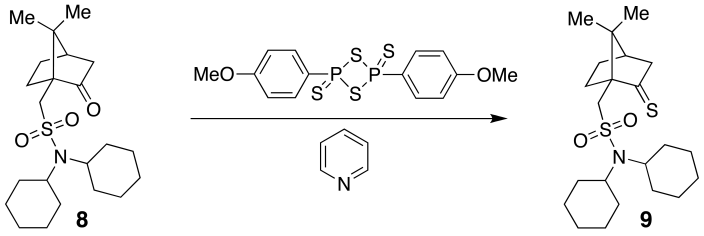


Sulfonamide 8. Sulfonyl chloride **7** was prepared following a literature procedure.[19] Freshly distilled thionyl chloride was added by syringe to (1*S*)-(+)-10-Camphorsulfonic acid that had been recrystallized from ethyl acetate (EtOAc). The reaction mixture was heated to 110 °C for 3 h. After the reaction mixture was cooled to room temperature, 5 mL of dry toluene was added, and the mixture was concentrated under reduced pressure. An additional 5 mL of dry toluene was

added, and the mixture was concentrated again. The spectroscopic data of sulfonyl chloride **7** matched the data reported[19]: ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.32–4.30 (d, *J* = 14.6 Hz, 1H), 3.74–3.71 (d, *J* = 14.6 Hz, 1H), 2.50–2.42 (m, 2H), 2.17–2.16 (m, 1H), 2.12–2.07 (m, 1H), 2.01–1.98 (d, *J* = 18.7 Hz, 1H), 1.80–1.75 (m, 1H), 1.53–1.47 (m, 1H), 1.15 (s, 3H), 0.93 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 212.8, 64.3, 59.7, 48.2, 42.8, 42.3, 26.9, 25.3, 19.8, 19.7.

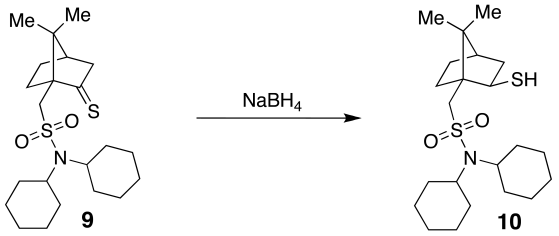
The unpurified sulfonyl chloride **7** was immediately subjected to previously described conditions to form sulfonamide **8**.[20] The sulfonyl chloride was dissolved in *N*,*N*-dimethylformamide (DMF, 1 M, 25 mL) and cooled to 0 °C. In another flame-dried flask, 4-(dimethylamino)pyridine (0.608 g, 4.98 mmol), isoquinoline (5.77 mL, 49.8 mmol), and dicyclohexylamine (9.9 mL, 49.8 mmol) were dissolved in DMF (25 mL) and cooled to 0 °C. The sulfonyl chloride solution was added by syringe pump over 2 h to the solution of amines. After 4 h of stirring at 0 °C, 50 mL of 10% citric acid in water were added. The resulting precipitate was filtered and washed with CH_2Cl_2 until the precipitate was white in color. The precipitate was dissolved in 50 mL of CH_2Cl_2 and washed with water (50 mL). The aqueous layer was extracted with CH_2Cl_2 (3 x 50 mL). The organic extracts were combined, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (12.5% EtOAc in hexanes) afforded sulfonamide **8** (5.64 g, 57%), whose spectroscopic data matched those reported[20]: mp 130–132 °C, lit 134–135 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.33–3.30 (d, *J* = 14.5 Hz, 1H), 2.81–2.78 (d, *J* = 14.5 Hz, 1H), 2.62–2.58 (m, 1H), 2.39–2.35 (m, 1H), 2.09–2.07 (m, 1H), 2.05–2.01 (m, 1H), 1.93 (s, 1H), 1.90 (s, 1H), 1.81–1.78 (m, 12H), 1.63–1.59 (m, 3H), 1.42–1.38 (m, 1H), 1.37–1.30 (m, 4H), 1.17 (s, 3H), 1.17–1.13 (m, 3H), 0.89 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 215.5, 59.0, 57.6, 52.2, 47.4, 42.9,

42.5, 32.9, 32.5, 26.8, 26.44, 26.43, 25.3, 25.2, 20.3, 19.8; HRMS (TOF MS ES+) *m/z* calcd for $C_{22}H_{37}NNaO_3S$ $(M + Na)^+$ 418.2386, found 418.2396; $[\alpha]_D^{23}$ +29 (*c* 0.41, $CHCl_3$).

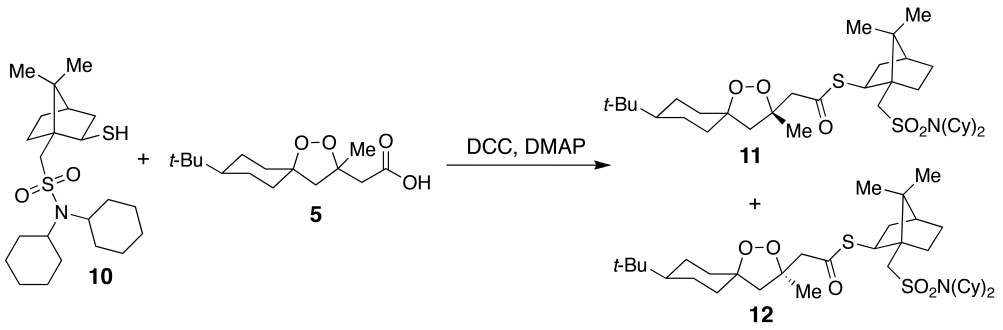


Thione 9. Thione **9** was prepared following a literature procedure.[21] Lawesson's reagent was recrystallized from toluene, and pyridine was dried over molecular sieves prior to use. A solution of sulfonamide **8** (1.22 g, 3.08 mmol), Lawesson's reagent (1.51 g, 3.72 mmol), and toluene (4.85 mL) were heated to 130 °C. After the solution started to reflux, pyridine (126 μL, 1.57 mmol) was added by syringe. After 19 h, aqueous sodium bicarbonate (5 mL) was added to the reaction mixture. The reaction mixture was partitioned between aqueous sodium bicarbonate (40 mL) and Et_2O (40 mL). The organic layer was washed with brine (40 mL). The combined aqueous layers were combined and extracted with Et_2O (3 **x** 50 mL). The organic extracts were combined, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (7% EtOAc in hexanes) afforded thione **9** as an orange solid (0.478 g, 38%) whose spectroscopic data matched those reported[21]: mp 155–157 °C, lit 145–150 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.91–3.87 (d, *J* = 14.6 Hz, 1H), 3.35–3.32 (m, 2H), 2.92–2.89 (d, *J* = 14.6 Hz, 1H), 2.81–2.67 (m, 2H), 2.50–2.45 (d, *J* = 20.8 Hz, 1H), 2.15–2.13 (m, 1H), 2.10–2.08 (m, 1H), 1.85–1.75 (m, 12H), 1.65–1.61 (m, 2H), 1.55–1.42 (m, 2H), 1.35–1.30 (m, 3H), 1.24 (s, 3H), 1.17–1.08 (m, 2H), 1.07–0.95 (m, 1H), 0.85 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 265.9, 69.9, 57.6, 54.91, 54.88, 49.8, 45.0, 33.1, 32.5, 29.7, 27.0, 26.5, 25.2, 20.5, 19.8;

HRMS (TOF MS ES+) *m/z* calcd for $C_{22}H_{37}NNaO_3S$ $(M + Na)^+$ 434.2163, found 434.2158; $[\alpha]_D^{23}$ +147 (*c* 1.03, $CHCl_3$).



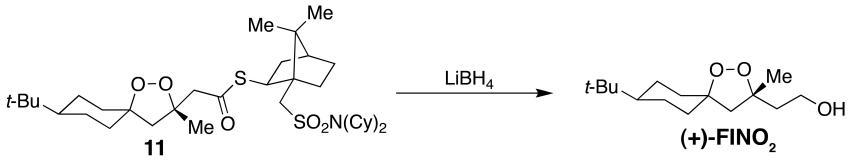
Thiol 10. Thiol **10** was prepared following a literature procedure.[21] To a cold (0 °C) solution of thione **9** (0.150 g, 0.364 mmol), tetrahydrofuran (1.79 mL, 0.204 M), and isopropanol (1.79 mL, 0.204 M) was added sodium borohydride (0.138 g, 3.64 mmol). The reaction mixture was stirred at 0 °C for 20 minutes before warming to room temperature for an additional 30 minutes. Excess sodium borohydride was quenched by drop-wise addition of 1 M HCl (aq) until bubbling stopped. The reaction mixture was partitioned between brine (30 mL) and Et_2O (35 mL). The aqueous layer was extracted with Et_2O (3 **x** 40 mL). The organic extracts were combined, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (4% EtOAc in hexanes) afforded thiol **10** as a white solid (0.1417 g, 94%) whose spectroscopic data matched those reported[21]: mp 122–125 °C, lit 105–110 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.74–3.71 (d, *J* = 13.4 Hz, 1H), 3.47–3.43 (m, 1H), 3.33–3.31 (m, 2H), 2.73–2.71 (d, *J* = 13.4 Hz, 1H), 2.57–2.56 (d, *J* = 7.5 Hz, 1H), 2.12–2.07 (m, 1H), 2.01–1.97 (m, 1H), 1.81–1.74 (m, 12H), 1.63–1.58 (m, 4H), 1.32–1.27 (m, 6H), 1.13–1.10 (m, 3H), 0.96 (s, 3H), 0.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 57.6, 55.5, 50.0, 49.7, 45.3, 44.3, 40.3, 33.6, 33.4, 32.4, 27.3, 26.6, 25.3, 21.1, 20.1; HRMS (TOF MS ES+) *m/z* calcd for $C_{22}H_{40}NO_2S_2$ $(M + H)^+$ 414.2495, found 414.2491; $[\alpha]_D^{23}$ +27 (*c* 0.51, $CHCl_3$).



1,2-Dioxolanes 11 and 12. To a solution of 1,2-dioxolane **5** (0.047 g, 0.172 mmol) and CH_2Cl_2 (866 μL, 0.2 M) were added 4-(dimethylamino)pyridine (DMAP, 0.005 g, 0.043 mmol) and *N*,*N*′-dicyclohexylcarbodiimide (DCC, 0.043 g, 0.021 mmol). After 5 min, thiol **10** (0.108 g, 0.260 mmol) was added to the solution. After 90 min, the reaction mixture was diluted with CH_2Cl_2 (10 mL), filtered through celite, and concentrated under reduced pressure. Purification by flash column chromatography (7% EtOAc in hexanes) afforded a mixture of 1,2-dioxolanes **11** and **12** as an oil (0.093 g, 80%). Further purification by flash column chromatography (15% Et_2O in hexanes) afforded 1,2-dioxolane **11** (0.026 g) as the first diastereomer to elute: ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.05–4.03 (dd, *J* = 9.3, 5.2 Hz, 1H), 3.27–3.22 (m, 2H), 3.21–3.19 (d, *J* = 13.7 Hz, 1H), 3.00–2.98 (d, *J* = 14.8 Hz, 1H), 2.90–2.88 (d, *J* = 14.8 Hz, 1H), 2.73–2.71 (d, *J* = 13.7 Hz, 1H), 2.57–2.55 (d, *J* = 12.6 Hz, 1H), 2.18–2.09 (m, 4H), 1.94–1.91 (m, 1H), 1.84–1.75 (m, 17H), 1.64–1.57 (m, 4H), 1.54–1.49 (m, 1H), 1.43 (s, 1H), 1.40 (s, 2H), 1.34–1.20 (m, 7H), 1.14–1.07 (m, 2H), 0.97– 0.93 (m, 1H), 0.89 (s, 3H), 0.88 (s, 3H), 0.83 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$, the multiplicity of resolvable carbon peaks was determined using HSQC) δ 194.2 (C), 85.0 (C), 83.6 (C), 57.4 (CH), 56.7, 55.6 (CH_2), 52.9 (CH_2), 50.6 (C), 49.6 (C), 48.0 (CH), 47.0, 45.5, 41.0, 36.0. 35.9, 33.8, 32.43, 32.37, 30.3, 27.5 (CH_3), 27.3, 26.6, 25.3, 23.9, 23.7, 23.6, 20.6 (CH_3), 20.2 (CH_3); IR (ATR) 2939, 2859, 1684, 1323, 1143 cm^{-1}; HRMS (TOF MS

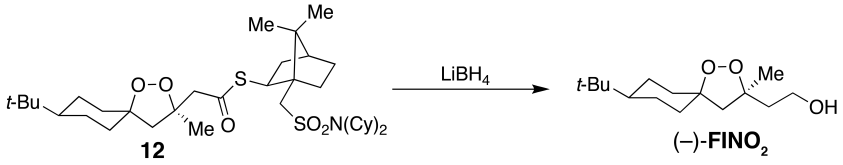
ES+) *m/z* calcd for $C_{37}H_{64}NO_5S_2$ $(M + H)^+$ 666.4220, found 666.4226; $[\alpha]_D^{23}$ +42 (*c* 0.86, $CHCl_3$).

1,2-Dioxolane **12** (0.0276 g) was the second product to elute: ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.04–4.01 (dd, *J* = 9.2, 5.2 Hz, 1H), 3.27–3.24 (m, 2H), 3.18–3.15 (d, *J* = 13.7 Hz, 1H), 3.00–2.98 (d, *J* = 14.5 Hz, 1H), 2.86–2.84 (d, *J* = 14.5 Hz, 1H), 2.72–2.69 (d, *J* = 13.7 Hz, 1H), 2.48–2.46 (d, *J* = 12.5 Hz, 1H), 2.19–2.07 (m, 4H), 1.95–1.93 (m, 1H), 1.83–1.74 (m, 17H), 1.63–1.58 (m, 4H), 1.55–1.49 (m, 1H), 1.46 (s, 2H) 1.43 (s, 1H), 1.33–1.21 (m, 7H), 1.13–1.06 (m, 2H), 0.98–0.93 (m, 1H), 0.90 (s, 3H), 0.89 (s, 3H), 0.83 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$, the multiplicity of resolvable carbon peaks was determined using HSQC) δ 194.3 (C), 84.9 (C), 83.8 (C), 57.3 (CH), 56.2, 55.6 (CH_2), 52.9 (CH_2), 50.4 (C), 49.6 (C), 48.1 (CH), 47.0, 45.5, 41.1, 36.0, 35.8, 33.9, 33.3, 32.4, 32.3, 30.3, 27.5 (CH_3), 27.4, 26.5, 26.5, 25.2, 24.2, 23.9, 23.6, 20.6 (CH_3), 20.2 (CH_3); IR (ATR) 2938, 2856, 1688, 1322, 1142 cm^{-1}; HRMS (TOF MS ES+) *m/z* calcd for $C_{37}H_{64}NO_5S_2$ $(M + H)^+$ 666.4220, found 666.4222; $[\alpha]_D^{23}$ +15 (*c* 1.2, $CHCl_3$). Both **11** and **12** were oils when concentrated under reduced pressure; however, slow evaporation at 0 °C of a solution of **11** in hexanes provided crystalline material of sufficient quality for X-ray crystallography (see below).



(+)-**FINO$_2$**. Conditions to reduce an ethyl ester in the presence of a 1,2-dioxane[22] were slightly modified to provide (+)-**FINO$_2$**. To a cooled (0 °C) solution of 1,2-dioxolane **11** (0.090 g, 0.135 mmol) in Et_2O (2.7 mL, 0.05 M) was added lithium borohydride ($LiBH_4$, 0.009 g, 0.406 mmol). After 20 minutes at 0 °C, the reaction mixture was allowed to warm to room temperature. After

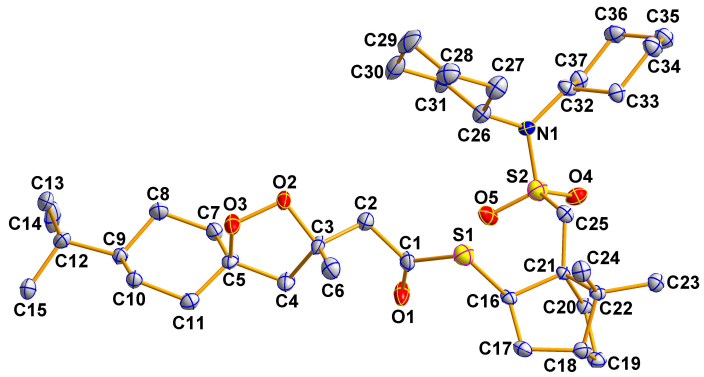
24 h, the excess $LiBH_4$ was quenched at 0 °C with saturated aqueous ammonium chloride (1 mL). The reaction mixture was partitioned between water (15 mL) and EtOAc (15 mL). The organic layer was washed with brine (20 mL). The aqueous layers were combined and extracted with Et_2O (3 x 40 mL). The organic extracts were combined, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (12–20% EtOAc in hexanes) afforded (+)-**FINO$_2$** as a white solid (0.022 g, 62%) whose spectroscopic data matched those reported: $[\alpha]_D^{23}$ +32 (*c* 0.60, $CHCl_3$).



(–)-**FINO$_2$**. Conditions to reduce an ethyl ester in the presence of a 1,2-dioxane[22] were slightly modified to provide (–)-**FINO$_2$**. To a cooled (0 °C) solution of 1,2-dioxolane **12** (0.090 g, 0.135 mmol) in Et_2O (2.7 mL, 0.05 M) was added lithium borohydride ($LiBH_4$, 0.009 g, 0.406 mmol). After 15 minutes at 0 °C, the reaction mixture was allowed to warm to room temperature. After 24 h, the excess $LiBH_4$ was quenched at 0 °C with saturated aqueous ammonium chloride (1 mL). The reaction mixture was partitioned between water (15 mL) and EtOAc (15 mL). The organic layer was washed with brine (20 mL). The aqueous layers were combined and extracted with Et_2O (3 x 40 mL). The organic extracts were combined, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by flash column chromatography (12–30% EtOAc in hexanes) afforded (–)-**FINO$_2$** as a white solid (0.018 g, 51%) whose spectroscopic data matched those reported: with the following optical rotation $[\alpha]_D^{23}$ –38 (*c* 0.62, $CHCl_3$).

X-ray Crystallographic Data

X-ray Data Collection, Structure Solution and Refinement for 1,2-Dioxolane **11**.



The molecular structure of dioxolane **11**. The H atoms are omitted for clarity.

A colorless needle-like crystal with the size of 0.02 · 0.04 · 0.54 mm^3 was selected for geometry and intensity data collection with a Bruker SMART APEXII CCD area detector on a D8 goniometer at 100 K. The temperature during the data collection was controlled with an Oxford Cryosystems Series 700+ instrument. Preliminary lattice parameters and orientation matrices were obtained from three sets of frames. Data were collected using graphite-monochromated and 0.5 mm-MonoCap-collimated Mo-Kα radiation (λ = 0.71073 Å) with the ω scan method [1]. Data were processed with the INTEGRATE program of the APEX2 software [1] for reduction and cell refinement. Multi-scan absorption corrections were applied by using the SCALE program for the area detector. The structure was solved by the direct method and refined on F^2 (SHELXTL) [2]. Non-hydrogen atoms were refined with anisotropic displacement parameters, and hydrogen atoms on carbons were placed in idealized positions (C-H = 0.98-1.00 Å) and included as riding with U_{iso}(H) = 1.2 or 1.5 U_{eq}(non-H).

References.

[1] APEX2 (version 2012.10). *Program for Bruker CCD X-ray Diffractometer Control*, Bruker AXS Inc., Madison, WI, 2012.

[2] G. M. Sheldrick, SHELXTL, version 6.14. *Program for solution and refinement of crystal structures*, Universität Göttingen, Germany, 2009.

Sample and Crystal Data

Chemical formula: $C_{37}H_{63}NO_5S_2$
Formula weight: 666.03
Temperature: 100(2) K
Wavelength: 0.71073 Å
Crystal size: 0.020 x 0.040 x 0.540 mm
Crystal habit: colorless needle
Crystal system: orthorhombic
Space group: P 21 21 21
Unit cell dimensions:
a = 6.5242(7) Å; α = 90°
b = 18.975(2) Å; β = 90°
c = 29.829(3) Å; γ = 90°
Volume: 3692.7(7) $Å^3$
Z: 4
Density (calculated): 1.198 g/cm^3
Absorption coefficient: 0.185 mm^{-1}
F(000): 1456

Data Collection and Structure Refinement

Diffractometer: Bruker APEX-II CCD
Radiation source: sealed tube, MoKα
Theta range for data collection: 1.27 to 26.37°
Index ranges: -7<=h<=8, -23<=k<=23, -36<=l<=37
Reflections collected: 30801
Independent reflections: 7524 [R(int) = 0.0877]
Absorption correction: multi-scan
Max. and min. transmission: 0.9963 and 0.9065
Structure solution technique: direct methods
Structure solution program: SHELXS-97 (Sheldrick, 2008)
Refinement method: Full-matrix least-squares on F^2
Refinement program: SHELXL-97 (Sheldrick, 2008)
Function minimized: $\Sigma\, w(F_o^2 - F_c^2)^2$

Data / restraints / parameters: 7524 / 0 / 413
Goodness-of-fit on F2 : 1.036
Δ/σmax: 0.001
Final R indices: 5683 data; I>2σ(I); R1 = 0.0503, wR2 = 0.1008
all data: R1 = 0.0792, wR2 = 0.1117
Weighting scheme: $w=1/[\sigma^2(F_o^2)+(0.0489P)^2+0.0000P]$
where $P=(F_o^2+2F_c^2)/3$
Absolute structure parameter: 0.0(1)
Largest diff. peak and hole: 0.226 and -0.371 eÅ^{-3}
R.M.S. deviation from mean: 0.056 eÅ^{-3a}

Atomic coordinates and equivalent isotropic atomic displacement parameters (Å^2):

U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x/a	y/b	z/c	U(eq)
S1	0.31155(12)	0.60129(4)	0.47390(3)	0.02229(19)
S2	0.40087(12)	0.53423(4)	0.35323(3)	0.01863(17)
O1	0.7114(3)	0.58204(13)	0.48444(8)	0.0345(6)
O2	0.5158(3)	0.42777(12)	0.58384(7)	0.0290(6)
O3	0.6349(3)	0.42529(11)	0.62540(7)	0.0283(5)
O4	0.4609(3)	0.55196(11)	0.30823(7)	0.0249(5)
O5	0.5565(3)	0.53002(11)	0.38713(7)	0.0268(5)
N1	0.2795(4)	0.45925(12)	0.35180(8)	0.0183(5)
C1	0.5418(5)	0.55989(17)	0.49172(10)	0.0231(7)
C2	0.5042(5)	0.49223(16)	0.51776(10)	0.0241(7)
C3	0.5558(5)	0.49850(16)	0.56717(10)	0.0212(7)
C4	0.7843(5)	0.50910(17)	0.57750(11)	0.0247(8)
C5	0.8364(4)	0.45085(15)	0.61134(10)	0.0206(7)
C6	0.4190(5)	0.55116(17)	0.59070(10)	0.0272(8)
C7	0.9580(5)	0.39065(17)	0.59032(10)	0.0238(7)
C8	0.0158(5)	0.33314(16)	0.62365(10)	0.0256(8)
C9	0.1332(5)	0.36390(15)	0.66372(9)	0.0183(7)
C10	0.9933(5)	0.41801(15)	0.68674(9)	0.0201(7)
C11	0.9380(5)	0.47723(16)	0.65420(10)	0.0221(7)
C12	0.2227(5)	0.30788(15)	0.69618(10)	0.0230(7)
C13	0.0560(6)	0.26720(18)	0.72064(11)	0.0339(9)
C14	0.3594(7)	0.25702(19)	0.66968(12)	0.0424(11)
C15	0.3588(5)	0.34437(17)	0.73091(11)	0.0267(8)
C16	0.4138(5)	0.66600(15)	0.43471(9)	0.0166(6)
C17	0.3983(5)	0.74374(16)	0.45087(10)	0.0222(7)
C18	0.3054(5)	0.78138(16)	0.41031(10)	0.0213(7)
C19	0.4670(5)	0.78186(16)	0.37291(10)	0.0216(7)
C20	0.4670(4)	0.70359(15)	0.35675(10)	0.0182(7)
C21	0.3067(4)	0.66801(14)	0.38786(9)	0.0141(6)

C22	0.1450(4)	0.72793(15)	0.39327(9)	0.0164(6)
C23	0.0418(5)	0.75050(16)	0.34924(10)	0.0206(7)
C24	0.9751(5)	0.71122(17)	0.42706(10)	0.0229(7)
C25	0.2174(4)	0.59891(15)	0.37085(10)	0.0174(6)
C26	0.2351(5)	0.42539(16)	0.39574(10)	0.0228(7)
C27	0.0075(5)	0.42234(18)	0.40725(11)	0.0292(8)
C28	0.9723(6)	0.38755(18)	0.45286(11)	0.0330(9)
C29	0.0748(7)	0.31544(19)	0.45584(12)	0.0424(10)
C30	0.3004(6)	0.31891(19)	0.44398(11)	0.0379(9)
C31	0.3366(6)	0.35353(16)	0.39867(10)	0.0272(8)
C32	0.1660(5)	0.43423(16)	0.31161(10)	0.0211(7)
C33	0.9914(5)	0.48193(16)	0.29678(10)	0.0213(7)
C34	0.8706(5)	0.44820(17)	0.25901(10)	0.0267(8)
C35	0.0042(5)	0.42609(18)	0.22041(11)	0.0285(8)
C36	0.1800(5)	0.37962(16)	0.23494(10)	0.0255(7)
C37	0.3042(5)	0.41394(17)	0.27299(10)	0.0247(7)

Bond lengths (Å):

S1-C1	1.776(3)	S1-C16	1.822(3)
S2-O5	1.435(2)	S2-O4	1.438(2)
S2-N1	1.629 (2)	S2-C25	1.793(3)
O1-C1	1.204(4)	O2-C3	1.455(4)
O2-O3	1.464(3)	O3-C5	1.462(3)
N1-C32	1.487(4)	N1-C26	1.488(4)
C1-C2	1.521(4)	C2-C3	1.516(4)
C2-H2A	0.99	C2-H2B	0.99
C3-C6	1.512(4)	C3-C4	1.535(4)
C4-C5	1.535(4)	C4-H4A	0.99
C4-H4B	0.99	C5-C11	1.525(4)
C5-C7	1.526(4)	C6-H6A	0.98
C6-H6B	0.98	C6-H6C	0.98
C7-C8	1.523(4)	C7-H7A	0.99
C7-H7B	0.99	C8-C9	1.535(4)
C8-H8A	0.99	C8-H8B	0.99
C9-C10	1.536(4)	C9-C12	1.552(4)
C9-H9	1	C10-C11	1.528(4)
C10-H10A	0.99	C10-H10B	0.99
C11-H11A	0.99	C11-H11B	0.99
C12-C13	1.520(5)	C12-C15	1.530(4)
C12-C14	1.533(5)	C13-H13A	0.98
C13-H13B	0.98	C13-H13C	0.98
C14-H14A	0.98	C14-H14B	0.98
C14-H14C	0.98	C15-H15A	0.98
C15-H15B	0.98	C15-H15C	0.98
C16-C17	1.555(4)	C16-C21	1.563(4)

C16-H16	1	C17-C18	1.530(4)
C17-H17A	0.99	C17-H17B	0.99
C18-C19	1.535(4)	C18-C22	1.543(4)
C18-H18	1	C19-C20	1.562(4)
C19-H19A	0.99	C19-H19B	0.99
C20-C21	1.553(4)	C20-H20A	0.99
C20-H20B	0.99	C21-C25	1.522(4)
C21-C22	1.560(4)	C22-C24	1.531(4)
C22-C23	1.537(4)	C23-H23A	0.98
C23-H23B	0.98	C23-H23C	0.98
C24-H24A	0.98	C24-H24B	0.98
C24-H24C	0.98	C25-H25A	0.99
C25-H25B	0.99	C26-C31	1.518(4)
C26-C27	1.525(4)	C26-H26	1
C27-C28	1.530(4)	C27-H27A	0.99
C27-H27B	0.99	C28-C29	1.526(5)
C28-H28A	0.99	C28-H28B	0.99
C29-C30	1.515(6)	C29-H29A	0.99
C29-H29B	0.99	C30-C31	1.521(4)
C30-H30A	0.99	C30-H30B	0.99
C31-H31A	0.99	C31-H31B	0.99
C32-C37	1.512(4)	C32-C33	1.521(4)
C32-H32	1	C33-C34	1.516(4)
C33-H33A	0.99	C33-H33B	0.99
C34-C35	1.504(4)	C34-H34A	0.99
C34-H34B	0.99	C35-C36	1.510(4)
C35-H35A	0.99	C35-H35B	0.99
C36-C37	1.539(4)	C36-H36A	0.99
C36-H36B	0.99	C37-H37A	0.99
C37-H37B	0.99		

Bond angles (°):

C1-S1-C16	100.39(15)		
O5-S2-O4	118.56(13)		
O5-S2-N1	108.28(13)	O4-S2-N1	108.19(13)
O5-S2-C25	107.69(13)	O4-S2-C25	107.17(13)
N1-S2-C25	106.33(14)	C3-O2-O3	102.9(2)
C5-O3-O2	102.92(18)	C32-N1-C26	118.4(2)
C32-N1-S2	122.83(19)	C26-N1-S2	116.7(2)
O1-C1-C2	122.4(3)	O1-C1-S1	124.7(2)
C2-C1-S1	113.0(2)	C3-C2-C1	113.2(3)
C3-C2-H2A	108.9	C1-C2-H2A	108.9
C3-C2-H2B	108.9	C1-C2-H2B	108.9
H2A-C2-H2B	107.7	O2-C3-C6	110.2(2)
O2-C3-C2	102.7(2)	C6-C3-C2	111.8(3)

O2-C3-C4	103.1(2)	C6-C3-C4	113.1(3)
C2-C3-C4	114.9(3)	C5-C4-C3	104.6(2)
C5-C4-H4A	110.8	C3-C4-H4A	110.8
C5-C4-H4B	110.8	C3-C4-H4B	110.8
H4A-C4-H4B	108.9	O3-C5-C11	105.0(2)
O3-C5-C7	109.7(2)	C11-C5-C7	111.3(2)
O3-C5-C4	103.2(2)	C11-C5-C4	114.3(3)
C7-C5-C4	112.6(2)	C3-C6-H6A	109.5
C3-C6-H6B	109.5	H6A-C6-H6B	109.5
C3-C6-H6C	109.5	H6A-C6-H6C	109.5
H6B-C6-H6C	109.5	C8-C7-C5	113.4(2)
C8-C7-H7A	108.9	C5-C7-H7A	108.9
C8-C7-H7B	108.9	C5-C7-H7B	108.9
H7A-C7-H7B	107.7	C7-C8-C9	111.0(2)
C7-C8-H8A	109.4	C9-C8-H8A	109.4
C7-C8-H8B	109.4	C9-C8-H8B	109.4
H8A-C8-H8B	108	C8-C9-C10	107.8(2)
C8-C9-C12	114.4(2)	C10-C9-C12	113.7(2)
C8-C9-H9	106.8	C10-C9-H9	106.8
C12-C9-H9	106.8	C11-C10-C9	110.3(2)
C11-C10-H10A	109.6	C9-C10-H10A	109.6
C11-C10-H10B	109.6	C9-C10-H10B	109.6
H10A-C10-H10B	108.1	C5-C11-C10	113.2(2)
C5-C11-H11A	108.9	C10-C11-H11A	108.9
C5-C11-H11B	108.9	C10-C11-H11B	108.9
H11A-C11-H11B	107.8	C13-C12-C15	108.7(3)
C13-C12-C14	110.1(3)	C15-C12-C14	107.3(3)
C13-C12-C9	112.2(3)	C15-C12-C9	109.3(2)
C14-C12-C9	109.2(2)	C12-C13-H13A	109.5
C12-C13-H13B	109.5	H13A-C13-H13B	109.5
C12-C13-H13C	109.5	H13A-C13-H13C	109.5
H13B-C13-H13C	109.5	C12-C14-H14A	109.5
C12-C14-H14B	109.5	H14A-C14-H14B	109.5
C12-C14-H14C	109.5	H14A-C14-H14C	109.5
H14B-C14-H14C	109.5	C12-C15-H15A	109.5
C12-C15-H15B	109.5	H15A-C15-H15B	109.5
C12-C15-H15C	109.5	H15A-C15-H15C	109.5
H15B-C15-H15C	109.5	C17-C16-C21	103.0(2)
C17-C16-S1	114.6(2)	C21-C16-S1	115.2(2)
C17-C16-H16	107.9	C21-C16-H16	107.9
S1-C16-H16	107.9	C18-C17-C16	102.9(2)
C18-C17-H17A	111.2	C16-C17-H17A	111.2
C18-C17-H17B	111.2	C16-C17-H17B	111.2
H17A-C17-H17B	109.1	C17-C18-C19	107.8(3)
C17-C18-C22	102.8(2)	C19-C18-C22	103.3(2)
C17-C18-H18	113.9	C19-C18-H18	113.9

C22-C18-H18	113.9	C18-C19-C20	102.6(2)
C18-C19-H19A	111.2	C20-C19-H19A	111.2
C18-C19-H19B	111.2	C20-C19-H19B	111.2
H19A-C19-H19B	109.2	C21-C20-C19	103.2(2)
C21-C20-H20A	111.1	C19-C20-H20A	111.1
C21-C20-H20B	111.1	C19-C20-H20B	111.1
H20A-C20-H20B	109.1	C25-C21-C20	115.7(2)
C25-C21-C22	113.8(2)	C20-C21-C22	101.6(2)
C25-C21-C16	116.6(2)	C20-C21-C16	104.1(2)
C22-C21-C16	103.2(2)	C24-C22-C23	107.6(2)
C24-C22-C18	114.2(2)	C23-C22-C18	113.3(2)
C24-C22-C21	114.0(2)	C23-C22-C21	114.3(2)
C18-C22-C21	93.1(2)	C22-C23-H23A	109.5
C22-C23-H23B	109.5	H23A-C23-H23B	109.5
C22-C23-H23C	109.5	H23A-C23-H23C	109.5
H23B-C23-H23C	109.5	C22-C24-H24A	109.5
C22-C24-H24B	109.5	H24A-C24-H24B	109.5
C22-C24-H24C	109.5	H24A-C24-H24C	109.5
H24B-C24-H24C	109.5	C21-C25-S2	115.6(2)
C21-C25-H25A	108.4	S2-C25-H25A	108.4
C21-C25-H25B	108.4	S2-C25-H25B	108.4
H25A-C25-H25B	107.4	N1-C26-C31	110.7(3)
N1-C26-C27	113.8(3)	C31-C26-C27	112.2(3)
N1-C26-H26	106.5	C31-C26-H26	106.5
C27-C26-H26	106.5	C26-C27-C28	111.3(3)
C26-C27-H27A	109.4	C28-C27-H27A	109.4
C26-C27-H27B	109.4	C28-C27-H27B	109.4
H27A-C27-H27B	108	C29-C28-C27	111.9(3)
C29-C28-H28A	109.2	C27-C28-H28A	109.2
C29-C28-H28B	109.2	C27-C28-H28B	109.2
H28A-C28-H28B	107.9	C30-C29-C28	111.9(3)
C30-C29-H29A	109.2	C28-C29-H29A	109.2
C30-C29-H29B	109.2	C28-C29-H29B	109.2
H29A-C29-H29B	107.9	C29-C30-C31	112.2(3)
C29-C30-H30A	109.2	C31-C30-H30A	109.2
C29-C30-H30B	109.2	C31-C30-H30B	109.2
H30A-C30-H30B	107.9	C26-C31-C30	111.8(3)
C26-C31-H31A	109.3	C30-C31-H31A	109.3
C26-C31-H31B	109.3	C30-C31-H31B	109.3
H31A-C31-H31B	107.9	N1-C32-C37	113.5(2)
N1-C32-C33	114.7(2)	C37-C32-C33	112.1(2)
N1-C32-H32	105.1	C37-C32-H32	105.1
C33-C32-H32	105.1	C34-C33-C32	110.7(2)
C34-C33-H33A	109.5	C32-C33-H33A	109.5
C34-C33-H33B	109.5	C32-C33-H33B	109.5
H33A-C33-H33B	108.1	C35-C34-C33	112.7(3)

C35-C34-H34A	109.1	C33-C34-H34A	109.1
C35-C34-H34B	109.1	C33-C34-H34B	109.1
H34A-C34-H34B	107.8	C34-C35-C36	112.5(3)
C34-C35-H35A	109.1	C36-C35-H35A	109.1
C34-C35-H35B	109.1	C36-C35-H35B	109.1
H35A-C35-H35B	107.8	C35-C36-C37	111.4(3)
C35-C36-H36A	109.4	C37-C36-H36A	109.4
C35-C36-H36B	109.4	C37-C36-H36B	109.4
H36A-C36-H36B	108	C32-C37-C36	110.8(3)
C32-C37-H37A	109.5	C36-C37-H37A	109.5
C32-C37-H37B	109.5	C36-C37-H37B	109.5
H37A-C37-H37B	108.1		

Anisotropic atomic displacement parameters (Å^2):

The anisotropic atomic displacement factor exponent takes the form: -2π2[h2 a*2 U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
S1	0.0167(4)	0.0293(4)	0.0209(4)	0.0076(3)	0.0003(4)	0.0012(4)
S2	0.0144(4)	0.0173(4)	0.0242(4)	0.0005(3)	0.0010(3)	0.0005(3)
O1	0.0193(12)	0.0461(16)	0.0381(14)	0.0239(12)	-0.0070(11)	-0.0075(11)
O2	0.0235(12)	0.0317(13)	0.0318(13)	0.0184(10)	-0.0114(11)	-0.0106(11)
O3	0.0188(12)	0.0360(13)	0.0300(12)	0.0170(10)	-0.0048(10)	-0.0086(10)
O4	0.0245(12)	0.0208(12)	0.0295(12)	0.0011(10)	0.0076(10)	-0.0023(10)
O5	0.0172(12)	0.0267(12)	0.0364(13)	-0.0061(10)	-0.0079(10)	0.0059(10)
N1	0.0204(13)	0.0141(13)	0.0204(13)	-0.0004(11)	0.0011(11)	-0.0024(11)
C1	0.0230(17)	0.0287(18)	0.0175(15)	0.0066(14)	-0.0031(14)	-0.0018(15)
C2	0.0254(18)	0.0214(17)	0.0255(17)	0.0051(14)	-0.0044(15)	-0.0011(14)
C3	0.0178(17)	0.0214(17)	0.0245(17)	0.0121(14)	-0.0009(14)	-0.0009(13)
C4	0.0180(17)	0.0280(18)	0.0282(18)	0.0094(14)	-0.0014(14)	-0.0047(14)
C5	0.0153(15)	0.0213(17)	0.0251(17)	0.0081(13)	-0.0003(13)	-0.0050(13)
C6	0.0243(18)	0.035(2)	0.0219(17)	0.0021(14)	0.0028(15)	-0.0022(16)
C7	0.0257(18)	0.0257(18)	0.0200(16)	0.0016(14)	-0.0042(14)	-0.0034(15)
C8	0.0318(19)	0.0199(17)	0.0251(17)	-0.0024(14)	-0.0042(15)	0.0015(15)
C9	0.0199(17)	0.0167(16)	0.0184(15)	0.0011(12)	-0.0011(13)	0.0025(13)
C10	0.0220(16)	0.0196(17)	0.0188(15)	0.0011(13)	-0.0016(14)	0.0020(14)
C11	0.0211(17)	0.0205(17)	0.0245(17)	0.0003(13)	0.0020(14)	-0.0008(14)
C12	0.0290(18)	0.0162(16)	0.0239(16)	0.0009(13)	-0.0035(15)	0.0016(14)
C13	0.047(2)	0.0247(19)	0.0304(18)	0.0115(15)	-0.0151(18)	-0.0085(17)
C14	0.058(3)	0.037(2)	0.0322(19)	-0.0019(16)	-0.0109(19)	0.032(2)
C15	0.027(2)	0.0243(17)	0.0285(18)	0.0036(14)	-0.0067(15)	0.0042(15)
C16	0.0126(15)	0.0217(16)	0.0157(15)	0.0010(12)	0.0004(13)	-0.0042(14)
C17	0.0207(16)	0.0250(17)	0.0209(15)	-0.0041(13)	-0.0021(15)	-0.0062(15)
C18	0.0195(16)	0.0187(16)	0.0257(17)	-0.0017(13)	-0.0011(15)	0.0001(15)

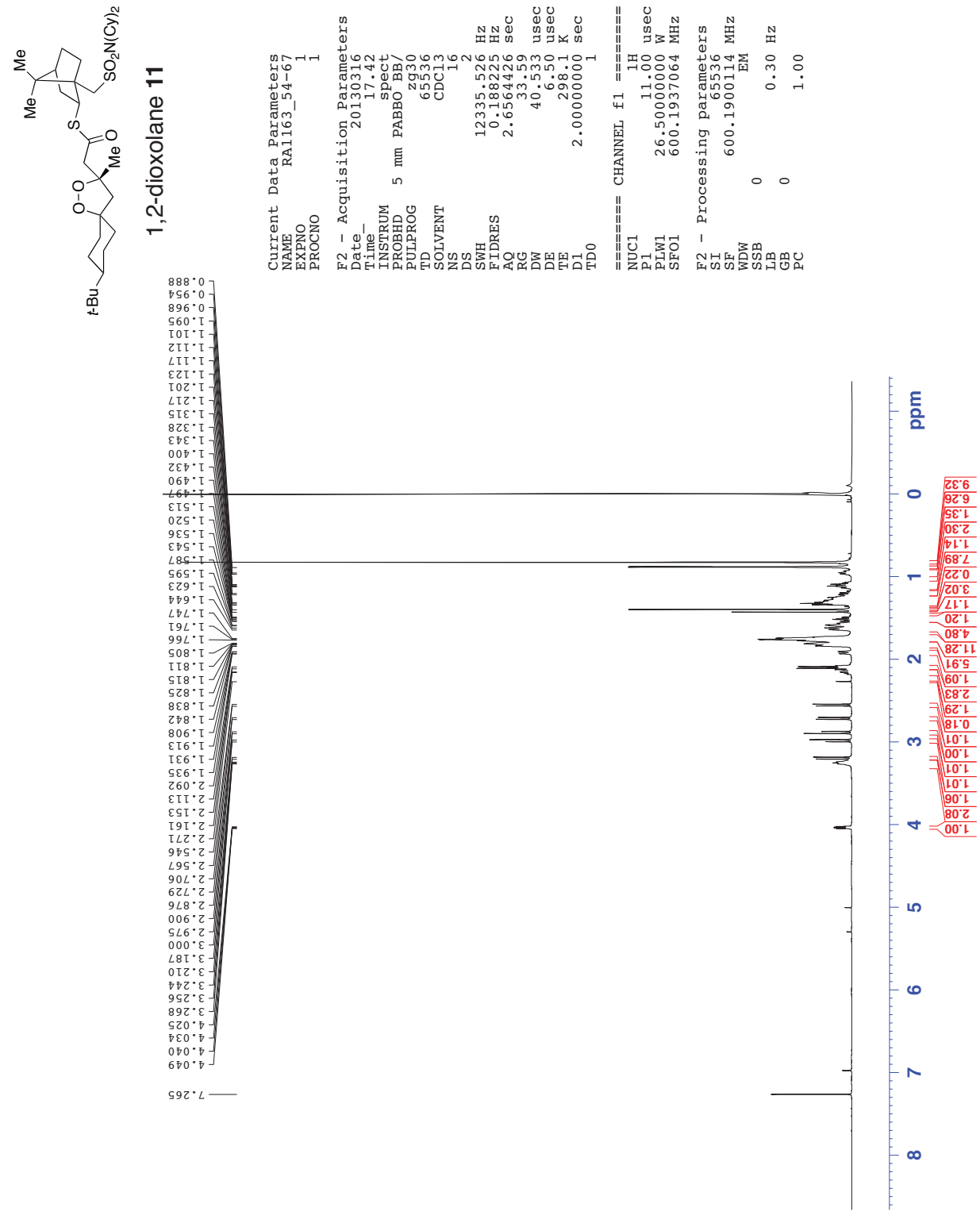
C19	0.0173(16)	0.0212(17)	0.0264(17)	0.0007(14)	-0.0007(14)	-0.0039(14)
C20	0.0149(15)	0.0197(16)	0.0200(15)	0.0025(13)	-0.0005(13)	-0.0006(13)
C21	0.0112(14)	0.0152(15)	0.0159(14)	0.0013(12)	-0.0011(13)	-0.0007(13)
C22	0.0128(16)	0.0165(15)	0.0197(15)	-0.0005(12)	0.0000(12)	-0.0006(12)
C23	0.0176(16)	0.0216(17)	0.0227(16)	0.0013(14)	0.0006(14)	0.0017(13)
C24	0.0195(17)	0.0276(18)	0.0217(16)	-0.0007(14)	0.0027(14)	0.0038(15)
C25	0.0123(15)	0.0216(16)	0.0183(15)	-0.0019(13)	0.0010(12)	0.0013(13)
C26	0.0249(18)	0.0203(17)	0.0233(16)	0.0029(14)	0.0014(14)	0.0004(14)
C27	0.0289(19)	0.030(2)	0.0292(18)	0.0035(15)	0.0084(16)	0.0036(16)
C28	0.038(2)	0.033(2)	0.0282(18)	0.0012(16)	0.0084(17)	-0.0060(17)
C29	0.066(3)	0.031(2)	0.0301(19)	0.0140(16)	0.010(2)	-0.009(2)
C30	0.058(3)	0.0245(19)	0.032(2)	0.0066(15)	0.003(2)	0.008(2)
C31	0.037(2)	0.0206(17)	0.0245(17)	0.0031(13)	0.0037(16)	0.0098(16)
C32	0.0160(16)	0.0234(17)	0.0238(16)	-0.0033(13)	-0.0016(14)	-0.0003(14)
C33	0.0174(16)	0.0240(17)	0.0225(16)	0.0003(14)	-0.0006(14)	0.0021(14)
C34	0.0231(17)	0.0281(19)	0.0289(18)	-0.0035(14)	-0.0032(15)	0.0034(15)
C35	0.0300(19)	0.0290(19)	0.0266(17)	-0.0044(15)	-0.0043(16)	0.0022(16)
C36	0.0310(19)	0.0227(17)	0.0228(16)	-0.0044(14)	0.0039(16)	-0.0012(16)
C37	0.0235(17)	0.0249(18)	0.0256(17)	-0.0019(14)	0.0003(15)	0.0068(15)

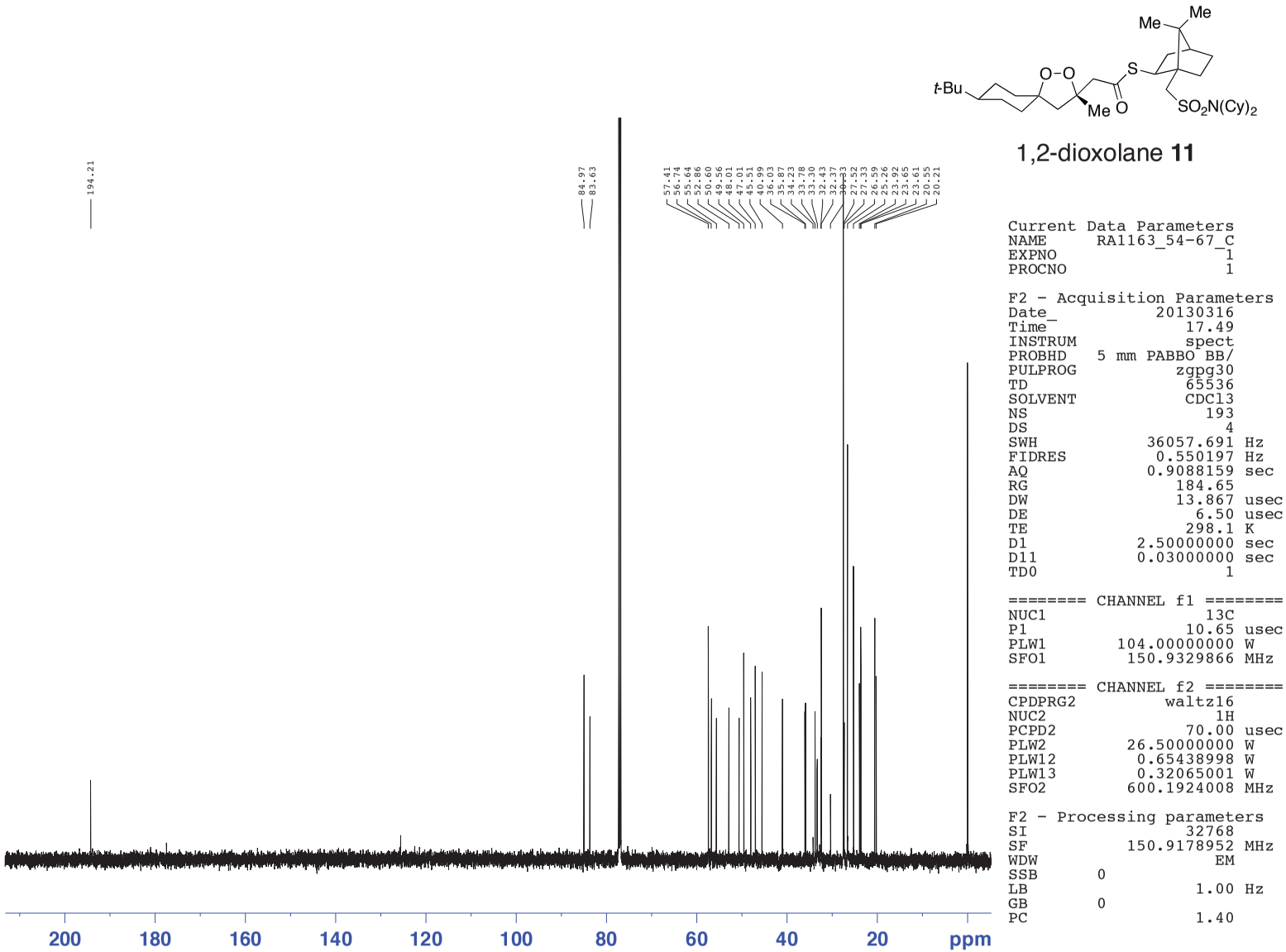
Hydrogen atomic coordinates and isotropic atomic displacement parameters (Å^2):

	x/a	y/b	z/c	U(eq)
H2A	0.3582	0.4788	0.5147	0.029
H2B	0.5878	0.454	0.5045	0.029
H4A	0.8678	0.5042	0.55	0.03
H4B	0.8089	0.5563	0.5906	0.03
H6A	0.4507	0.5988	0.58	0.041
H6B	0.4425	0.5486	0.6231	0.041
H6C	0.2753	0.5402	0.5842	0.041
H7A	0.8758	0.3695	0.5659	0.029
H7B	1.0848	0.41	0.5768	0.029
H8A	1.102	0.2974	0.6085	0.031
H8B	0.89	0.3095	0.6345	0.031
H9	1.2521	0.3907	0.6512	0.022
H10A	0.8666	0.3945	0.6972	0.024
H10B	1.064	0.438	0.7132	0.024
H11A	0.8441	0.5105	0.6694	0.026
H11B	1.0642	0.5033	0.6462	0.026
H13A	0.9683	0.2432	0.6987	0.051
H13B	0.9731	0.2999	0.7385	0.051
H13C	1.1191	0.2322	0.7405	0.051
H14A	1.274	0.2278	0.6501	0.064
H14B	1.4349	0.2267	0.6906	0.064
H14C	1.4567	0.284	0.6515	0.064

H15A	1.4645	0.372	0.7155	0.04
H15B	1.4241	0.3088	0.75	0.04
H15C	1.2748	0.3757	0.7495	0.04
H16	0.562	0.655	0.4298	0.02
H17A	0.3082	0.7478	0.4774	0.027
H17B	0.5352	0.763	0.4583	0.027
H18	0.2476	0.8289	0.4173	0.026
H19A	0.6032	0.7958	0.3846	0.026
H19B	0.4276	0.8143	0.3484	0.026
H20A	0.4256	0.7001	0.3249	0.022
H20B	0.604	0.6819	0.3605	0.022
H23A	0.1471	0.7614	0.3269	0.031
H23B	-0.0425	0.7924	0.3546	0.031
H23C	-0.0451	0.7121	0.3382	0.031
H24A	-0.1051	0.7539	0.4329	0.034
H24B	0.0364	0.6945	0.4551	0.034
H24C	-0.1147	0.6746	0.4148	0.034
H25A	0.1257	0.6094	0.3453	0.021
H25B	0.1323	0.5782	0.3949	0.021
H26	0.3013	0.4555	0.4191	0.027
H27A	-0.0659	0.3953	0.3838	0.035
H27B	-0.0492	0.4707	0.4077	0.035
H28A	0.0275	0.4184	0.4767	0.04
H28B	-0.1768	0.3822	0.458	0.04
H29A	0.0597	0.2969	0.4867	0.051
H29B	0.005	0.2824	0.4352	0.051
H30A	0.3575	0.2706	0.4435	0.046
H30B	0.374	0.3459	0.4674	0.046
H31A	0.4859	0.3588	0.3937	0.033
H31B	0.2816	0.3228	0.3747	0.033
H32	0.0987	0.3893	0.3212	0.025
H33A	-0.1008	0.4911	0.3225	0.026
H33B	0.0476	0.5277	0.2866	0.026
H34A	-0.2026	0.4064	0.2707	0.032
H34B	-0.2334	0.4821	0.2481	0.032
H35A	0.0596	0.4687	0.2055	0.034
H35B	-0.0803	0.4004	0.1982	0.034
H36A	0.2712	0.3708	0.209	0.031
H36B	0.1257	0.3337	0.2453	0.031
H37A	0.41	0.3805	0.2837	0.03
H37B	0.3746	0.4565	0.2615	0.03

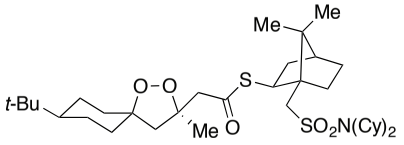
Selected Spectra



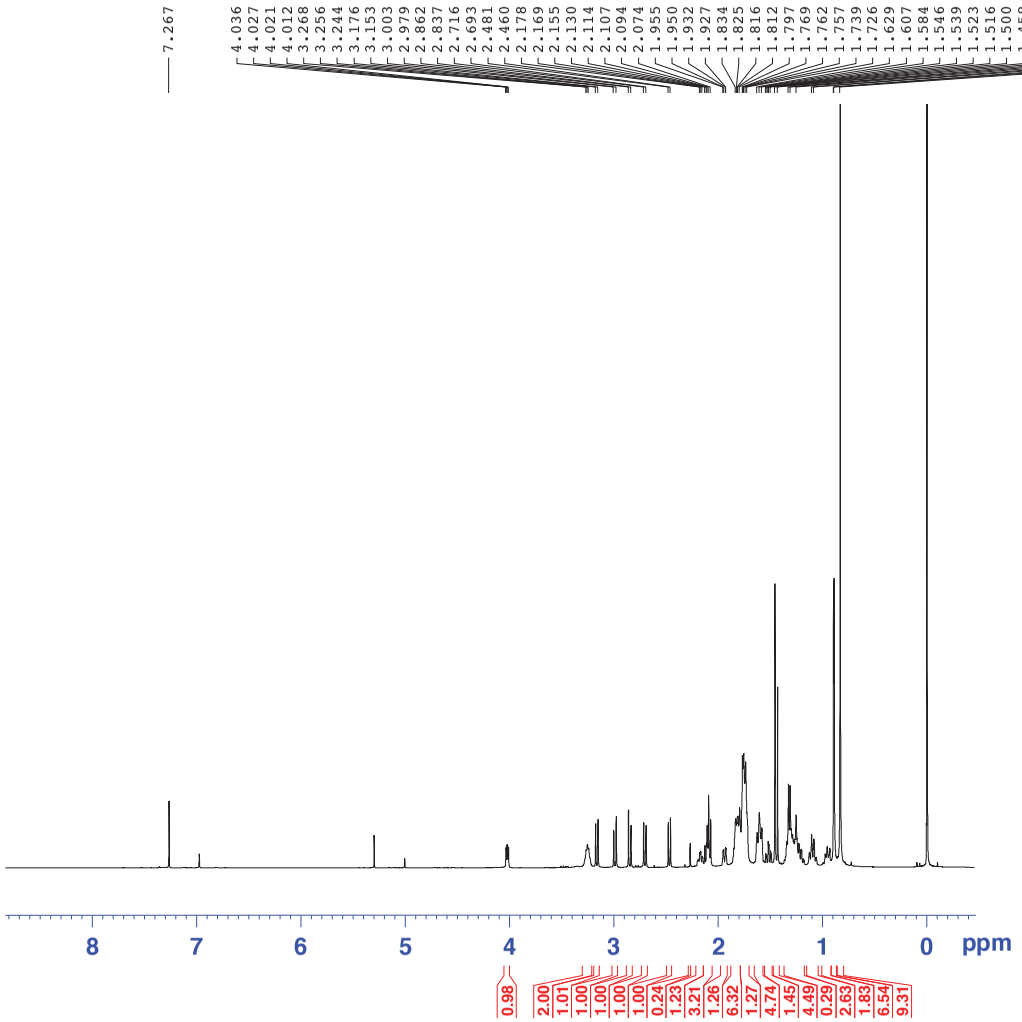


1,2-dioxolane **11**

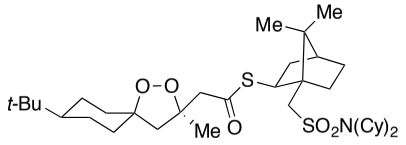
```
Current Data Parameters
NAME      RA1163_54-67_C
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130316
Time              17.49
INSTRUM           spect
PROBHD   5 mm PABBO BB/
PULPROG         zgpg30
TD                65536
SOLVENT           CDCl3
NS                  193
DS                    4
SWH           36057.691 Hz
FIDRES         0.550197 Hz
AQ            0.9088159 sec
RG               184.65
DW               13.867 usec
DE                 6.50 usec
TE                298.1 K
D1           2.50000000 sec
D11          0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                 13C
P1                 10.65 usec
PLW1       104.00000000 W
SFO1        150.9329866 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                 1H
PCPD2              70.00 usec
PLW2        26.50000000 W
PLW12        0.65438998 W
PLW13        0.32065001 W
SFO2        600.1924008 MHz

F2 - Processing parameters
SI                32768
SF          150.9178952 MHz
WDW                  EM
SSB       0
LB                1.00 Hz
GB        0
PC                1.40
```



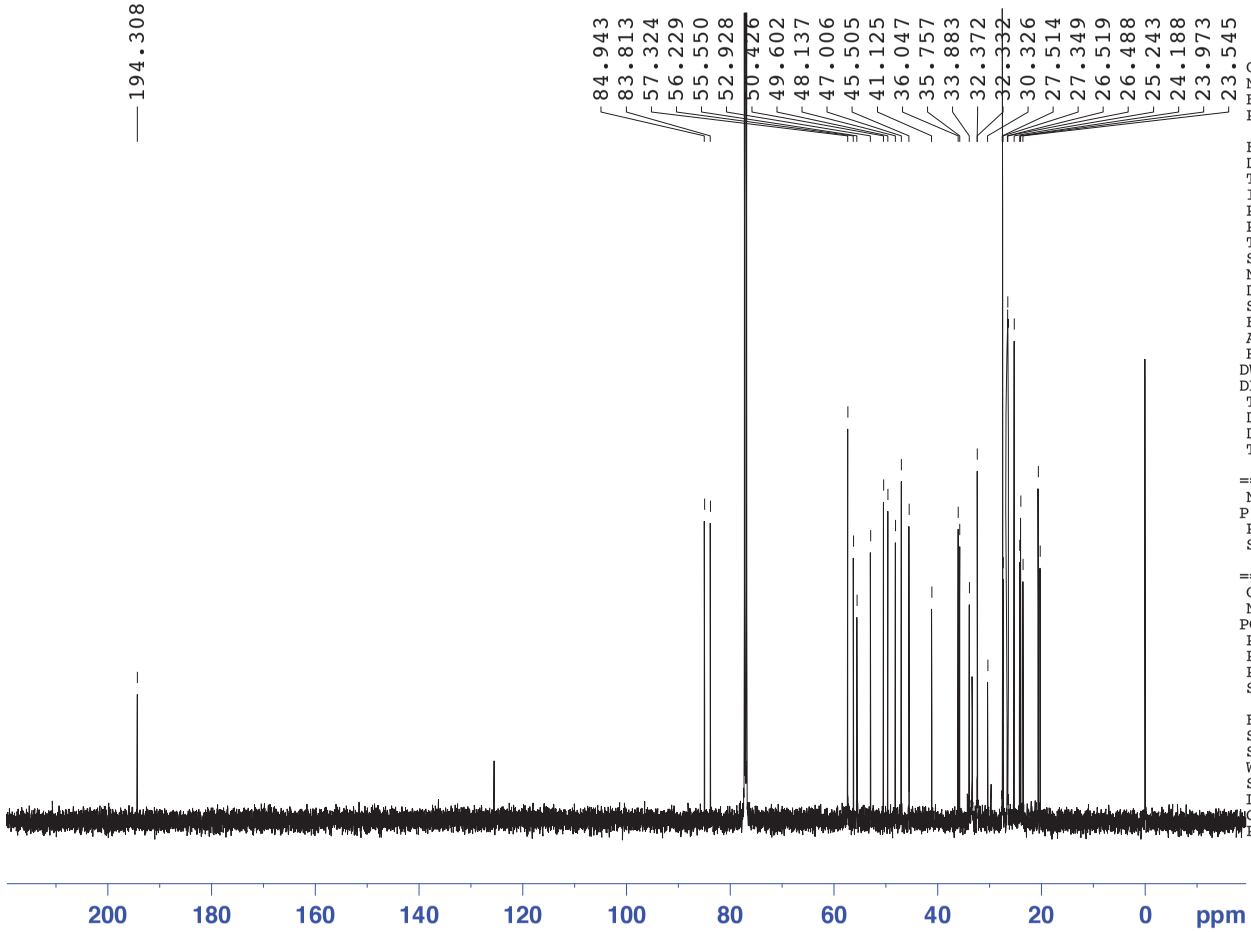
1,2-dioxolane **12**




```
Current Data Parameters
NAME      RA1163_90-end
EXPNO                 1
PROCNO                1

F2 - Acquisition Parameters
Date_          20130316
Time               18.17
INSTRUM            spect
PROBHD   5 mm PABBO BB/
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH            12335.526 Hz
FIDRES          0.188225 Hz
AQ              2.6564426 sec
RG                 33.59
DW                40.533 usec
DE                 6.50 usec
TE                298.1 K
D1             2.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                 11.00 usec
PLW1          26.50000000 W
SFO1          600.1937064 MHz

F2 - Processing parameters
SI                 65536
SF            600.1900106 MHz
WDW                   EM
     SSB       0
LB                  0.30 Hz
     GB        0
PC                  1.00
```

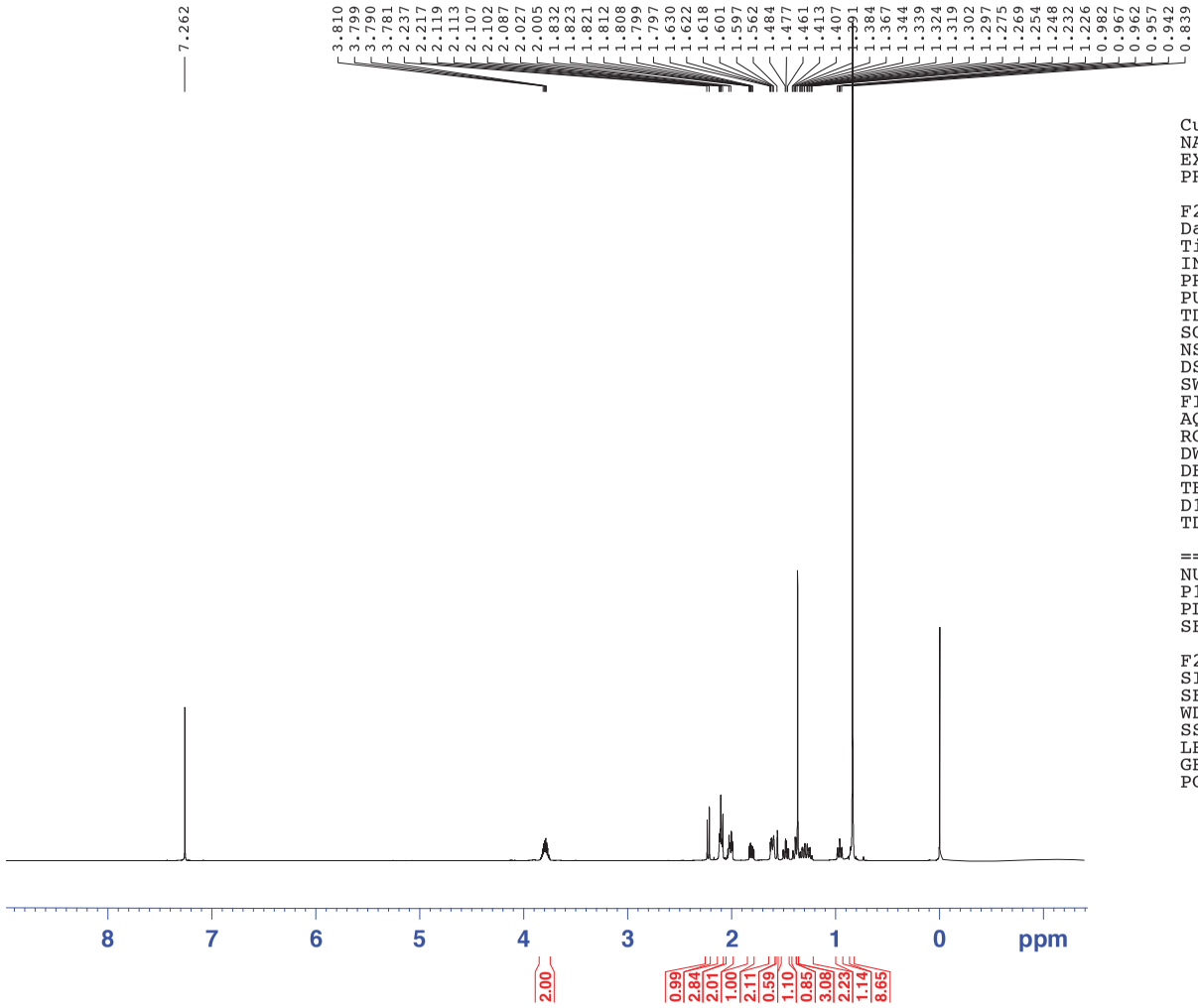


1,2-dioxolane **12**

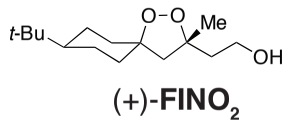



```
Current Data Parameters
NAME      RA1163_90-end_C
EXPNO                   1
PROCNO                  1

F2 - Acquisition Parameters
Date_           20130316
Time              18.25
INSTRUM           spect
PROBHD   5 mm PABBO BB/
PULPROG         zgpg30
TD                65536
SOLVENT           CDCl3
NS                  166
DS                    4
SWH           36057.691 Hz
FIDRES         0.550197 Hz
AQ            0.9088159 sec
RG               184.65
DW              13.867 usec
DE               6.50 usec
TE               298.1 K
D1           2.50000000 sec
D11          0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                 13C
P1                10.65 usec
PLW1        104.00000000 W
SFO1         150.9329866 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                 1H
PCPD2             70.00 usec
PLW2         26.50000000 W
PLW12         0.65438998 W
PLW13         0.32065001 W
SFO2         600.1924008 MHz

F2 - Processing parameters
SI                32768
SF           150.9178954 MHz
WDW                  EM
SSB       0
LB                1.00 Hz
GB        0
PC                1.40
```

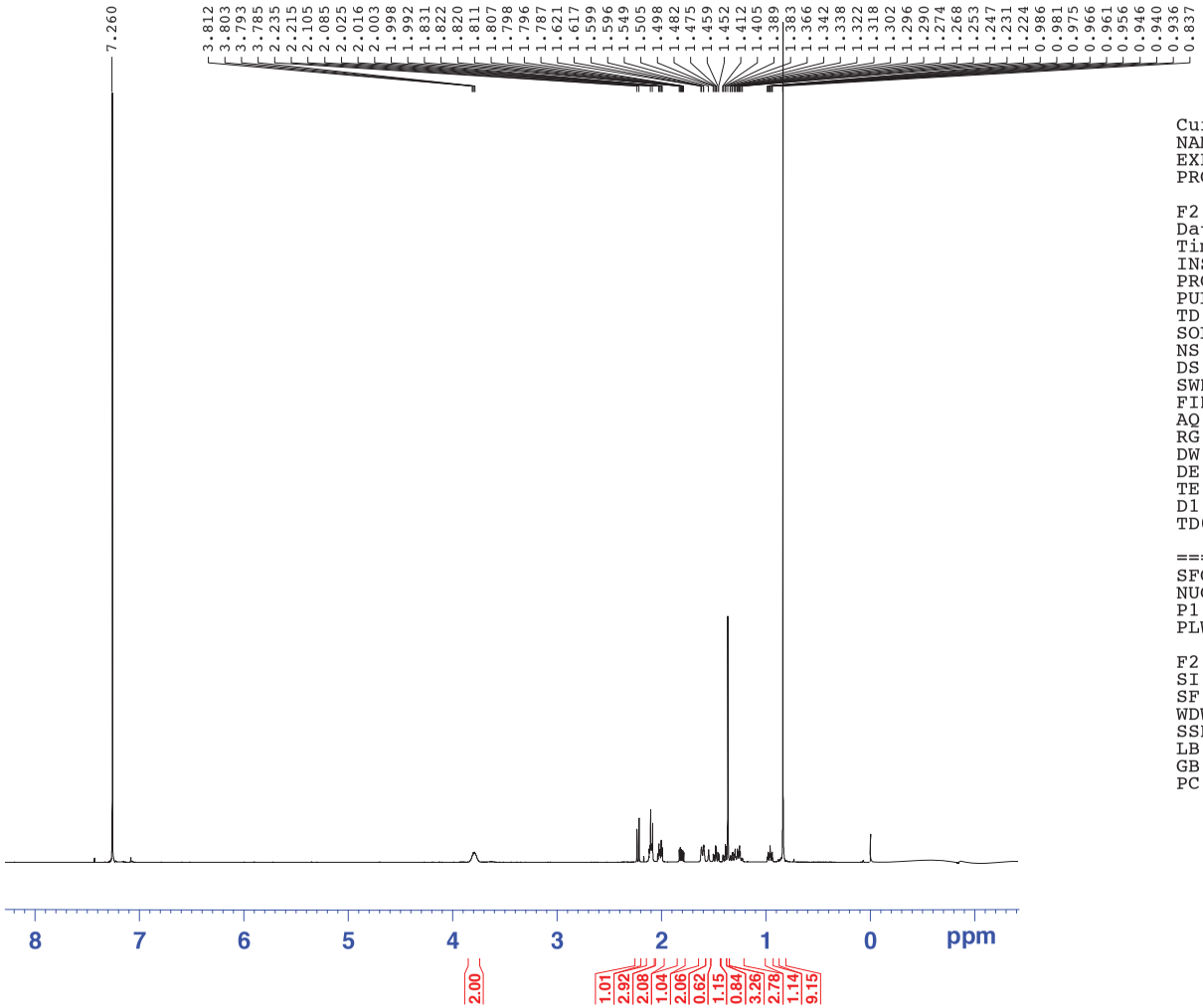
FINO$_2$



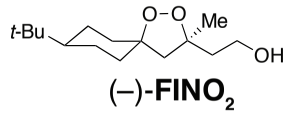

```
Current Data Parameters
NAME       RA1174_84-107
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130606
Time               16.50
INSTRUM            spect
PROBHD   5 mm PAQXI 1H/
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH           12335.526 Hz
FIDRES         0.188225 Hz
AQ            2.6564426 sec
RG               164.46
DW               40.533 usec
DE                 6.50 usec
TE                298.1 K
D1           2.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                 9.79 usec
PLW1         9.30000019 W
SFO1        600.1937064 MHz

F2 - Processing parameters
SI                 65536
SF          600.1900134 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```



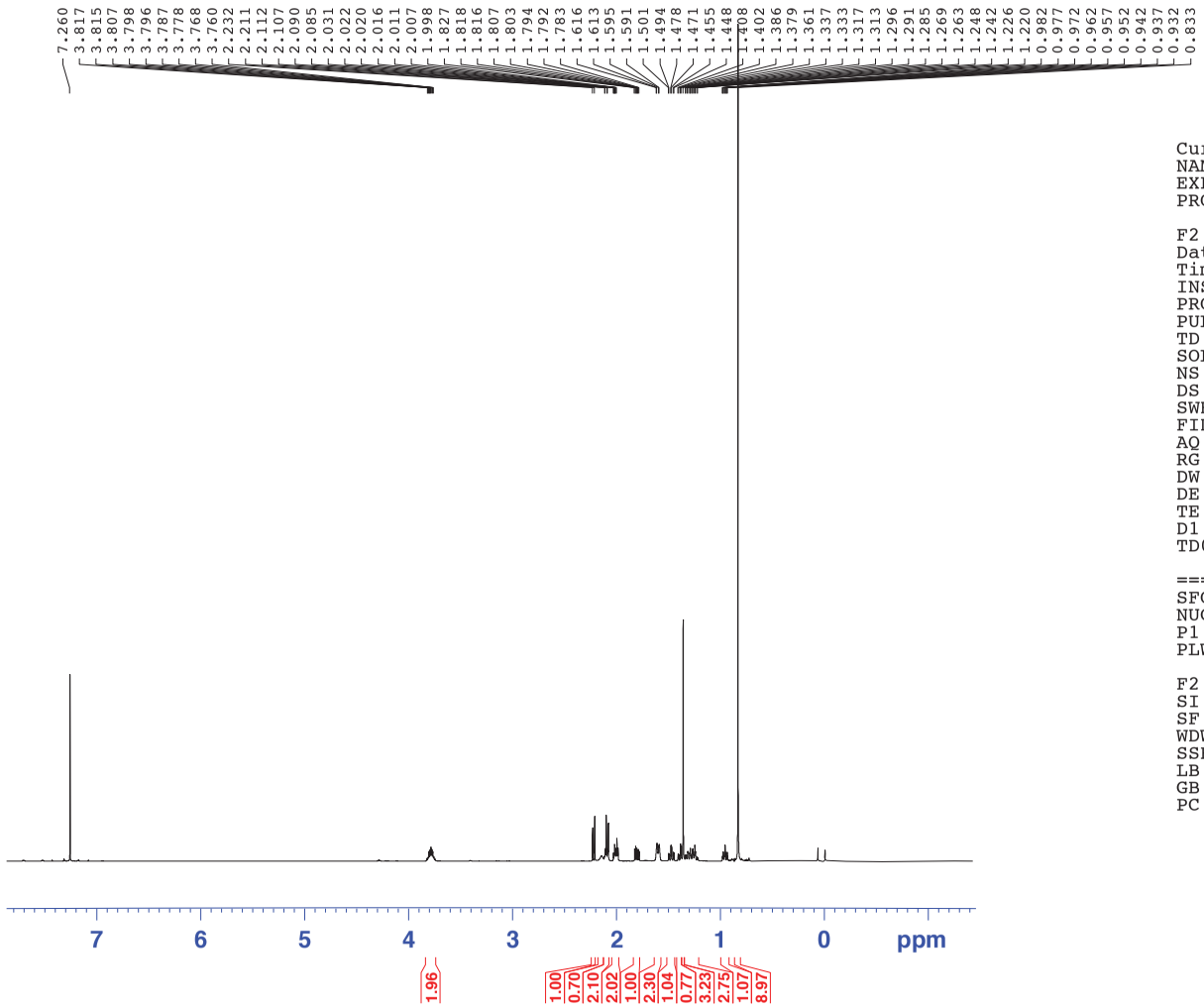
(+)-**FINO$_2$**




```
Current Data Parameters
NAME      RA1194_2_61-73
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20150411
Time               20.31
INSTRUM            spect
PROBHD   5 mm PAQXI 1H/
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH            12335.526 Hz
FIDRES         0.188225 Hz
AQ             2.6564426 sec
RG                184.65
DW                40.533 usec
DE                 6.50 usec
TE                298.1 K
D1           2.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         600.1937064 MHz
NUC1                1H
P1                 10.00 usec
PLW1          9.60000038 W

F2 - Processing parameters
SI                 65536
SF           600.1900143 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```



(–)-**FINO$_2$**




```
Current Data Parameters
NAME          RA1192_RA1
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20150403
Time               12.07
INSTRUM            spect
PROBHD   5 mm PAQXI 1H/
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     0
SWH            12335.526 Hz
FIDRES         0.188225 Hz
AQ             2.6564426 sec
RG                184.65
DW                40.533 usec
DE                 6.50 usec
TE                298.1 K
D1           2.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         600.1937064 MHz
NUC1                1H
P1                 10.00 usec
PLW1          9.60000038 W

F2 - Processing parameters
SI                 65536
SF           600.1900150 MHz
WDW                   no
SSB       0
LB        0 Hz
GB        0
PC                 1.00
```

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