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Ring Enlargement versus Selenoetherification on the Reaction of Allenyl Oxindoles with Selenenylating Reagents

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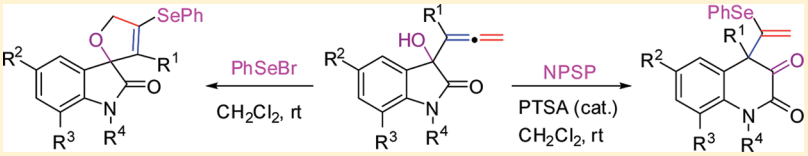
Supporting Information

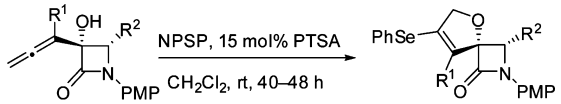


ABSTRACT: Lactam-tethered allenols, readily prepared from α-oxolactams, were used as starting materials for divergent reactivity with selenenylating reagents. Either oxycyclization (spirocyclic selenolactams) or ring expansion (selenoquinolones) can be achieved through the choice of both reagents and substrates. The biological activity of some of the synthesized heterocycles has additionally been evaluated in four human cancer cell lines.

The carbon−carbon double bond of allenes, a class of compounds with two π-orbitals perpendicular to each other, is around 10 kcal mol^{-1} less stable than that of simple alkenes,[1] rendering them significantly more reactive. Thus, allenes have metamorphosed from a laboratory curiosity to a versatile and uniquely reactive functional group, allowing chemists to prepare a variety of compounds of chemical and biological interest.[2] In addition, interest in the chemistry of organoselenium compounds has increased remarkably due to their biological activities and pharmaceutical potential.[3] Selenocyclizations are stereospecific *anti* addition reactions of selenium electrophiles to olefins bearing internal nucleophiles leading to cyclic products.[4,5] The reaction of selenium electrophiles with allenes has attracted much attention because it provides functionalized derivatives.[6] Following up on our combined interest in the area of lactams and allenes,[7] we have recently communicated the preparation of spirocyclic seleno β-lactams **2** from 2-azetidinone-tethered allenols **1** and *N*-phenylselenophthalimide (Scheme 1).[8] We wish to report here an unprecedented behavior of selenium electrophilic reagents, namely, the ring enlargement of 2-indolinone-tethered allenols in preference to selenoetherification on reacting with selenenylating reagents.

Starting allenols **3a−e** were achieved via indium-mediated Barbier-type allenylation reactions of isatins in aqueous media following our previously described methodology.[9] PhSeBr, NPSS (*N*-phenylselenosuccinimide), or diphenyl diselenide in the presence of (diacetoxyiodo)benzene were shown to serve as donors of PhSe$^+$ in reactions with 2-indolinone-tethered allenol **3a**, affording exclusively the expected spirocyclic seleno-oxindole **4a** (Table 1, entries 1−3).[10] To further test the reactivity of 2-indolinone-tethered allenols **3**, we examined the reaction of allenol **3a** with NPSP (*N*-phenylselenophthalimide), a well-known source of seleniranium ion.[11] Interestingly, it was found that the combined use of NPSP and catalytic amounts of PTSA in dichloromethane at room temperature gave rise to quinoline-2,3-dione **5a** as major product; quinoline-2,4-dione **6a** and spirocycle **4a** were also isolated as minor components (Table 1, entry 4). Worthy of note, the reaction of 2-indolinone-tethered allenols **3** with NPSP exhibited a chemoselectivity different from that previously observed for 2-azetidinone-tethered allenols **1**, namely, ring enlargement versus selenocycloetherification. The comparative studies of quinolone formation with addition of PTSA demonstrated that the presence of the Brønsted acid gives higher yields and that the acid additive acts as an activator but not as a catalyst.[12] A brief optimization of the reaction conditions revealed that

Scheme 1. NPSP-Mediated Preparation of Spirocyclic Seleno β-Lactams through Selenocyclization of Allenols[a]



1a R^1 = Ph, R^2 = Diox — **2a**
1b R^1 = Me, R^2 = Diox — **2b**
1b R^1 = Me, R^2 = Tol — **2c**
1c R^1 = Me, R^2 = Az — **2d**

[a]PMP = 4-MeOC$_6$H$_4$. Az = (*R*)-3-methoxy-1-(4-methoxyphenyl)-azetidinyl-2-one. Diox = (*S*)-2,2-dimethyl-1,3-dioxolan-4-yl. Tol = 4-MeC$_6$H$_4$. NPSP = *N*-phenylselenophthalimide.

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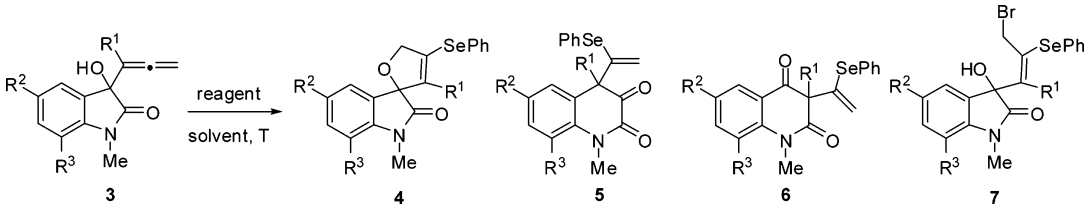
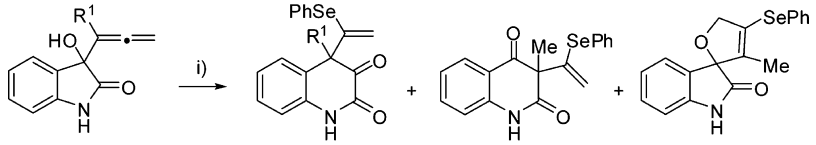
Table 1. Controlled Selenocycloetherification versus Ring Expansion Reactions of 2-Indolinone-Tethered Allenols 3 under Modified Selenenylation Conditions



entry	reagent	solvent	time (h)	additive	T (°C)	R^1, R^2, R^3	product	yield **4**/**5**/**6**/**7** (%)[a]
1	PhSeBr	CH_2Cl_2	1		20	Me, H, H	**4a**	71/0/0/0
2	PhSeSePh	DCE	72	DIB	40	Me, H, H	**4a**	60/0/0/0
3	NPSS	CH_2Cl_2	96	PTSA (15 mol %)	20	Me, H, H	**4a**	70/0/0/0
4	NPSP	CH_2Cl_2	24	PTSA (15 mol %)	20	Me, H, H	**4a**/**5a**/**6a**	26/56/17/0
5	NPSP	CH_2Cl_2	5	PTSA (15 mol %)	110	Me, H, H	**4a**/**5a**/**6a**	80/2/13/0
6	NPSP	CH_2Cl_2	240	PTSA (15 mol %)	−15	Me, H, H	**4a**/**5a**/**6a**	43/40/12/0
7	NPSP	CH_2Cl_2	24	PTSA (15 mol %)	20	Ph, H, H	**5b**	0/79/0/0
8	PhSeBr	CH_2Cl_2	1		20	Ph, H, H	**7b**	0/0/0/56
9	NPSP	CH_2Cl_2	24	PTSA (15 mol %)	20	PMP, H, H	**5c**	0/65/0/0
10	NPSP	CH_2Cl_2	1	PTSA (15 mol %)	20	Me, Cl, H	**4d**	44/0/0/0
11	PhSeBr	CH_2Cl_2	1		20	Me, Cl, H	**4d**/**7d**	55/0/0/9[b]
12	NPSP	CH_2Cl_2	72	PTSA (15 mol %)	20	Me, H, Cl	**4e**/**5e**/**6e**	25/10/5/0
13	PhSeBr	CH_2Cl_2	0.5		20	Me, H, Cl	**4e**/**7e**	43/0/0/19[b]

[a]Yield of pure, isolated product with correct analytical and spectral data. NPSS = *N*-Phenylselenosuccinimide. NPSP = *N*-Phenylselenophthalimide. DCE = 1,2-Dichloroethane. DIB = (Diacetoxyiodo)benzene. PMP = 4-$MeOC_6H_4$. PTSA = *p*-Toluenesulfonic acid. [b]Compounds **4d**/**7d** and **4e**/**7e** were obtained as unseparable mixtures.

Scheme 2. Rearrangement Reaction of *NH*-Indolinone-Tethered Allenols 8a−c to Quinoline-2,3-diones 9a−c by NPSP Treatment[a]



[a]Conditions: (i) NPSP, 15 mol % PTSA, CH_2Cl_2, rt, **8a**: 72 h; **8b**: 72 h, **8c**: 24 h. PMP = 4-$MeOC_6H_4$. NPSP = *N*-phenylselenophthalimide. PTSA = *p*-toluenesulfonic acid.

employment of other solvents (acetonitrile, THF, or 1,4-dioxane) did not improve the yield of **5a**. The reaction of allenol **3a** with the binary system NPSP/PTSA in 1,2-dichloroethane at 110 °C gave as the major product the spirocyclic component **4a** (Table 1, entry 5). A general trend can be deduced on the basis of this result: the spirocycle **4a** is the thermodynamic control product, while the quinoline-2,3-dione **5a** is the kinetic control product. With the optimized conditions in hand, the generality of this transformation was examined (Table 1). Fortunately, compounds **4**, **5**, and **6** are easily separated by flash chromatography. Happily, the ring expansion products **5b** and **5c** were isolated in good yields as the sole isomers from the skeletal reorganization of 2-indolinone-tethered allenols **3b** and **3c** bearing an aromatic substituent at the allenic moiety (Table 1, entries 7 and 9). Despite that the presence of halide substituents at the aromatic ring is anticipated to provide the same reactivity pattern, the 5-chloroindolinone **3d** led to spirocyclic selenooxindole **4d** as the sole product, while 7-chloroindolinone **3e** afforded **4e** as the major product; the expected 1,2-dicarbonylic compound **5e** was the minor component (Table 1, entries 10 and 12). It should be noted that the presence of a chlorine atom at the aromatic ring as in chloroindolinones **3d** and **3e** encumbers or even avoids the migration of the benzene nucleus toward ring expansion, which makes spirocyclization more feasible. This interesting change in the ratio of ring expansion products versus spirocyclic products, with the introduction of a chlorine substituent in a rather distant part of the molecule, may be explained invoking the deactivating effect of the chlorine substituent toward the aromatic ring. This deactivating effect may be related to the decreased migration ability of the chlorobenzene moiety to form quinolinediones. Surprisingly, the reaction of phenyl-substituted allenol **3b** with PhSeBr afforded the allene 1,2-addition adduct **7b** as exclusive reaction product (Table 1, entry 8). Despite that a priori NPSP and PhSeBr are similar sources of $PhSe^+$, different products, namely, **5b** and **7b**, were obtained starting from the common precursor **3b** (Table 1, entries 7 and 8). This different behavior for both selenenylating reagents may be explained taking into account their different chemical nature. The initial common addition of $PhSe^+$ cation to the central sp carbon atom of the allene group forms a carbocationic sp^2 center, which induces an intramolecular oxycyclization for the

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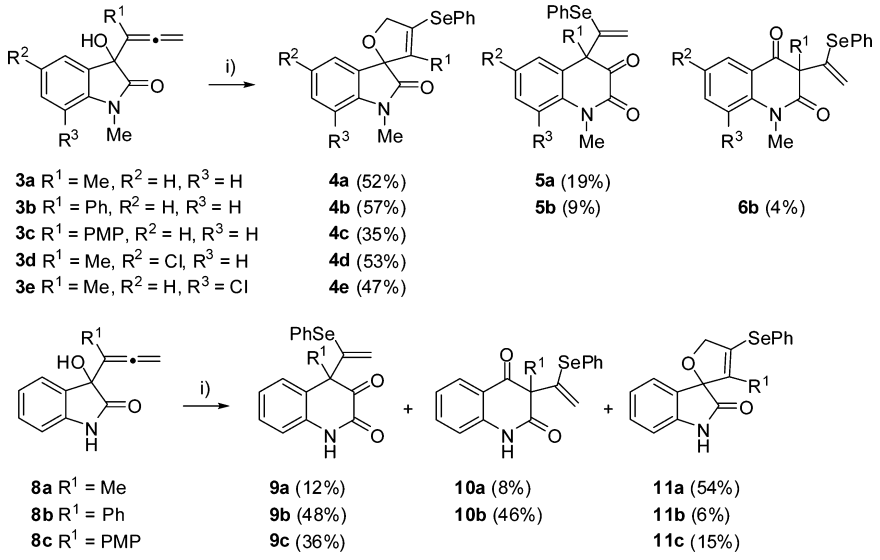
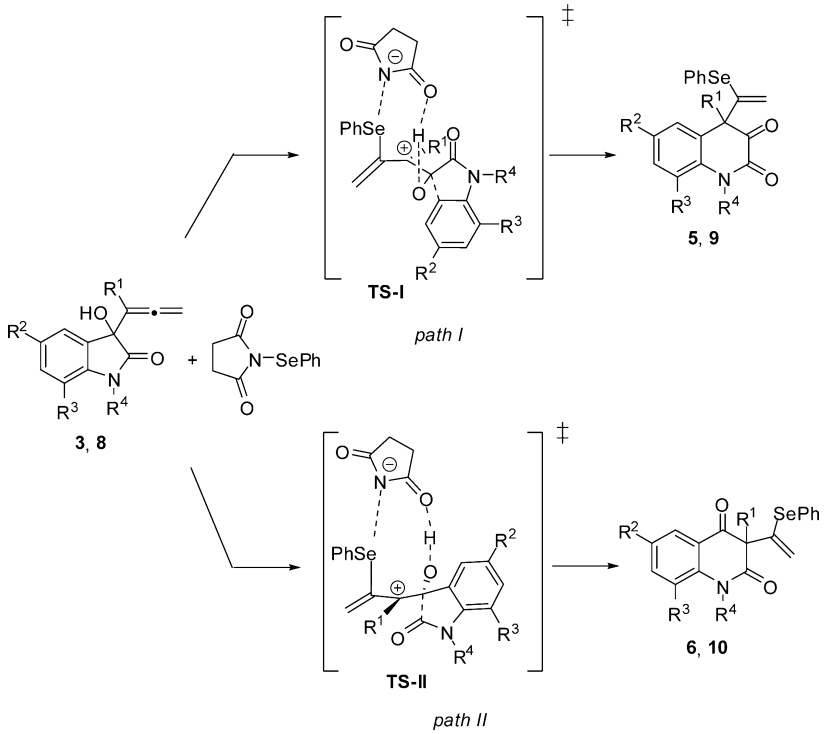
Scheme 3. Reaction of Indolinone-Tethered Allenols 3 and 8 with NPSP under Gold Catalysis[a]



[a]Conditions: (i) NPSP, 5 mol % $AuCl_3$, CH_2Cl_2, rt, **3a**: 1 h; **3b**: 2 h, **3c**: 1 h; **3d**: 1 h, **3e**: 2 h; **8a**: 2 h; **8b**: 1 h, **8c**: 1 h. PMP = 4-$MeOC_6H_4$. NPSP = *N*-phenylselenophthalimide.

Scheme 4. Mechanistic Explanation for the Ring Expansion of 2-Indolinone-Tethered Allenols through Reaction with NPSP



NPSP case, while an intermolecular attack of the bromide counteranion is observed for PhSeBr.

The structural assignments of selenylquinoline-2,3-dione **5a** and selenyloxindole **7b** were confirmed by means of an X-ray diffraction analysis (Supplementary Figures S1 and S2).[13,14] The intermolecular contact O(1)···H(2) in compound **7b** may indicate hydrogen bonding; these contacts link the molecules into dimers (Supplementary Figure S3).

Having established the feasibility of the reaction for *N*-methyl oxindoles **3**, we investigated the generality of the protocol for allenic *NH*-oxindoles **8a–c** under the optimized reaction conditions. In general, the lack of substitution at the indole nitrogen gave both selectivity and yields very comparable to those attained using *N*-methyl derivatives and could be considered excellent in the context of constructing multiple bonds in a selective manner. When using the methyl-substituted allenol **8a**, the ring enlargement/spirocyclization ratio was 88:12. Gratifyingly, allenols **8b** and **8c** containing an aromatic motif were completely and exclusively converted to selenylquinoline-2,3-diones **9b** and **9c**, spirocycle formation being suppressed (Scheme 2).

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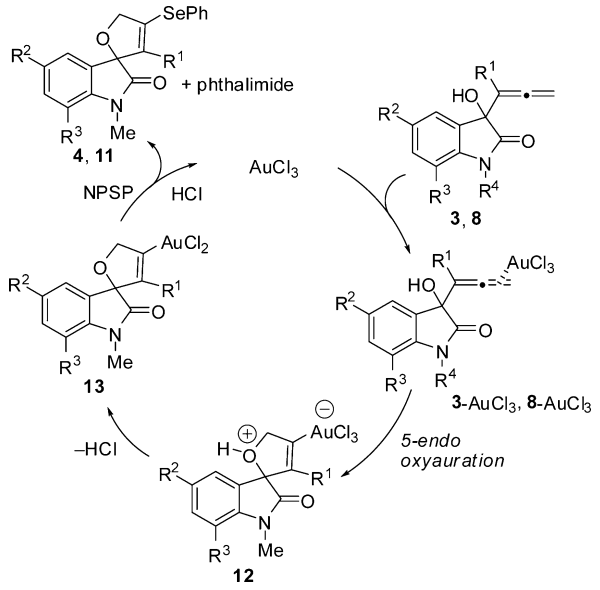
The use of gold salts has gained a lot of attention in the recent times because of their powerful soft Lewis acidic nature.[15] In particular, gold activation of allenes toward attacks by oxygen nucleophiles is an important C−O bond-forming reaction.[16] However, gold-catalyzed protocols for the reaction of allenols in the presence of selenylated reagents have not yet been available. Despite the anticipated difficulty, we decided to test the reactivity of our allenic 2-indolinones **3** and **8** with NPSP under gold-catalyzed conditions. The stage was thus set for the Au(III)-catalyzed reaction of 2-indolinone-tethered allenol **3a** with NPSP. Preliminary studies demonstrated that the combined use of NPSP and catalytic amounts of both $AuCl_3$ and PTSA gave rise to messy reactions. When allenol **3a** was treated with NPSP in dichloromethane at room temperature using 5 mol % of $AuCl_3$, a clean and fast reaction occurred to give selenyloxindole **4a** (major product) and selenylquinoline-2,3-dione **5a** (minor product). Similar results were obtained for the rest of allenols **3** and **8** (Scheme 3); the selenocycloetherification was the major or exclusive path in most cases. Probably, the presence of the phenyl group (R^1 = Ph) at the allene moiety forms a benzylic-like carbocation that is more prone to suffer rearrangement in the case of *NH*-indolone **8b** than for **3b**, because the ring opening of *NH*-indolones is normally easier than the cleavage of *N*-methyl indolones. Interestingly, replacement of PTSA by $AuCl_3$ resulted in a much faster reaction favoring spirocyclization, with both the acceleration and the selectivity being interesting issues.

For the NPSP-promoted ring expansion of indolinone-tethered allenols **3** and **8**, two regioisomeric reaction pathways presenting a one-step mechanism may be considered. They are related to the migration of the aryl group, *path I*, or the migration of carbonyl group, *path II*, along the ring expansion (Scheme 4). These NPSP-promoted ring expansions involve two distinct processes: (i) addition of $PhSe^+$ cation from NPSP to the proximal allenic double bond and (ii) a ring expansion. Therefore, two regioisomeric TSs for the reaction of oxindoles **3** and **8**, **TS-I** and **TS-II**, and the corresponding products have been depicted in Supplementary Scheme S4. The addition of $PhSe^+$ cation to the central sp carbon atom of the allene group forms a carbocationic sp^2 center, which induces the concomitant ring expansion, the migration of the phenyl group being favored over the migration of the carbonyl one.

A possible pathway for the achievement of spirocyclic selenooxindoles **4** and **11** from allenols **3** and **8** may initially involve the formation of the complexes **3**-$AuCl_3$ and **8**-$AuCl_3$ through coordination of the gold trichloride to the distal allenic double bond. Next, regioselective 5-*endo* oxyauration forms zwitterionic species **12**. Loss of HCl generates neutral species **13**, which followed by electrophilic capture of the σ-gold species (selenolysis of the carbon−gold bond) affords spirocycles **4** and **11** and regenerates the gold catalyst (Scheme 5). The fact that related metal salts such as $InCl_3$ or $FeCl_3$ were not effective for the selenoetherification sequence ruled out the hypothesis of simple Lewis acid catalysis, with the gold salt $AuCl_3$ activating the allene group. With the aim of trapping the organogold intermediate to confirm the mechanism of this reaction, we performed studies with water. Under otherwise identical conditions, but with the addition of 2 equiv of H_2O, selenoetherification reaction of 2-indolinone-tethered allenol **3d** with NPSP catalyzed by $AuCl_3$ in dichloromethane afforded **4d** (50%) accompanied by **14** in 10% yield, indicating that a hydrogen atom was incorporated at the alkenyl carbon

Scheme 5. Mechanistic Explanation for the Gold-Catalyzed Selenoetherification of 2-Indolinone-Tethered Allenols through Reaction with NPSP



(Supplementary Scheme S1). The fact that the $AuCl_3$-catalyzed conversion of allenol **3d** into spirocycle **4d** in the presence of 2 equiv of H_2O afforded **14** suggests that protonolysis of the carbon−gold in species **13** has occurred.

As the combination of two different heterocycles within the same molecule is known to enhance biological activity,[17] a biological evaluation of representative compounds of types **2**, **4**, and **5** (Supplementary Figure S4) was next planned . The cytotoxicity of the mentioned compounds was examined in the human cancer cell line HL-60. The results clearly show that there is significant difference between the three series of compounds. Interestingly, all compounds **2** showed higher toxicity toward HL-60 cells than compounds **4a** and **5a** (Supplementary Table S1). The cytotoxicity of the mentioned compounds **2a−2d** was examined in four different cancer cell lines, namely, HL-60 (human promyelocytic leukemia), HT-1080 (human fibrosarcoma), HT-29 (human colon adenocarcinoma), and MDA-MB-231 (human breast carcinoma). The results of this investigation are summarized in Supplementart Table S1. Compounds **2** showed typical dose−response curves for all the cell lines assayed, with a sharp decrease of cell survival at concentrations that are close to the IC_{50} values (Supplementary Figures S5−S8, Tables S2−S5). Data indicate that, in the seleno β-lactam group of compounds, **2a** and **2c** exhibited the higher cytotoxic activity for all cell types. The best results were obtained with **2a**, which showed values of IC_{50} around 5 μg/mL for the leukemia, fibrosarcoma, and breast carcinoma cell lines. On the contrary, compound **2d** was the least active compound for all cell lines tested. This could be due to a lower solubility of this compound, since some crystals appeared in the assay wells throughout the experiment (Supplementary Figure S9).

In conclusion, an unprecedented and divergent preparation of spirocyclic selenolactams and selenoquinolone derivatives by reaction of lactam-tethered allenols with selenenylating reagents has been developed. Chemoselectivity (oxycyclization versus ring expansion) control in the reaction of lactam-tethered allenols can be achieved through the choice of both

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reagents and substrates. These selenofunctionalization reactions have been developed experimentally, and the biological activity of some of the synthesized heterocycles has additionally been evaluated in four cancer cell lines (see Supporting Information).

EXPERIMENTAL SECTION

General Methods. ^{1}H NMR and ^{13}C NMR spectra were recorded on 700, 500, 300, or 200 MHz spectrometers. NMR spectra were recorded in $CDCl_3$ solutions, except when otherwise stated. Chemical shifts are given in ppm relative to TMS (^{1}H, 0.0 ppm), or $CDCl_3$ (^{13}C, 76.9 ppm). Low and high resolution mass spectra were taken using the electronic impact (EI) or electrospray modes (ES) unless otherwise stated. Specific rotation $[\alpha]_D$ is given in 10^{-1} deg cm^2 g^{-1} at 20 °C, and the concentration (c) is expressed in grams per 100 mL. All commercially available compounds were used without further purification.

Materials and Methods for the Biological Evaluation. *Cell Culture.* Compounds **2**, **4**, and **5** were dissolved in dimethylsufoxide (DMSO) and stored at −20 °C until use. All cancer cell lines used in this study were obtained from the American Type Culture Collection (ATCC). Human fibrosarcoma HT-1080 cells were maintained in Dulbecco's modified Eagle's medium (DMEM) containing glucose (4.5 g/L), glutamine (2 mM), penicillin (50 IU/mL), streptomycin (50 μg/mL), and amphotericin (1.25 μg/mL) supplemented with 10% FBS. Human colon adenocarcinoma HT-29 cells were maintained in McCoy's 5A medium containing glutamine (2 mM), penicillin (50 IU/mL), streptomycin (50 μg/mL), and amphotericin (1.25 μg/mL) supplemented with 10% FBS. Human breast cancer carcinoma MDA-MB-231 and human promyelocytic leukemia HL-60 cells were maintained in RPMI1640 medium containing glutamine (2 mM), penicillin (50 IU/mL), streptomycin (50 μg/mL), and amphotericin (1.25 μg/mL) supplemented with 10% and 20% FBS, respectively.

Cytotoxicity Assay. The 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide dye reduction assay was performed in 96-well microplates by using the Mosmann's method [Mosmann, T. *J. Immunol. Methods* **1983**, *65*, 55]. Here, 2×10^3 tumor cells in a total volume of 100 μL of their respective growth media were incubated with serial dilutions of the tested compounds. After 3 days of incubation (37 °C, 5% CO_2 in a humid atmosphere), 10 μL of MTT (5 mg/mL in PBS) was added to each well, and the plate was incubated for a further 4 h (37 °C). The resulting formazan was dissolved in 150 μL of 0.04 N HCl-2 propanol and read at 550 nm. All determinations were carried out in triplicate. IC_{50} values were calculated from semilogarithmic dose−response plots as the concentration of compound yielding 50% cell survival.

General Experimental Procedures for the Synthesis of Organoselenium Compounds. *Procedure A. Reaction between Allenols **1** or **3** and N-Phenylselenophthalimide.* To a solution of the appropriate allenols **1** or **3** (0.15 mmol) in dichloromethane were sequentially added *N*-phenylselenophthalimide (0.195 mmol) and *p*-toluenesulphonic acid monohydrate (0.0225 mmol) under argon. The reaction mixture was stirred at RT until the starting material disappeared as indicated by TLC. Saturated aqueous sodium hydrogen carbonate (1.5 mL) was added to the reaction mixture, before being partitioned between dichloromethane and water. The organic extract was washed with brine, dried ($MgSO_4$), concentrated under vacuum, and purified by flash column chromatography eluting with ethyl acetate/hexanes mixtures or dichloromethane/ethyl acetate mixtures. Spectroscopic and analytical data for pure forms of compounds **4**, **5**, **6**, and **7** follow.

*Procedure B. Reaction between Allenols **3** and N-Phenylselenyl Bromide.* To a solution of the corresponding allenol **3** (0.14 mmol) in dichloromethane (2.8 mL) was added PhSeBr (0.21 mmol) under argon. The reaction mixture was stirred at RT until the starting material disappeared as indicated by TLC. Saturated aqueous sodium hydrogen carbonate (1.5 mL) was added to the reaction mixture, before being partitioned between dichloromethane and water. The organic extract was washed with brine, dried ($MgSO_4$), concentrated under vacuum, and purified by flash column chromatography eluting with ethyl acetate/hexanes mixtures.

*Procedure C. Reaction between Allenols **3** and Diphenyl Diselenide.* To a solution of the corresponding allenol **3** (0.18 mmol) in dichloroethane (1.5 mL) were sequentially added PhSeSePh (0.18 mmol), (diacetoxy)iodobenzene (0.36 mmol), and water (0.18 mmol). The reaction mixture was stirred at 40 °C until the starting material disappeared as indicated by TLC. The reaction was concentrated under vacuum and purified by flash column chromatography eluting with ethyl acetate/hexanes mixtures.

*Procedure D. Gold-Catalyzed Reaction between Allenols **3** and N-Phenylselenophthalimide.* A solution of *N*-phenylselenophthalimide (0.20 mmol) and $AuCl_3$ (0.008 mmol) in dichloromethane (4 mL) under argon was stirred for 5 min. Then, the appropriate allenol **3** (0.15 mmol) was added, and the resulting mixture was stirred at RT until the starting material disappeared as indicated by TLC. Saturated aqueous sodium hydrogen carbonate (1.5 mL) was added to the reaction mixture, before it was partitioned between dichloromethane and water. The organic extract was washed with brine, dried ($MgSO_4$), concentrated under vacuum, and purified by flash column chromatography eluting with ethyl acetate/hexanes mixtures or dichloromethane/ethyl acetate mixtures.

Cyclization of Allenol 3a. Preparation of Spirocycle 4a, Quinoline-2,3-dione 5a, and Quinoline-2,4-dione 6a. Procedure A. From 193 mg (0.90 mmol) of allenol **3a** and after chromatography of the residue using dichloromethane/ethyl acetate (98:2) as eluent, 58 mg (17%) of the less polar compound **6a**, 186 mg (56%) of compound **5a** (intermediate polarity), and 87 mg (26%) of the more polar compound **4a** were obtained.

Cyclization of Allenol 3a. Preparation of Spirocyclic Seleno Indolone 4a. Procedure B. From 30 mg (0.14 mmol) of allenol **3a** and after chromatography of the residue using hexanes/ethyl acetate (2:1) as eluent, the procedure gave compound **4a** (36 mg, 71%) as a colorless solid: mp 163−165 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 7.50 (d, J = 7.7 Hz, 2H), 7.26 (m, 5H), 7.07 (t, J = 7.5 Hz, 1H), 6.81 (d, J = 7.7 Hz, 1H), 4.94 and 4.78 (dq, J = 11.8, 2.0 Hz, each 1H), 3.18 (s, 3H), 1.50 (t, J = 2.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ 174.9, 143.9, 139.0, 131.8, 130.3, 129.4, 128.1, 127.8, 127.3, 124.5, 124.4, 123.2, 108.4, 93.2, 79.9, 26.3, 11.3; IR (CH_2Cl_2) ν 1725 cm^{-1}; HRMS (ES) calcd for $C_{19}H_{17}NO_2Se$ $[M + H]^+$ 372.0503, found 372.0508.

Cyclization of Allenol 3a. Procedure C. From 40 mg (0.18 mmol) of allenol **3a** and after chromatography of the residue using hexanes/ethyl acetate (3:1) as eluent, the procedure gave gave compound **4a** (40 mg, 60%).

Cyclization of Allenol 3a. Preparation of Spirocycle 4a and Quinoline-2,3-dione 5a. Procedure D. From 30 mg (0.14 mmol) of allenol **3a** and after chromatography of the residue using hexanes/ethyl acetate (2:1) as eluent, 27 mg (52%) of the less polar compound **4a** and 10 mg (19%) of the more polar compound **5a** were obtained.

Spirocycle 4a. Colorless solid; mp 163−165 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 7.50 (d, J = 7.7 Hz, 2H), 7.26 (m, 5H), 7.07 (t, J = 7.5 Hz, 1H), 6.81 (d, J = 7.7 Hz, 1H), 4.94 and 4.78 (dq, J = 11.8, 2.0 Hz, each 1H), 3.18 (s, 3H), 1.50 (t, J = 2.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ 174.9, 143.9, 139.0, 131.8, 130.3, 129.4, 128.1, 127.8, 127.3, 124.5, 124.4, 123.2, 108.4, 93.2, 79.9, 26.3, 11.3; IR (CH_2Cl_2) ν 1725 cm^{-1}; HRMS (ES) calcd for $C_{19}H_{17}NO_2Se$ $[M + H]^+$ 372.0503, found 372.0508.

Quinoline-2,3-dione 5a. Colorless solid; mp 219−221 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 7.80 and 7.29 (m, each 4H), 7.01 (d, J = 8.8 Hz, 1H), 5.56 and 5.23 (d, J = 2.1 Hz, each 1H), 3.44 (s, 3H), 1.78 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ 191.7, 167.8, 157.3, 143.7, 138.3, 135.5, 134.3, 132.6, 129.7, 129.4, 128.5, 128.0, 124.0, 123.5, 120.1, 115.4, 59.1, 30.0, 21.1; IR (CH_2Cl_2) ν 3202, 1774, 1746, 1370 cm^{-1}; HRMS (ES) calcd for $C_{19}H_{17}NO_2Se$ $[M + H]^+$ 372.0503, found 372.0503.

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Quinoline-2,4-dione 6a. Pale yellow oil; ^{1}H NMR (700 MHz, $CDCl_3$, 25 °C) δ 7.95 (d, J = 7.7 Hz, 1H), 7.62 (m, 1H), 7.45 (d, J = 7.7 Hz, 1H), 7.20 (m, 5H), 7.11 (d, J = 7.7 Hz, 1H), 5.93 and 5.55 (d, J = 1.4 Hz, each 1H), 3.39 (s, 3H), 1.71 (s, 3H); ^{13}C NMR (176 MHz, $CDCl_3$, 25 °C) δ 194.2, 170.9, 142.9, 139.3, 135.9, 134.3, 129.4, 129.0, 128.4, 127.9, 123.1, 122.7, 120.4, 114.7, 64.6, 29.9, 22.6; IR (CH_2Cl_2) ν 2931, 1698, 1600, 1471 cm^{-1}; HRMS (ES) calcd for $C_{19}H_{17}NO_2Se$ $[M + H]^+$ 372.0503, found 372.0501.

Cyclization of Allenol 3b. Procedure A. From 30 mg (0.11 mmol) of allenol **3b** and after chromatography of the residue using hexanes/ethyl acetate (3:1) as eluent, the procedure gave compound **5b** (37 mg, 79%).

Cyclization of Allenol 3b. Procedure B. From 27 mg (0.09 mmol) of allenol **3b** and after chromatography of the residue using hexanes/ethyl acetate (2:1) as eluent, the procedure gave compound **7b** (26 mg, 56%).

Cyclization of Allenol 3b. Preparation of Spirocycle 4b, Quinoline-2,3-dione 5b, and Quinoline-2,4-dione 6b. Procedure D. From 31 mg (0.11 mmol) of allenol **3b** and after chromatography of the residue using hexanes/ethyl acetate (5:1) as eluent, 1.8 mg (4%) of the less polar compound **6b**, 27 mg (57%) of compound **4b** (intermediate polarity), and 4 mg (9%) of the more polar compound **5b** were obtained.

Spirocycle 4b. Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 7.65 (m, 2H), 7.33 (m, 5H), 7.18 (m, 3H), 7.07 (t, J = 7.9 Hz, 1H), 6.97 (m, 2H), 6.72 (d, J = 7.9 Hz, 1H), 5.01 and 4.83 (d, J = 12.5 Hz, each 1H), 3.10 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ 174.7, 143.9, 137.7, 134.3, 131.9, 130.4, 129.5, 129.3, 128.3, 128.2, 128.1, 128.0, 126.4, 124.9, 123.1, 108.4, 93.7, 79.9, 26.2; IR (CH_2Cl_2) ν 1725 cm^{-1}; HRMS (ES) calcd for $C_{24}H_{19}NO_2Se$ $[M + H]^+$ 434.0659, found 434.0644.

Quinoline-2,3-dione 5b. Colorless solid; mp 153−155 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 7.87, 7.77, and 7.65 (m, each 2H), 7.48 (t, J = 8.5 Hz, 1H), 7. Nineteen (m, 7H), 5.59 and 5.36 (d, J = 1.5 Hz, each 1H), 3.40 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ 189.2, 167.8, 156.5, 142.3, 138.2, 135.7, 135.2, 134.2, 132.6, 130.8, 129.9, 129.6, 129.3, 128.8, 128.7, 128.5, 125.2, 123.8, 123.5, 115.7, 70.8, 30.2; IR (CH_2Cl_2) ν 3205, 1747, 1686, 1371 cm^{-1}; HRMS (ES) calcd for $C_{24}H_{19}NO_2Se$ $[M + H]^+$ 434.0659, found 434.0667.

Quinoline-2,4-dione 6b. Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 8.03 (d, J = 7.7 Hz, 1H), 7.77 (m, 1H), 7.56 (m, 1H), 7.30 (m, 7H), 7.14 (t, J = 7.3 Hz, 1H), 7.06 (d, J = 8.6 Hz, 1H), 5.70 and 5.23 (d, J = 1.0 Hz, each 1H), 3.55 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$, 25 °C) δ 192.8, 169.4, 142.5, 140.5, 135.8, 134.3, 133.8, 131.4, 129.1, 129.0, 128.9, 128.6, 128.3, 128.2, 127.7, 127.5, 127.2, 123.2, 121.5, 114.8, 53.4, 30.4; IR (CH_2Cl_2) ν 1698, 1660, 1351 cm^{-1}; HRMS (ES) calcd for $C_{24}H_{19}NO_2Se$ $[M + H]^+$ 434.0644, found 434.0644.

Quinoline-2,3-dione 5c. Procedure A. From 23 mg (0.07 mmol) of allenol **3c** and after chromatography of the residue using hexanes/ethyl acetate (2:1) as eluent, the procedure gave compound **5c** (21 mg, 65%) as a pale yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 7.81 (d, J = 9.0 Hz, 2H), 7.65 (m, 2H), 7.33 (m, 7H), 6.92 (d, J = 9.0 Hz, 2H), 6.13 and 5.66 (d, J = 1.1 Hz, each 1H), 5.30 (s, 3H), 3.87 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ 193.2, 165.7, 163.4, 159.5, 143.5, 137.9, 136.5, 132.0, 131.7, 131.4, 129.6, 129.1, 128.9, 127.7, 127.3, 124.6, 113.6, 77.1, 55.4, 25.6; IR (CH_2Cl_2) ν 3205, 1747, 1686, 1371 cm^{-1}; HRMS (ES) calcd for $C_{25}H_{21}NO_3Se$ $[M + H_2O + K]^+$ 520.0429, found 520.0443.

Cyclization of Allenol 3c. Procedure D. From 31 mg (0.10 mmol) of allenol **3c** and after chromatography of the residue using dichloromethane/ethyl acetate (98:2) as eluent, the procedure gave compound **4c** (16 mg, 35%).

Spirocycle 4c. Colorless solid; mp 73−75 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 7.88 (m, 2H), 7.77 (m, 2H), 7.63 (m, 2H), 7.33 (m, 3H), 7.08 (t, J = 7.5 Hz, 1H), 6.90 (d, J = 8.9 Hz, 1H), 6.71 (m, 2H), 5.00 and 4.82 (d, J = 12.4 Hz, each 1H), 3.75 (s, 3H), 3.13 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ 174.8, 159.4, 143.9, 137.7, 134.3, 134.0, 132.6, 130.4, 129.3, 129.2, 128.4, 128.3, 128.2, 126.7, 124.8, 124.2, 123.6, 123.1, 113.7, 108.4, 93.4, 79.8, 55.0, 26.3; IR ($CHCl_3$) ν 1725 cm^{-1}; HRMS (ES) calcd for $C_{25}H_{21}NO_3Se$ $[M + H]^+$ 464.0765, found 464.0748.

Cyclization of Allenol 3d. Procedure A. From 27 mg (0.11 mmol) of allenol **3d** and after chromatography of the residue using dichloromethane/ethyl acetate (99:1) as eluent, the procedure gave compound **4d** (19 mg, 44%).

Cyclization of Allenol 3d. Preparation of Spirocycle 4d and Selenooxindole 7d. Procedure B. From 30 mg (0.12 mmol) of allenol **3d** and after chromatography of the residue using dichloromethane/ethyl acetate (9:1) as eluent, the procedure gave an isomeric mixture (90:10) of nonseparable compounds **4d** and **7d** (31.5 mg, 64%).

Cyclization of allenol 3d. Procedure D. From 25 mg (0.10 mmol) of allenol **3d** and after chromatography of the residue using hexanes/ethyl acetate (3:1) as eluent, the procedure gave compound **4d** (21.5 mg, 53%).

Spirocycle 4d. Colorless solid; mp 209−211 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 7.54 (m, 2H), 7.26 (m, 5H), 6.77 (d, J = 8.4 Hz, 1H), 4.95 and 4.79 (dd, J = 11.9, 2.0 Hz, each 1H), 3.20 (s, 3H), 1.53 (t, J = 2.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ 174.5, 142.4, 137.7, 134.3, 132.5, 132.2, 130.2, 129.4, 128.7, 127.5, 125.0, 123.6, 109.4, 93.1, 80.1, 26.5, 11.2; IR (CH_2Cl_2) ν 1748 cm^{-1}; HRMS (ES) calcd for $C_{19}H_{16}ClNO_2Se$ $[M + H]^+$ 406.0113, found 406.0093.

Cyclization of Allenol 3e. Preparation of Spirocycle 4e, Quinoline-2,3-dione 5e, and Quinoline-2,4-dione 6e. Procedure A. From 30 mg (0.12 mmol) of allenol **3e** and after chromatography of the residue using hexanes/ethyl acetate (7:1) as eluent, 12 mg (25%) of the less polar compound **4e**, 2.5 mg (5%) of compound **6e** (intermediate polarity), and 5 mg (10%) of the more polar compound **5e** were obtained.

Cyclization of Allenol 3e. Preparation of Spirocycle 4e and Selenooxindole 7e. Procedure B. From 30 mg (0.12 mmol) of allenol **3e** and after chromatography of the residue using dichloromethane/ethyl acetate (98:2) as eluent, the procedure gave an isomeric mixture (70:30) of nonseparable compounds **4e** and **7e** (32.5 mg, 62%).

Cyclization of Allenol 3e. Procedure D. From 40 mg (0.16 mmol) of allenol **3e** and after chromatography of the residue using hexanes/ethyl acetate (5:1) as eluent, the procedure gave compound **4e** (30.5 mg, 47%).

Spirocycle 4e. Colorless solid; mp 85−87 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 7.53 (m, 2H), 7.30 (m, 4H), 7.10 (dd, J = 7.3, 1.3 Hz, 1H), 7.00 (m, 1H), 4.95 and 4.79 (dq, J = 11.9, 2.0 Hz, each 1H), 3.58 (s, 3H), 1.53 (t, J = 2.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ 175.2, 139.8, 138.2, 132.6, 132.1, 130.8, 129.4, 127.9, 127.5, 125.0, 124.0, 123.1, 115.9, 92.6, 80.0, 29.7, 11.2; IR (CH_2Cl_2) ν 1732 cm^{-1}; HRMS (ES) calcd for $C_{19}H_{16}ClNO_2Se$ $[M + H]^+$ 406.0113, found 406.0102.

Quinoline-2,3-dione 5e. Pale yellow solid; mp 94−96 °C; ^{1}H NMR (700 MHz, $CDCl_3$, 25 °C) δ 7.45 (m, 3H), 7.32 (m, 4H), 7.20 (t, J = 7.9 Hz, 1H), 5.42 and 5.09 (d, J = 2.1 Hz, each 1H), 3.49 (s, 3H), 1.75 (s, 3H); ^{13}C NMR (176 MHz, $CDCl_3$, 25 °C) δ 191.8, 161.0, 144.0, 137.4, 136.3, 132.5, 130.6, 129.6, 129.0, 127.6, 126.1, 125.8, 125.3, 118.8, 58.9, 36.4, 19.7; IR (CH_2Cl_2) ν 3205, 1747, 1686, 1371 cm^{-1}; HRMS (ES) calcd for $C_{19}H_{16}ClNO_2Se$ $[M + H]^+$ 406.0113, found 406.0105.

Quinoline-2,4-dione 6e. Colorless oil; ^{1}H NMR (700 MHz, $CDCl_3$, 25 °C) δ 7.61 and 7.57 (dd, J = 8.1, 1.4 Hz, each 1H), 7.34 (d, J = 8.1 Hz, 2H), 7.21 (m, 2H), 7.11 (m, 2H), 5.67 and 5.16 (d, J = 1.5 Hz, each 1H), 3.55 (s, 3H), 1.66 (s, 3H); ^{13}C NMR (176 MHz, $CDCl_3$, 25 °C) δ 194.5, 170.6, 141.4, 140.6, 137.3, 134.6, 129.3, 128.8, 128.2, 126.8, 126.2, 125.2, 122.8, 120.9, 65.8, 36.9, 19.5; IR (CH_2Cl_2) ν 3205 cm^{-1}; HRMS (ES) calcd for $C_{19}H_{16}ClNO_2Se$ $[M + H]^+$ 406.0113, found 406.0120.

Selenyloxindole 7b. Procedure B. From 27 mg (0.09 mmol) of allenol **3b** and after chromatography of the residue using hexanes/ethyl acetate (2:1) as eluent, the procedure gave compound **7b** (26 mg, 56%) as a colorless solid: mp 166−168 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 7.69 (d, J = 7.3 Hz, 1H), 7.56 (d, J = 8.0 Hz, 1H), 7.24 (m, 8H), 6.99 (t, J = 7.8 Hz, 1H), 6.62 (d, J = 6.6 Hz, 1H), 6.32

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(d, J = 7.8 Hz, 1H), 4.89 and 4.62 (d, J = 10.2 Hz, each 1H), 2.84 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ 178.2, 146.5, 144.4, 140.9, 139.0, 138.3, 133.4, 132.9, 132.2, 131.9, 131.6, 131.4, 131.3, 131.0, 130.9, 130.5, 127.9, 126.5, 111.4, 85.1, 34.2, 28.9; IR (CH_2Cl_2) ν 1701, 1579, 1434, 1376 cm^{-1}; HRMS (ES) calcd for $C_{24}H_{20}BrNO_2Se$ [(M + H) − H_2O]$^+$ 495.9815, found 495.9818.

Cyclization of Allenol 8a. Preparation of Quinoline-2,3-dione 9a, Quinoline-2,4-dione 10a, and Spirocycle 11a. Procedure A. From 28 mg (0.13 mmol) of allenol **8a** and after chromatography of the residue using hexanes/ethyl acetate (2:1) as eluent, 4.5 mg (9%) of the less polar compound **11a**, 12 mg (23%) of compound **10a** (intermediate polarity), and 21 mg (46%) of the more polar compound **9a** were obtained.

Cyclization of Allenol 8a. Preparation of Quinoline-2,3-dione 9a, Quinoline-2,4-dione 10a, and Spirocycle 11a. Procedure D. From 25 mg (0.12 mmol) of allenol **8a** and after chromatography of the residue using hexanes/ethyl acetate (2:1) as eluent, 23 mg (54%) of the less polar compound **11a**, 3.5 mg (8%) of compound **10a** (intermediate polarity), and 5 mg (12%) of the more polar compound **9a**, were obtained.

Quinoline-2,3-dione 9a. Pale yellow solid; mp 159−161 °C; ^{1}H NMR (700 MHz, $CDCl_3$, 25 °C) δ 9.07 (s, 1H), 7.88 (m, 1H), 7.77 (m, 1H), 7.34 (m, 5H), 7.15 (t, J = 7.7 Hz, 1H), 6.92 (d, J = 7.7 Hz, 1H), 5.72 (s, 1H), 5.33 (s, 1H), 1.77 (s, 3H); ^{13}C NMR (176 MHz, $CDCl_3$, 25 °C) δ 192.2, 167.8, 155.8, 143.2, 135.5, 134.3, 129.6, 129.4, 128.7, 128.5, 128.4, 126.3, 124.3, 123.6, 119.8, 116.5, 60.1, 23.0; IR (CH_2Cl_2) ν 3202, 1774, 1746, 1370 cm^{-1}; HRMS (ES) calcd for $C_{18}H_{15}NO_2Se$ [M + H]$^+$ 358.0346, found 358.0336.

Quinoline-2,4-dione 10a. Colorless solid; mp 221−223 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 8.97 (br s, 1H), 7.89 (m, 2H), 7.77 (m, 2H), 7.53 (m, 2H), 7.16 (m, 2H), 6.97 (d, J = 7.7 Hz, 1H), 6.05 and 5.65 (d, J = 1.5 Hz, each 1H), 1.73 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ 194.0, 172.5, 168.0, 140.4, 138.4, 136.1, 134.3, 132.5, 129.0, 128.3, 127.9, 123.7, 123.6, 123.3, 116.1, 64.7, 22.7; IR (CH_2Cl_2) ν 3202, 1748, 1379, 1306 cm^{-1}; HRMS (ES) calcd for $C_{18}H_{15}NO_2Se$ [M + H]$^+$ 358.0346, found 358.0334.

Spirocycle 11a. Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 8.90 (br s, 1H), 7.88 (m, 1H), 7.77 (m, 2H), 7.53 (d, J = 6.9 Hz, 1H), 7.31 (m, 2H), 7.21 (d, J = 7.5 Hz, 1H), 7.08 (t, J = 7.5 Hz, 1H), 6.88 (d, J = 7.5 Hz, 1H),), 4.97 and 4.83 (dd, J = 12.0, 1.9 Hz, each 1H), 1.58 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ 176.8, 140.7, 138.6, 135.5, 134.3, 132.5, 132.0, 130.3, 129.4, 128.1, 127.4, 124.9, 124.7, 123.5, 110.2, 93.5, 80.0, 11.2; IR (CH_2Cl_2) ν 1725 cm^{-1}; HRMS (ES) calcd for $C_{18}H_{15}NO_2Se$ [M + H]$^+$ 358.0346, found 358.0342.

Cyclization of Allenol 8b. Procedure A. From 26 mg (0.10 mmol) of allenol **8b** and after chromatography of the residue using hexanes/ethyl acetate (2:1) as eluent, the procedure gave compound **9b** (31 mg, 74%).

Cyclization of Allenol 8b. Preparation of Quinoline-2,3-dione 9b, Quinoline-2,4-dione 10b, and Spirocycle 11b. Procedure D. From 30 mg (0.11 mmol) of allenol **8a** and after chromatography of the residue using hexanes/ethyl acetate (3:1) as eluent, 21 mg (46%) of the less polar compound **10b**, 22 mg (48%) of compound **9b** (intermediate polarity), and 3 mg (6%) of the more polar compound **11b** were obtained.

Quinoline-2,3-dione 9b. Colorless solid; mp 177−179 °C; ^{1}H NMR (300 MHz, acetone-d_6, 25 °C) δ 10.14 (br s, 1H), 7.67 (m, 2H), 7.43 (m, 6H), 7.19 (m, 4H), 7.07 (m, 2H), 5.59 and 5.34 (d, J = 1.3 Hz, each 1H); ^{13}C NMR (75 MHz, acetone-d_6, 25 °C) δ 191.5, 169.4, 156.3, 144.0, 136.7, 136.3, 135.1, 134.1, 131.7, 131.3, 130.9, 130.8, 130.4, 129.8, 129.7, 129.6, 125.2, 124.2, 123.9, 117.8, 117.7, 72.9; IR (CH_2Cl_2) ν 3203, 1746, 1698, 1376 cm^{-1}; HRMS (ES) calcd for $C_{23}H_{17}NO_2Se$ [M + H]$^+$ 420.0498, found 420.0503.

Quinoline-2,4-dione 10b. Pale yellow solid; mp 61−63 °C; ^{1}H NMR (300 MHz, acetone-d_6, 25 °C) δ 10.24 (br s, 1H), 7.90 (m, 2H), 7.76 (m, 2H), 7.61 (m, 2H), 7.35 (m, 6H), 7.15 (m, 2H), 5.65 and 5.26 (d, J = 1.0 Hz, each 1H); ^{13}C NMR (75 MHz, acetone-d_6, 25 °C) δ 193.9, 170.4, 142.2, 137.2, 135.5, 135.1, 134.1, 133.9, 133.7, 132.1, 130.3, 130.0, 129.9, 129.8, 129.7, 128.5, 128.3, 128.1, 124.1, 123.9, 117.2, 117.1, 78.4; IR (CH_2Cl_2) ν 3202, 1748, 1379, 1306 cm^{-1}; HRMS (ES) calcd for $C_{23}H_{17}NO_2Se$ [M + H]$^+$ 420.0503, found 420.0484.

Spirocycle 11b. Pale yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 7.48 (m, 13H), 6.67 (d, J = 8.0 Hz, 1H), 4.94 and 4.71 (d, J = 11.3, Hz, each 1H); ^{13}C NMR (175 MHz, $CDCl_3$, 25 °C) δ 176.8, 140.8, 138.9, 138.5, 136.1, 131.5, 130.4, 129.8, 129.3, 129.1, 128.5, 128.2, 127.6, 126.2, 125.4, 123.5, 123.0, 110.3, 90.9, 76.0; IR (CH_2Cl_2) ν 1720 cm^{-1}; HRMS (ES) calcd for $C_{23}H_{17}NO_2Se$ [M + H]$^+$ 420.0510, found 420.0498.

Cyclization of Allenol 8c. Procedure A. From 26 mg (0.09 mmol) of allenol **8c** and after chromatography of the residue using hexanes/ethyl acetate (2:1) as eluent, the procedure gave compound **9c** (35 mg, 89%).

Cyclization of Allenol 8c. Preparation of Quinoline-2,3-dione 9c and Spirocycle 11c. Procedure D. From 26 mg (0.09 mmol) of allenol **8c** and after chromatography of the residue using hexanes/ethyl acetate (2:1) as eluent, 15 mg (36%) of the less polar compound **9c** and 6 mg (15%) of the more polar compound **11c** were obtained.

Quinoline-2,3-dione 9c. Pale yellow solid; mp 197−199 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 8.85 (br s, 1H), 7.82 (m, 7H), 7.47 (t, J = 8.0 Hz, 1H), 7.33 (d, J = 8.9 Hz, 1H), 7.23 (m, 1H), 7.11 (t, J = 7.2 Hz, 1H), 6.85 (m, 2H), 5.75 and 5.38 (d, J = 1.0 Hz, each 1H), 3.75 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ 192.5, 170.8, 167.9, 159.8, 139.9, 139.7, 135.8, 134.3, 133.7, 131.8, 130.2, 129.0, 128.3, 127.6, 127.5, 125.4, 123.7, 123.6, 115.9, 114.3, 77.3, 55.2; IR (CH_2Cl_2) ν 3202, 1748, 1662, 1380 cm^{-1}; HRMS (ES) calcd for $C_{24}H_{19}NO_3Se$ [M + H]$^+$ 450.0608, found 450.0605.

Spirocycle 11c. Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 7.64 (m, 2H), 7.28 (m, 6H), 7.07 (t, J = 7.2 Hz, 1H), 6.94 (m, 2H), 6.72 (m, 2H), 5.00 and 4.82 (d, J = 12.5 Hz, each 1H), 3.73 (s, 3H); ^{13}C NMR (175 MHz, $CDCl_3$, 25 °C) δ 176.5, 159.4, 140.7, 137.1, 135.6, 134.3, 134.2, 132.5, 131.4, 130.4, 129.3, 129.2, 129.1, 128.5, 128.3, 126.5, 125.4, 124.0, 123.3, 113.7, 110.2, 93.5, 79.9, 55.0; IR (CH_2Cl_2) ν 1726 cm^{-1}; HRMS (ES) calcd for $C_{24}H_{19}NO_3Se$ [M + H]$^+$ 450.0608, found 450.0620.

Spirocycle 14. Pale yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 7.30 (dd, J = 8.3, 2.2 Hz, 1H), 7.18 (d, J = 2.2 Hz, 1H), 6.75 (d, J = 8.3 Hz,1H), 5.98 (m, 1H), 4.95 (ddm, J = 31.3, 12.4, 2.0 Hz, 2H), 3.18 (s, 3H), 1.44 (q, J = 2.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ 175.1, 142.5, 135.2, 130.0, 129.9, 128.6, 125.3, 124.9, 109.2, 92.3, 76.5, 26.4, 11.1; IR (CH_2Cl_2) ν 1740 cm^{-1}; HRMS (ES) calcd for $C_{13}H_{13}ClNO_2$ [M + H]$^+$ 250.0635, found 250.0639.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of the ^{1}H NMR and ^{13}C NMR spectra for all new compounds; ORTEP plots for compounds **5a** and **7b**; in vitro dose−response curves of compounds **2a−d**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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(12) The reaction of allenol **3a** with NPSP in the absence of the Brønsted acid additive (PTSA) proceeded to afford the corresponding products **4a**, **5a**, and **6a** in a slightly lower yield. The Brønsted acid present in solution seems to act as a scavenger for the free phthalimide from the NPSP.

(13) X-ray data of **5a**: crystallized from ethyl acetate/*n*-hexane at 20 °C; $C_{19}H_{17}NO_2Se$ (M_r = 370.30); monoclinic; space group = $P2(1)/n$; a = 12.360(2) Å, b = 12.862(3) Å; c = 22.211(4) Å; α = 90°; β = 104.886(4)°; γ = 90°; V = 3412.6(11) Å^3; Z = 8; cd = 1.441 mg m^{-3}; μ = 2.209 mm^{-1}; F(000) = 1504. A transparent crystal of 0.17 × 0.11 × 0.09 mm^3 was used. 6688 [R(int) = 0.0976] independent reflections were collected on a Bruker Smart CCD difractomer using graphite-monochromated Mo Kα radiation (λ = 0.71073 Å) operating at 50 Kv and 30 mA. Data were collected over a hemisphere of the reciprocal space by combination of three exposure sets. Each exposure of 20 s covered 0.3 in ω. The cell parameters were determined and refined by a least-squares fit of all reflections. The first 100 frames were recollected at the end of the data collection to monitor crystal decay, and no appreciable decay was observed. The structure was solved by direct methods and Fourier synthesis and refined by full-matrix least-squares procedures on F^2 (SHELXL-97). All non-hydrogen atoms were refined anisotropically. All hydrogen atoms were included in calculated positions and refined riding on the respective carbon atoms. Final R(Rw) values were R1 = 0.0609, wR2 = 0.1495. CCDC-765453 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via the www.ccdc.cam.ac.uk/data_request/cif (or from The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB21EZ, U.K.; Fax (+44)1223−336033; or deposit@cccdc.cam.ac.uk).

(14) X-ray data of **7b**: crystallized from ethyl acetate/*n*-hexane at 20 °C; $C_{24}H_{20}BrNO_2Se$ (M_r = 513.28); triclinic; space group = P-1; a = 9.2292(13) Å, b = 13.5016(19) Å; c = 18.493(3) Å; α = 72.535(2)°; β = 81.060(3)°; γ = 76.979(3)°; V = 2132.1(5) Å^3; Z = 4; cd = 1.599 mg m^{-3}; μ = 3.655 mm^{-1}; F(000) = 1024. A transparent crystal of 0.21 × 0.10 × 0.07 mm^3 was used. 9841 [R(int) = 0.1727] independent reflections were collected on a Bruker Smart CCD difractomer using graphite-monochromated Mo Kα radiation (λ = 0.71073 Å) operating at 50 Kv and 30 mA. Data were collected over a hemisphere of the reciprocal space by combination of three exposure sets. Each exposure of 20s covered 0.3 in ω. The cell parameter were determined and refined by a least-squares fit of all reflections. The first 100 frames were recollected at the end of the data collection to monitor crystal decay, and no appreciable decay was observed. The structure was solved by direct methods and Fourier synthesis. It was refined by full-matrix least-squares procedures on F^2 (SHELXL-97). All non-hydrogen atoms were refined anisotropically. All hydrogen atoms were included in calculated positions and refined riding on the respective carbon atoms. Final R(Rw) values were R1 = 0.0785, wR2 = 0.1265. CCDC-827677 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via the www.ccdc.cam.ac.uk/data_request/cif (or from The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB21EZ, U.K.; Fax (+44) 1223−336033; or deposit@cccdc.cam.ac.uk).

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