# Antitumor Agents. 233.[1] Lantalucratins A−F, New Cytotoxic Naphthoquinones from *Lantana involucrata*

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In a continuing study to isolate novel antitumor agents from rainforest plants, three new isopropenylfurano-$\beta$-naphthoquinones, designated lantalucratins A (**1**), B (**2**), and C (**3**), and three new isoprenyl-α-naphthoquinones, designated lantalucratins D (**4**), E (**5**), and F (**6**), were isolated from *Lantana involucrata*. Their structures were determined on the basis of NMR and X-ray crystallographic analyses. Compounds **1** and **2** showed cytotoxic activities against various human tumor cell lines, including drug-resistant variants, with $IC_{50}$ values of 1.0−4.9 $\mu$M.

In our continuing collaboration with the National Cancer Institute to discover antitumor agents from rainforest plants, extracts of *Lantana involucrata* showed significant in vitro cytotoxic activity against various human tumor cell lines. Bioactivity-directed fractionation of the $CHCl_3$ extract of the leaves led to the isolation of three new isopropenyl furano-1,2-($\beta$)-naphthoquinones (**1**−**3**) and three new isoprenyl-1,4-(α)-naphthoquinones (**4**−**6**), together with two known isopropenylfuranonaphthoquinones (**7** and **8**). Previously, two *Lantana* species, *L. achyrantifolia* and *L. camara*,[2] were reported to contain furano-1,4-(α)-naphthoquinones, and many furano-α-naphthoquinones have been isolated from various plant sources. However, to date, only four furano-$\beta$-naphthoquinones (**3**−**6**) have been reported from two plant genera, *Streptocarpus* and *Calceolaria*.[3−5] This report deals with the structural determination of six new naphthoquinones, designated lantalucratins A−F (**1**−**6**), and evaluation of cytotoxic activities of the new and known compounds.

## Results and Discussion

Lantalucratin A (**1**) was obtained as dark orange crystals. HRFABMS analysis gave a molecular formula of $C_{16}H_{14}O_4$. No hydroxyl absorption was present in the IR spectrum; however, absorptions at 1682 and 1651 $cm^{-1}$ (ketocarbonyl) and two $^{13}C$ NMR signals at $\delta$ 175.2 and 179.9 indicated that **1** is a quinone. This hypothesis was supported by a pH-dependent color change (acidic, yellow; alkaline, orange). The $^1H$ NMR spectrum showed 1,2,3-trisubstituted benzene ring protons at $\delta$ 7.19, 7.30, and 7.59 (each 1H), an allyl oxymethine at $\delta$ 5.45, isopropenyl methylene protons at $\delta$ 5.01 and 5.13 (each 1H), a methoxy signal at $\delta$ 3.99 (s, 3H), *gem*-methylene protons at $\delta$ 2.91 and 3.26, and isopropenylmethyl protons at $\delta$ 1.79 (s, 3H). The $^{13}C$ NMR spectrum displayed 16 signals including six aromatic and four olefinic signals. These data together with the molecular formula suggested that **1** is an isoporpenylfuranonaphthoquinone. The presence of the isopropenyl group was confirmed by $^1H-^1H$ COSY (H-2 to H-3) and HMBC spectroscopic (H-12 to C-2, -10, and -11) data. The positions of the isopropenyl and methoxy groups were located at C-2 and C-6, respectively, on the basis of HMBC correlations (H-11 and -12 to C-2 and methoxy protons to C-6). Thus, **1** was determined to be 2-isopropenyl-6-methoxufurano-$\beta$-naphthoquinone as shown in Figure 1 from HMBC correlations (H-3 and -9 to C-9b and H-3 to C-4) and by comparison with NMR data of related α-naphthoquinones such as **8** (C-9b for **1**; $\delta_C$ 169.2 ppm and C-3a for **8**; $\delta_C$ 160.8 ppm).[6] The assignments of $^{13}C$ NMR signals are shown in Table 1. In addition to NMR and mass analyses, single-crystal X-ray analysis confirmed the structure for lantalucratin A (**1**) established above.

Lantalucratin B (**2**), red crystals, has a molecular formula of $C_{15}H_{12}O_4$, as shown by HREIMS analysis. The IR spectrum showed absorptions attributed to hydroxy (3490 $cm^{-1}$) and ketocarbonyl (1662, 1645 $cm^{-1}$) groups. $^1H$ and $^{13}C$ NMR spectra of **2** afforded signals similar to those of **1**, except for an additional phenolic proton signal at $\delta$ 11.93 and the disappearance of an *O*-methyl signal observed in **1**. The $^{13}C$ NMR spectrum contained 15 carbon signals including two quinone ketocarbonyl, six aromatic, two olefinic, and isopropenyl signals. The $^1H$ NMR spectrum of **2** displayed 1,2,3-trisubstituted benzene, isopropenyl, *gem*-methylene, and phenolic proton signals. The presence of a 1,2-($\beta$)-naphthoquinone structure and the position of the hydroxyl group were confirmed by HMBC correlations and by comparison with the NMR data of **1**. Thus, **2** was identified as the demethylated analogue of **1**. The structure and NMR assignments of **2** are indicated in Figure 1 and Table 1, respectively.

Lantalucratin C (**3**) was established by ESI-mass and $^1H$ and $^{13}C$ NMR spectral data. The molecular formula $C_{15}H_{12}O_4$ was assigned by HREIMS measurement. The IR spectrum suggested the presence of hydroxyl (3300 $cm^{-1}$) and ketocarbonyl groups (1700 and 1645 $cm^{-1}$). Compounds **3** and **1** showed similar $^1H$ and $^{13}C$ NMR spectra, except for the aromatic ring proton (H-6 to H-9) couplings, suggesting **3** is related structurally to **1**. The $^1H$ NMR spectrum of **3** showed 1,4,5-trisubstituted benzene ring protons at 7.19 (dd, $J$ = 2.4, 8.0 Hz, H-8), 7.46 (d, $J$ = 2.4

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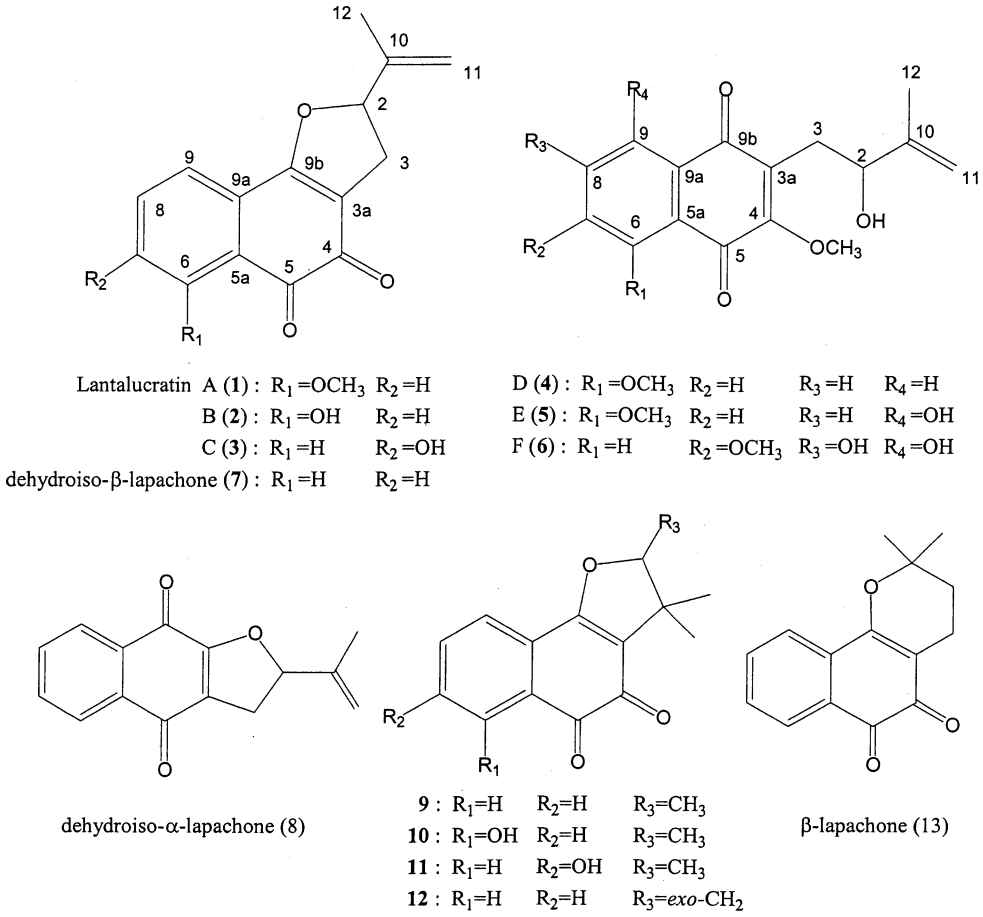


**Figure 1.** Structures of lantalucratins A−D and related compounds.

**Table 1.** $^{13}$C NMR Data for Compounds **1**−**6**

| position | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|
| 2 | 89.3 | 89.8 | 90.2 | 74.8 | 74.7 | 74.6 |
| 3 | 31.1 | 31.0 | 31.6 | 30.2 | 29.6 | 29.6 |
| 3a | 114.5 | 115.2 | 113.3 | 128.8 | 128.5 | 128.5 |
| 4 | 175.2 | 174.8 | 175.5 | 159.6 | 160.0 | 160.1 |
| 5 | 179.9 | 185.2 | 181.6 | 180.1 | 179.2 | 178.9 |
| 5a | 117.8 | 113.4 | 133.8 | 119.8 | 117.1 | 117.2 |
| 6 | 161.8 | 164.5 | 116.9 | 159.4 | 154.0 | 123.6 |
| 7 | 116.8 | 123.4 | 161.8 | 117.3 | 122.0 | 153.0 |
| 8 | 135.8 | 137.6 | 121.2 | 134.9 | 127.0 | 133.2 |
| 9 | 117.1 | 117.5 | 127.2 | 119.1 | 155.8 | 153.6 |
| 9a | 129.1 | 127.1 | 119.8 | 134.0 | 114.0 | 114.2 |
| 9b | 169.2 | 169.2 | 170.2 | 186.4 | 191.2 | 191.3 |
| 10 | 142.0 | 141.8 | 143.8 | 146.9 | 146.9 | 146.9 |
| 11 | 113.5 | 113.9 | 113.3 | 110.5 | 110.6 | 110.6 |
| 12. | 16.7 | 16.8 | 16.9 | 18.1 | 18.0 | 18.1 |
| OMe | 56.3 | | | 61.4 | 61.5 | 61.6 |
| OMe | | | | 56.5 | 56.8 | 56.8 |

Hz, H-6), and 7.60 (d, $J$ = 8.0 Hz, H-9), together with oxymethine, isopropenyl, and *gem*-methylene signals. The $^{13}$C NMR spectrum displayed 15 carbon signals, including two quinone ketocarbonyl, six aromatic, two olefinic, and isopropenyl signals. The position of the phenolic group and a 1,2-(*β*)-naphthoquinone structure were established by HMBC correlations (H-6 to C-5 and H-9 to C-9b) and comparison with the NMR data of **1**, resulting in the determination of structure of **3** as indicated in Figure 1. The $^{13}$C NMR assignments of **3** are shown in Table 1.

Lantalucratin D (**4**) was analyzed for $C_{17}H_{18}O_5$ by HREIMS measurement. The IR spectrum indicated ketocarbonyl and free hydroxyl absorptions at 1668 and 3520 cm$^{-1}$, respectively. The $^1$H NMR spectrum revealed 1,2,3-trisubstututed benzene ring, isopropenyl methylene, *gem*-methylene, one methyl, oxymethine, and two methoxy signals. Seventeen carbon signals in the $^{13}$C NMR spectrum included a benzene ring, two ketocarbonyl, and four olefinic signals. In comparing the spectra of compounds **4** and **1**, one ketocarbonyl signal [$\delta_C$ 180.1 (C-5) for **4**; 179.9 (C-5) for **1**] was analogous, while the other [$\delta_C$ 186.4 (C-9b) for **4**, 175.2 (C-4) for **1**] was not. These data suggested that **4** is a 1,4-(α)-naphthoquinone rather than a 1,2-(*β*)-naphthoquinone. $^1$H−$^1$H COSY and HMBC correlations (Figure 2) were used to establish the identity [−$CH_2CH(OH)C(CH_3)$=$CH_2$] and linkage (C-12 to C-3a) of the isoprenyl group. The ketocarbonyl carbon (C-9b) was positioned between C-3a and C-9a on the basis of HMBC correlations (H-9 and -3 to C-9b; H-8 to C-9a; and H-3 to C-3a and -4). Likewise, the remaining ketocarbonyl carbon (C-5) was connected between C-4 and C-5a. The positions of two methoxy groups were established to be C-4 and C-6 by HMBC correlations. The resulting structure of **4** was determined to be as shown in Figure 1. The $^{13}$C NMR assignments are listed in Table 1.

Lantalucratin E (**5**) was obtained as a red oil and has a molecular formula of $C_{17}H_{18}O_6$, as shown by HREIMS analysis. Absorptions for hydroxyl (3519 cm$^{-1}$) and ketocarbonyl (1665, 1629 cm$^{-1}$) groups were observed in the IR spectrum. The $^1$H and $^{13}$C NMR spectra were similar to those of **4**, suggesting that **5** is a 1,4-(α)-naphthoquinone with an added hydroxyl group. The $^1$H NMR spectrum displayed an *ortho*-coupled benzene, isopropenyl, *gem*-methylene, and two methoxy proton signals. The hydroxyl group was located at C-9 on the basis of HMBC correlations (hydroxyl proton to C-8, -9a, and -9) and the downfield shift of the ketone signal (C-9b, $\delta_C$ 191.2), most likely caused by hydrogen bonding with the phenolic proton. As in **4**, the

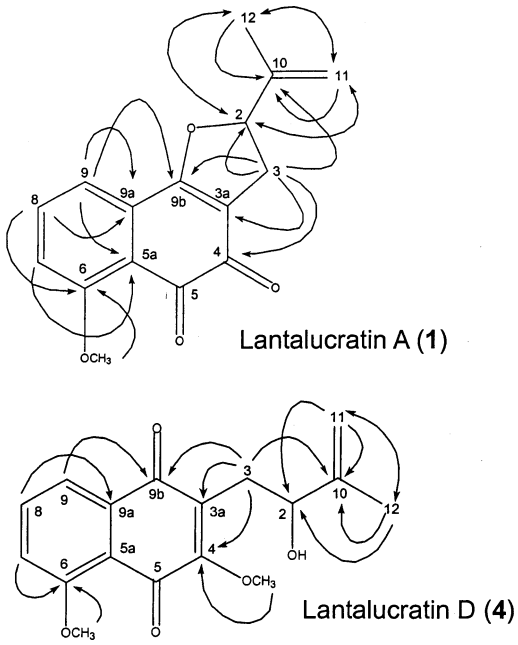


**Figure 2.** HMBC correlations of lantalucratins A (**1**) and D (**4**).

isoprenyl linkage (C-12 to C-3a) and location of the methoxy groups (C-4 and -6) were established by HMBC correlations. Thus, compound **5** was determined to be a C-9 hydroxylated analogue of **4** as shown in Figure 1. $^{13}C$ NMR assignments are listed in Table 1.

Lantalucratin F (**6**), red powder, showed a molecular formula of $C_{17}H_{18}O_7$, indicating one oxygen atom larger than the molecular formula of **5**. Compounds **5** and **6** had similar NMR spectra, except for the benzene proton signals, suggesting that **6** is a hydroxylated derivative of **5**. The $^1H$ NMR spectrum displayed a singlet benzene proton ($\delta_H$ 7.45) and a phenolic proton signal ($\delta_H$ 13.40). Likewise, the $^{13}C$ NMR spectrum of **6** was similar to those of **4** and **5**, except for the benzene ring signals. The positions of the phenolic and two methoxy groups were determined by HMBC correlations (hydroxyl proton at C-9 to C-8, -9a, and -9; methoxy proton to C-7 and -4; H-6 to C-5a and -5). The remaining connections from C-12 to C-3a were established by HMBC correlations, identical to **4**. The structure of **6** was determined as shown in Figure 1, and $^{13}C$ NMR assignments are listed in Table 1.

Compounds **1**−**8** were assayed for cytotoxic activity using NCI's standard procedure.[7] The test panel included several drug-resistant cell sublines that represent varied, and clinically important, mechanisms of anticancer drug resistance. The positive control was $\beta$-lapachone (**9**), a synthetic antitumor pyranonaphthoquinone of current interest.[8−10] Among the tested compounds, **1**, **2**, **3**, **7**, and **8** showed broad spectrum inhibition of human tumor cell replication with $IC_{50}$ values ranging from 1.0 to 10.0 $\mu$M (Table 2). In general, compound **2** was the most potent, with equivalent and similar patterns of activity to $\beta$-lapachone. Compounds **1** and **3** were ca. two- and 3-fold less potent, respectively, than **2**. Interestingly, α-naphthoquinone **5** exhibited moderate cytotoxic activity and selectivity against 1A9 (ovarian) cells ($IC_{50}$ =1.3 $\mu$g/mL), although related α-quinones **4** and **6** were not active. The position of the quinone carbonyls (α or $\beta$) would not explain the different activity and cell line profile based on the almost identical activity of **7** and **8**. Additional biological and mode of action studies are currently being performed.

## Experimental Section

**General Experimental Procedures.** Column chromatography was carried out on silica gel 60 (230−400 mesh, Merck). $^1H$ and $^{13}C$ NMR spectra were recorded on Bruker ARX400 and JEOL 500 NMR spectrometers with TMS as an internal standard. Specific rotation was measured with a HORIBA SEPT-200 polarimeter. IR spectroscopic analysis was performed on a JASCO FTIR-410 spectrometer (FTIR). HREIMS and HRFABMS spectra were obtained with a JEOL JMS-700 spectrometer.

**Plant Material.** *Lantana involucrata* was collected and identified by Dr. G. Castilleja of the New York Botanical Garden under contract to the National Cancer Institute in March 1988 from the Guanica Forest in Puerto Rico. A voucher specimen is deposited in the Botany Department, Museum of Natural History, Smithsonian Institution, Washington, DC.

**Extraction and Isolation.** The $CHCl_3$-soluble crude extract (5.7 g) of the roots was fractionated using silica gel chromatography with a stepwise elution gradient ($CHCl_3$/acetone) to give 10 fractions. Fractions 2, 3, 4, and 6 showed significant cytotoxic activity against MCF-7 and A549 cell lines. The active fraction 2 (2.0 g) was further purified by repeated silica gel chromatography to yield lantalucratin B (**2**, 240 mg) and compounds **7** (58 mg) and **8** (109 mg). The active fraction 4 (0.97 g) was applied on a silica gel column and eluted with a hexane and acetone solvent system to afford lantalucratin A (**1**, 410 mg). Another portion from fraction 4 was purified by silica gel chromatography (toluene/EtOAc, 9:1) and HPLC (Waters RCM 25 × 10 Nova pack ODS, $H_2O$/MeOH, 3:7) to yield lantalucratins D (**4**, 18 mg), E (**5**, 11 mg), and F (**6**, 16 mg). Lantalucratin C (**3**, 30 mg) was isolated from active fraction 6 by silica gel chromatography (hexane/acetone, 7:3) and preparative TLC (hexane/EtOAc, 55:45).

**Lantalucratin A (1):** dark orange crystals; mp 146−158 °C; $[\alpha]_D$ −21.7° (*c* 0.97, $CHCl_3$); HREIMS *m*/*z* 271.0975 [M +

**Table 2.** Cytotoxicity Data for **1**, **2**, and $\beta$-Lapachone against Parental and Drug-Resistant Human Tumor Cell Lines

| | $IC_{50}$ ($\mu$M) [b−d] | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| cell line[a] | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | $\beta$-lapachone |
| KB | >5 (46) | 2.3 | 6.9 | NA | NA | NA | 3 | 4.1 | 1.2 |
| KB-VIN | >5 (17) | 2.4 | 6.3 | NA | NA | NA | 3.9 | 5.7 | 2.2 |
| KB-7d | >5 (43) | 2.1 | 5.8 | NA | NA | NA | 3 | 3.5 | 1.8 |
| KB-CPT | 2.1 | 1 | 5.2 | NA | NA | NA | 2.2 | 3.2 | 1 |
| A549 | 3.3 | 1.8 | 6 | >10 (7) | 8.7 | NA | 2.7 | 6.4 | 1.5 |
| 1A9 | 3.9 | 1.5 | 9.4 | NA | 1.3 | NA | 2.1 | 2.6 | 0.8 |
| 1A9-PTX10 | >5 (45) | 2.1 | 6.5 | >10 (14) | 2.5 | NA | 2.3 | 2.8 | 0.8 |
| CAKI | NA | >5 (16) | NA | NA | >10 (8) | >10 (13) | 9.6 | >10 (26) | >5 (42) |
| MCF-7 | 1.6 | 1 | 4.9 | >10 (20) | 5.5 | >10 (9) | 1.2 | 1.2 | 0.8 |
| HOS | 4.8 | 2.5 | 4.7 | NA | 8.7 | NA | 4 | 3.6 | 1.4 |
| U87-MG | 4.7 | 1.9 | 7.3 | >10 (8) | 7 | NA | 3.4 | 2.6 | 2 |

[a] KB, nasopharyngeal; KB-VIN, vincristine resistant; KB-7d, etoposide resistant, KB-CPT, camptothecin resistant; A549, lung; 1A9, ovarian; 1A9-PTX10, paclitaxel resistant; CAKI, kidney; MCF-7, breast; HOS, bone; U87-MG, gliobastoma. [b] $IC_{50}$ = concentration that causes a 50% reduction in absorbance at 562 nm relative to untreated cells using SRB assay. [c] If inhibition < 50% at 10 $\mu$M, then percent inhibition observed is given as the value in parentheses. [d] NA = not active at 10 $\mu$M.

H]$^+$ (calcd for $C_{16}H_{14}O_4$, Δ 0.4 mmu); IR (neat) 1682, 1651, 1626, 1578, 1462 cm$^{-1}$; UV ($CHCl_3$) $\lambda_{max}$ nm, (log $\epsilon$), 240 (4.27), 261 (4.29), 395 (3.75); $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 1.79 (s, H-12), 2.91 (dd, $J$ = 8.1, 15.8 Hz, H-3), 3.26 (dd, $J$ = 10.5, 15.8 Hz, H-3), 3.99 (s, MeO), 5.01, 5.13 (each s, H-11), 5.45 (dd, $J$ = 8.1, 10.5 Hz, H-2), 7.19 (d, $J$ = 8.4 Hz, H-7), 7.30 (d, $J$ = 7.5 Hz, H-9), 7.59 (dd, $J$ = 7.5, 8.4 Hz, H-8).

**X-ray Crystal Structure Analysis of Lantalucratin A (1).** Crystal data: $C_{16}H_{14}O_4$; MW = 270.29, orthorhombic, space group $P2_12_12_1$ ($D_2^4$), $a$ = 18.220(2) Å, $b$ = 43.020(6) Å, $c$ = 6.824-(1) Å, $V$ = 5349(2) Å$^3$, $Z$ = 16, $D_c$ = 1.342 g cm$^{-3}$, $\mu$(Cu Kα radiation) = 7.6 cm$^{-1}$; crystal dimensions 0.20 × 0.40 × 0.40 mm.

An Enraf-Nonius CAD-4 diffractometer (Cu Kα radiation, graphite monochromator, $\lambda$ = 1.5418 Å) was used for all measurements. Intensity data (+$h$,+$k$,+$l$, $\theta_{max}$ = 75°, 6213 nonequivalent reflections), recorded at 296 K by $\omega$−2$\theta$ scans [scanwidth (1.00 + 0.14 tan $\theta$)°], were corrected for the usual Lorentz and polarization effects. The crystal structure was solved by direct methods using Enraf-Nonius Structure Determination Package (SDP 3.0). Full-matrix least-squares calculations with anisotropic temperature factors for the non-hydrogen atoms and isotropic factors for the hydrogen atoms converged to a final $R$-factor of 0.047 over 4175 reflections with $I > 2.0\alpha(I)$.

Final atomic positional and thermal parameters, bond lengths and angles, and torsion angles have been deposited at the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, U.K.

**Lantalucratin B (2):** red crystals; mp 179−181 °C; $[\alpha]_D$ −70.7° (*c* 0.95, $CHCl_3$); IR (neat) 3490, 1662, 1645, 1614, 1593, 1453 cm$^{-1}$; HREIMS *m/z* 257.0814 (calcd for $C_{15}H_{12}O_4$, Δ 0.6 mmu); UV ($CHCl_3$) $\lambda_{max}$ nm, (log $\epsilon$), 242 sh (4.15), 262 (4.26), 292 (3.75), 418 (3.67); $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 1.79 (s, H-12), 2.94 (dd, $J$ = 7.6, 15.6 Hz, H-3), 3.28 (dd, $J$ = 10.5, 15.6 Hz, H-3), 5.01, 5.13 (each s, H-11), 5.47 (dd, $J$ = 7.6, 10.5 Hz, H-2), 7.11 (d, $J$ = 8.6 Hz, H-7), 7.22 (d, $J$ = 7.4 Hz, H-9), 7.55 (dd, $J$ = 7.4, 8.6 Hz, H-8), 11.93 (br s, OH).

**Lantalucratin C (3):** purple needles; mp 199 °C; $[\alpha]_D$ −420.3° (*c* 0.07, $CHCl_3$); IR (neat) 3300, 3019, 1700, 1645, 1611, 1569, 1456 cm$^{-1}$; HREIMS *m/z* 256.0735 [M]$^+$ (calcd for $C_{15}H_{12}O_4$, Δ 0.0 mmu); UV (MeOH) $\lambda_{max}$ nm (log $\epsilon$) 202.0 (4.13), 270.8 (4.18), 277.6 (4.20), 304.8 (3.61), 502.0 (3.04); $^1$H NMR (500 MHz, acetone-$d_6$) $\delta$ 1.82 (s, H-12), 2.83 (dd, $J$ = 8.0, 15.0 Hz, H-3), 3.24 (dd, $J$ = 10.4, 15.0 Hz, H-3), 5.02 (s, H-11), 5.17 (s, H-11), 5.61 (dd, $J$ = 8.0, 10.4 Hz, H-2), 7.19 (dd, $J$ = 2.4, 8.0 Hz, H-8), 7.46 (d, $J$ = 2.4 Hz, H-6), 7.60 (d, $J$ = 8.0 Hz, H-9).

**Lantalucratin D (4):** yellow oil; $[\alpha]_D$ +5.3° (*c* 0.31, $CHCl_3$); IR (neat) 3520, 3018, 2947, 1668, 1646, 1473, 1449, 1278 cm$^{-1}$; HREIMS *m/z* 302.1161 [M]$^+$ (calcd for $C_{17}H_{18}O_5$, Δ 0.7 mmu); UV (MeOH) $\lambda_{max}$ nm (log $\epsilon$) 246.0 (3.96), 278.0 (3.85), 388.0 (3.44); $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 1.83 (s, H-12), 2.82 (dd, $J$ = 8.0, 13.0 Hz, H-3), 2.90 (dd, $J$ = 4.3, 13.0 Hz, H-3), 4.02 (s, OMe), 4.15 (s, OMe), 4.26 (dd, $J$ = 4.3, 8.0 Hz, H-2), 4.83 (s, H-11), 4.97 (s, H-11), 7.27 (d, $J$ = 8.1 Hz, H-7), 7.65 (t, $J$ = 8.1 Hz, H-8), 7.74 (dd, $J$ = 0.8, 8.1 Hz, H-9).

**Lantalucratin E (5):** red oil; $[\alpha]_D$ +2.3° (*c* 0.44, $CHCl_3$); HREIMS *m/z* 318.1103 [M]$^+$ (calcd for $C_{17}H_{18}O_6$, Δ 0.0 mmu); IR (neat) 3519, 3023, 2948, 1665, 1629, 1472, 1439, 1382, 1301, 1269 cm$^{-1}$; UV (MeOH) $\lambda_{max}$ nm (log $\epsilon$) 204.8 (4.40), 286.0 (3.98), 476.0 (3.72); $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 1.84 (s, H-12), 2.82 (dd, $J$ = 9.4, 14.6 Hz, H-3), 2.88 (dd, $J$ = 4.2, 14.6 Hz, H-3), 3.98 (s, OMe), 4.18 (s, OMe), 4.27 (dd, $J$ = 4.2, 9.4 Hz, H-2), 4.85 (s, H-11), 4.98 (s, H-11), 7.26 (d, $J$ = 9.2 Hz, H-7 or 8), 7.29 (d, $J$ = 9.2 Hz, H-7 or −8), 12.70 (s, OH).

**Lantalucratin F (6):** red powder; mp 227 °C, $[\alpha]_D$ −204.0° (*c* 0.15, $CHCl_3$); HRESIMS *m/z* 357.0971 [M+Na]$^+$ (calcd for $C_{17}H_{18}O_7Na$, Δ 2.1 mmu); IR (neat) 3502, 3020, 2946, 1659, 1623, 1456, 1420, 1382, 1301, 1259 cm$^{-1}$; UV (MeOH) $\lambda_{max}$ nm (log $\epsilon$) 224.4 (4.10), 242.0 (4.24), 296.4 (3.90), 505.6 (3.82); $^1$H NMR (500 MHz, $CDCl_3$ ) $\delta$ 1.85 (s, H-12), 2.85∼2.89 (m, H-3), 3.97 (s, OMe), 4.21 (s, OMe), 4.31 (t, $J$ = 6.3 Hz, H-2), 4.87 (s, H-11), 5.00 (s, H-11), 7.45 (s, H-6), 13.4 (s, OH).

**Dehydroiso-*β*-lapachone (7):** red powder; mp 97.0 °C; $[\alpha]_D$ −45.1° (*c* 0.40, $CHCl_3$); HREIMS *m/z* 240.0778 [M]$^+$ (calcd for $C_{15}H_{12}O_3$, Δ 0.8 mmu); IR (neat) 3019, 1700, 1652, 1635, 1616, 1591, 1573, 1481, 1455, 1407, 1360, 1336, 1277, 1244 cm$^{-1}$; UV (MeOH) $\lambda_{max}$ nm (log $\epsilon$) 213.2 (4.11), 260.4 (4.24), 268.0 (4.19), 333.2 (3.22), 436.4 (3.23); $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 1.81 (s, 3H), 2.97 (dd, $J$ = 7.9, 15.6 Hz, 1H), 3.31 (dd, $J$ = 10.5, 15.6 Hz, 1H), 5.04 (s, 1H), 5.15 (s, 1H), 5.51 (dd, $J$ = 7.9, 10.5 Hz, 1H), 7.09 (d, $J$ = 7.2 Hz, 1H), 7.58−7.62 (m, 1H), 7.65−7.70 (m, 2H).

**Dehydroiso-α-lapachone (8):** yellow crystals; mp 96.5 °C; $[\alpha]_D$ −4.3° (*c* 1.63, $CHCl_3$); HREIMS *m/z* 240.0787 [M]$^+$ (calcd for $C_{15}H_{12}O_3$, Δ 0.0 mmu); IR (neat) 3020, 2924, 1768, 1682, 1647, 1628, 1596, 1575, 1456, 1389, 1374, 1289, 1269 cm$^{-1}$; UV (MeOH) $\lambda$ max nm (log $\epsilon$) 202.0 (4.26), 248.4 (4.30), 253.2 (3.32), 288.4 (4.06), 336.8 (2.50), 390.0 (3.29); $^1$HNMR (400 MHz, $CDCl_3$) $\delta$ 1.81 (s, 3H), 3.03 (dd, $J$ = 8.8 Hz, 17.0, 1H), 3.36 (dd, $J$ = 10.9, 17.0 Hz, 1H), 5.01 (s, 1H), 5.15 (s, 1H), 5.43 (dd, $J$ = 8.8 Hz, 10.7, 1H), 7.66−7.74 (m, 2H), 8.03−8.07 (m, 2H).

**Cytotoxicity Assay.** All stock cultures were grown in T-25 flasks (5 mL of RPMI-1640 medium supplemented with 25 mM HEPES, 0.25% sodium bicarbonate, 10% fetal bovine serum, and 100 $\mu$g/mL kanamycin). Freshly trypsinized cell suspensions were seeded in 96-well microtiter plates at densities of 1500−7500 cells per well with test compounds from DMSO-diluted stock. After 3 days in culture, cells attached to the plastic subtractum were fixed with cold 50% trichloroacetic acid and then stained with 0.4% sulforhodamine B (SRB). The absorbance at 562 nm was measured using a microplate reader after solubilizing the bound dye. The $IC_{50}$ is the concentration of test compound that reduced cell growth by 50% over a 3-day assay period.

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**Supporting Information Available:** Tables of crystal data and an ORTEP diagram of **1**. This material is available free of charge via the Internet at http://pubs.acs.org.

## References and Notes

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