# New Cuparene-Derived Sesquiterpenes with Unprecedented Oxygenation Patterns from the Sea Hare *Aplysia dactylomela*

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Five new sesquiterpenes, cyclolaurene (2), cyclolaurenol (3), cyclolaurenol acetate (4), cupalaurenol (5), and cupalaurenol acetate (6), were isolated from the sea hare *Aplysia dactylomela*. Their structures including absolute configurations were deduced from spectroscopic data and chemical interconversion. The terpenes 3–6 are the first examples in which bromine and hydroxyl or acetoxy substituents are reversed in their positions from those usually found in related compounds, e.g., laurinterol (1).

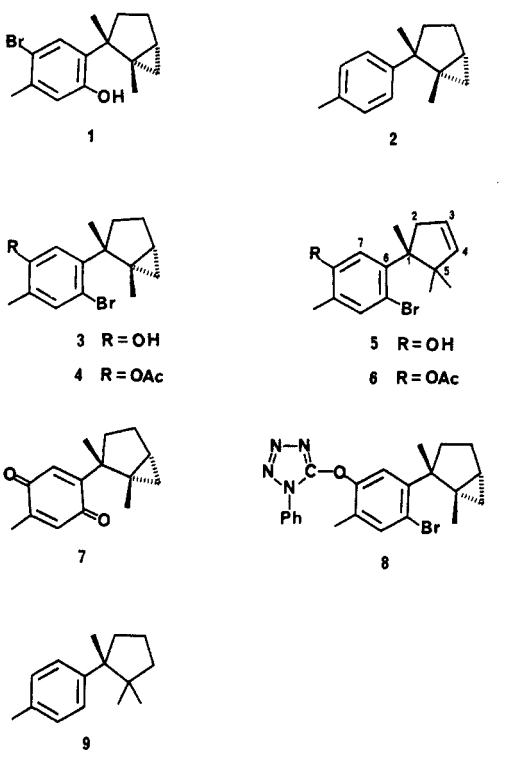
Over the two decades since Yamamura and Hirata first reported the isolation of aplysin and related compounds from the sea hare *Aplysia kurodai*,[1] a significant number of cuparene-derived sesquiterpenes have been isolated from the red algal genus *Laurencia* and some sea hares that prey on it.[2,3] These terpenoids, mostly halogenated with bromine and a few even with iodine,[4] comprise a class of characteristic metabolites of *Laurencia*. Most of them are either phenols or their cyclic ethers.[3,5] Interestingly, all the phenolic compounds known to date have oxygen attached exclusively at the ortho position to the junction of the five-membered ring as in laurinterol (1) (see Chart I). We herein describe the isolation and structure determination of four cuparene-related sesquiterpenes (3–6) having oxygen at the meta position. Also isolated for the first time is cyclolaurene (2), the parent hydrocarbon of laurinterol (1).

A single specimen of *Aplysia dactylomela* collected at Kohama Island, Okinawa, was homogenized with acetone. The ethyl acetate soluble portion of this extract was subjected to several chromatographic separations to give cyclolaurene (2), cyclolaurenol (3), cyclolaurenol acetate (4), cupalaurenol (5), and cupaluarenol acetate (6).

Cyclolaurene (2) was obtained as a colorless oil, $[\alpha]_D$ −9.0°. The compound was shown to be a hydrocarbon with molecular formula $C_{15}H_{20}$ by high-resolution mass spectrometry. The IR spectrum indicated the presence of aromatic (3045, 3025 $cm^{-1}$) as well as aliphatic moieties (2965, 2935, 2875, 1445, 1380, 1365 $cm^{-1}$). The $^1H$ NMR spectrum exhibited two 2 H doublets at $\delta$ 7.38 and 7.12 ($J$ = 8.8 Hz), indicating the presence of a 1,4-disubstituted benzene ring. One of the substituents was a methyl group [$\delta$ 2.24 (3 H, s)]. The other substituent was suggested to be a dimethyl[3.1.0]bicyclohexyl group by the presence of two additional methyl singlets ($\delta$ 1.31, 1.20) and a cyclopropyl signal [$\delta$ 0.67–0.26 (2 H, m)] and also by considering the number of unsaturation sites in the molecule. The structure 2, including the absolute configuration, was confirmed by a chemical correlation with cyclolaurenol (3) (vide infra).

Cyclolaurenol (3) was a crystalline compound, mp 109–109.5 °C, $[\alpha]_D$ −9.3°. The molecular formula $C_{15}H_{19}BrO$ was secured by combustion analysis and by EIMS ($M^+$ at $m/z$ 196, 194). The presence of a hydroxyl group

**Chart I**




was evident from the IR band at 3320 $cm^{-1}$. The $^1H$ NMR spectrum showed the presence of two aromatic protons [$\delta$ 7.16 (1 H, s), 7.01 (1 H, s)], an aromatic methyl ($\delta$ 2.14), two quarternary methyls ($\delta$ 1.48, 1.28), and cyclopropyl protons [$\delta$ 0.46 (2 H, m)]. Although the spectrum as a whole was similar to that of laurinterol (1), the chemical shifts of the two aromatic protons were distinctively different from those [$\delta$ 6.36 (1 H, s), 7.56 (1 H, s)] of 1, suggesting that 1 and 3 were different only in the positions of bromine and hydroxyl substituents. Irradiation of the aromatic methyl signal at $\delta$ 2.14 sharpened the somewhat broad singlet at $\delta$ 7.16 but did not affect the signal at $\delta$ 7.01. This observation suggested that the proton ($\delta$ 7.16) deshielded by bromine at an ortho position is also located next to the methyl group. When 3 was treated with *p*-toluenesulfonic acid under the same conditions that effected the smooth conversion of 1 into aplysin,[6] 3 was recovered unchanged. These results are consistent with the proposed structure of 3 in which the positions of bromine and hydroxyl are reversed from those of 1.

(1) Yamamura, S.; Hirata, Y. *Tetrahedron* **1963**, *19*, 1485.
(2) Martin, J. D.; Darias, J. In *Marine Natural Products*; Scheuer, P. J., Ed.; Academic: New York, 1978; Vol. I, p 125.
(3) Erickson, K. L., In *Marine Natural Products*; Scheuer, P. J., Ed.; Academic: New York, 1983; Vol. V, p 132.
(4) Izac, R. R.; Sims, J. J. *J. Am. Chem. Soc.* **1979**, *101*, 6136.
(5) Higa, T. In *Marine Natural Products*; Scheuer, P. J., Ed.; Academic: New York, 1981; Vol. IV, p 93.
(6) Irie, T.; Suzuki, M.; Kurosawa, E.; Masamune, T. *Tetrahedron* **1970**, *26*, 327.

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Treatment of **3** with chromium trioxide in acetic acid[7] gave a yellow oil as a major product. This oil, $[\alpha]_D$ −49.3°, was identical in all respects with laurequinone (**7**), $[\alpha]_D$ −53.5°, isolated recently from *laurencia nidifica*.[8] Since the absolute stereochemistry of **7** has been established by correlation with **1**, **3** must also have the same configuration as **1** and **7**.

Correlation of **3** and **2** was effected by removing the bromine and hydroxyl substituents from **3**. Thus, **3** was treated with 1-phenyl-5-chlorotetrazole[9] to give a quantitative yield of the tetrazoyl ether **8**. Hydrogenolysis of **8** over palladium on charcoal afforded an oily product, $[\alpha]_D$ −7.4°, which was identical in all respects with cyclolaurene (**2**).

Cupalaurenol (**5**) was isolated as a colorless oil, $[\alpha]_D$ +87.9°. The molecular formula $C_{15}H_{19}BrO$ was secured by EIMS ($M^+$ at $m/z$ 296, 294) of **5** and combustion analysis of its acetate **6**. The phenolic nature of the compound was shown by an IR band at 3520 $cm^{-1}$ and UV absorption at 282 nm. The $^1H$ NMR spectrum revealed the presence of two para-disposed protons [δ 7.10, (s), 6.76, (s)], two mutually coupling olefinic protons [δ 5.53 (1 H, ddd, $J$ = 5.8, 2.4, 1.9 Hz), 5.17 (1 H, ddd, $J$ = 5.8, 2.0, 1.0 Hz)], an allylic methylene [δ 3.20 (1 H, br d, $J$ = 16 Hz), 2.56 (1 H, br d, $J$ = 16 Hz)], an aromatic methyl [δ 2.08, (s)], and three quarternary methyls (δ 1.37, 1.27, 0.84). The same substitution pattern in the benzene ring with that of **3** was confirmed by irradiation of the signal at δ 2.08, increasing the height of the signal at δ 7.10 relative to that of δ 6.76. The NMR data suggested the aliphatic portion of the molecule to be a 1,5,5-trimethylcyclopentenyl. The double bond could be placed either at the 2,3- or 3,4-position on the cyclopentenyl. The assignment was made by NOESY study[10] with the acetate **6**. NOE correlation was observed between H-7 (δ 7.00) and three aliphatic methyls and one (δ 3.26) of the methylene protons and also between one (δ 5.25) of the olefinic protons and two C-5 methyls (δ 1.33, 0.87). No correlation was seen between olefinic protons and aromatic protons or C-1 methyl (δ 1.40). These observations are consistent only with the structure having the double bond at the 3,4-position.

Conversion of cupalaurenol (**5**) to cuparene (**9**) was carried out by the same two-step reaction that effected the transformation of **3** to **2**. The product thus obtained from **5** was shown to be the hydrocarbon (+)-cuparene (**9**) by comparison of spectral data and optical rotation with those reported.[11] The result confirms the absolute configuration of **5** to be *S*, the same configuration of (+)-cuparene.[11]

The acetates **4** and **6** were isolated as an inseparable mixture. Thus, the mixture was saponified and separated to give the phenols **3** and **5**, each of which was reacetylated for spectral characterization.

To the best of our knowledge this is the first report for the isolation of the parent hydrocarbon cyclolaurene **1**, although the trivial name has been coined for a class of sesquiterpenes related to laurinterol (**1**).[3] Of more than 40 cuparene-derived sesquiterpenes known from marine sources the present compounds are first examples having a phenolic oxygen in the meta position. Compounds **3–6** showed antibacterial activity against *Bacillus subtilis*. Compounds **3**, **5**, and **6** were also antifungal against *Aspergillus* sp., while **5** was active against *Trichoderma* sp. as well. All four metabolites **3–6** were ichthyotoxic against guppies at a concentration level of 5–10 ppm.

## Experimental Section

Infrared spectra were recorded on a Hitachi infrared spectrophotomer 260-10; UV spectra on a Jasco UVIDEC 610 spectrometer; optical rotation on an Atago AA-5 digital polarimeter; electron-impact mass spectra including high-resolution mass measurements on a JEOL JMS D-300 instrument. $^1H$ NMR spectra were taken at 60 MHz on a JEOL JNM-PMX 60. Melting points were measured on Mitamura Riken micromelting point apparatus.

**Extraction and Isolation.** A single specimen (wet weight, 290 g) of *Aplysia dactylomela*, collected in Kohama Island, Okinawa, in July, 1984, was homogenized with acetone in a blender. The acetone extract was concentrated and extracted with ethyl acetate (4 × 100 mL) to give 9.2 g of oil. The oil was grossly separated on a silica gel column into nine fractions by eluting with 1:2 hexane-chloroform (fractions 1–4), chloroform (fractions 5–7), ethyl acetate (fraction 8), and 3:1 ethyl acetate–acetone (fraction 9).

Fraction 1 (1 g) was separated on a Lobar Si-60 column (hexane) to give a crude sample of cyclolaurene (**2**). Purification of this sample on a TLC plate with silica gel impregnated with 12.5% silver nitrate using hexane as developing solvent gave 13.4 mg of **2** as a colorless oil. Fractions 2–5 (total 5.3 g) were combined as they showed the same spots by TLC and separated on a silica gel column (5:1 hexane–acetone) into three portions (200 mL each). Further separation of the second portion (3.0 g) on a Lobar Si-60 column (1:3 hexane–chloroform) furnished 273 mg of **3** and 660 mg of **5**. The first portion (1.6 g) was repeatedly chromatographed on the same column to give an oil, which showed one spot by TLC, but it was apparently a mixture of the acetates **4** and **6** as shown by $^1H$ NMR measurement. Since further separation of the mixture was deemed impractical, it was saponified by treating with 1% KOH in ethanol to yield, after usual workup, a mixture of the alcohols **3** and **5**. The alcohol mixture was chromatographed in the same manner as above to give pure samples of **3** and **5**, which on reacetylation (acetic anhydride/pyridine) afforded 49 mg of **4** and 69 mg of **6**.

**Cyclolaurene (2):** $[\alpha]_D$ −9.0° (*c* 0.22, $CHCl_3$); IR ($CCl_4$) 3045, 3025, 2965, 2935, 2875, 1445, 1380, 1365, 1065, and 1015 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 7.38 (2 H, d, $J$ = 8.8 Hz), 7.12 (2 H, d, $J$ = 8.8 Hz), 2.24 (3 H, s), 2.02–1.44 (4 H, m), 1.31 (3 H, s), 1.20 (3 H, s), 1.00 (1 H, m), and 0.67–0.26 (2 H, m); HRMS, obsd $m/z$ 200.1573 (calcd for $C_{15}H_{20}$ $m/z$ 200.1588); LRMS, $m/z$ (relative intensity) 200 ($M^+$, 54), 185 (52), 159 (61), 157 (54), 144 (17), 143 (30), 142 (12), 132 (100), 131 (12), 129 (19), 128 (13), 119 (14), 117 (18), 115 (14), 105 (38), 93 (15), and 91 (18).

**Cyclolaurenol (3):** mp 109–109.5 °; $[\alpha]^{21}_D$ −9.3° (*c* 4.04, $CHCl_3$); UV (EtOH) $\lambda_{max}$ 206 (ε 12 000), 269 (570), and 278 nm (sh) (560); IR (KBr) 3320, 2920, 2850, 1480, 1450, 1395, 1245, 1150, 1130, and 880 $cm^{-1}$; $^1H$ NMR ($CCl_4$) δ 7.16 (1 H, s), 7.01 (1 H, s), 4.51 (1 H, s), 2.56 (1 H, dd, $J$ = 12, 6 Hz), 2.14 (3 H, s), 1.70 (2 H, m), 1.48 (3 H, s), 1.28 (3 H, s), 1.03 (2 H, s), and 0.46 (2 H, m); LRMS, $m/z$ (relative intensity) 296 (13), 294 ($M^+$, 12), 281 (5), 279 (5), 255 (4), 253 (6), 228 (86), 226 (100), 215 (52), 214 (8), 212 (8), 201 (15), 200 (17), 199 (14), 187 (16), 186 (12), 185 (11), 174 (69), 173 (28), 172 (19), 159 (41), 115 (16), 91 (18), and 77 (19). Found: C, 61.22; H, 6.46; Br, 27.16. Calcd for $C_{15}H_{19}BrO$: C, 61.03; H, 6.49; Br, 27.07.

**Cyclolaurenol acetate (4):** $[\alpha]^{19}_D$ −9.2° (*c* 0.82, $CHCl_3$); UV (MeOH) $\lambda_{max}$ 206 (ε 17 000), 270 (700), and 278 nm (700); IR ($CCl_4$) 2965, 2930, 2870, 1760, 1425, 1365, 1210, 1145, 1125, and 910 $cm^{-1}$; $^1H$ NMR ($CCl_4$) δ 7.30 (1 H, s), 7.23 (1 H, s), 2.26 (3 H, s), 2.08 (3 H, s), 1.53 (3 H, s), 1.31 (3 H, s), and 0.50 (2 H, m); LRMS, $m/z$ (relative intensity) 338 (4), 336 ($M^+$, 3.5), 323 (1.8), 321 (2), 296 (16), 294 (15), 281 (8), 279 (9), 270 (38), 268 (40), 257 (58), 255 (14), 253 (14), 228 (98), 226 (100), 215 (57), 200 (22), 187 (15), 174 (85), 173 (37), and 159 (28).

**Cupalaurenol (5):** $[\alpha]^{19}_D$ +87.9° (*c* 1.0, $CHCl_3$); UV (EtOH) $\lambda_{max}$ 206 (ε 14 200), 224 (sh) (6550), and 282 nm (1530); IR ($CCl_4$) 3520, 3050, 2970, 1480, 1375, 1275, 1200, 1170, 1145, and 880 $cm^{-1}$;

(7) Lyons, J. M.; Thomson, R. H. *J. Chem. Soc.* **1953**, 2910.
(8) Shizuri, Y.; Yamada, A.; Yamada, K. *Phytochemistry* **1984**, *23*, 2672.
(9) Musliner, W. J.; Gates, Jr., J. W. *J. Am. Chem. Soc.* **1966**, *88*, 4271.
(10) NOESY spectrum was recorded by Ryuichi Sakai under the guidance of Professor Yoel Kashman on a Bruker AM 360 instrument at Harbor Branch Foundation-SeaPharm Research Laboratories. We thank both of them and SeaPharm for this service.
(11) Enzell, C.; Erdtman, H. *Tetrahedron* **1958**, *4*, 361.

$^1$H NMR ($CCl_4$) δ 7.10 (1 H, s), 6.76 (1 H, s), 5.53 (1 H, ddd, $J$ = 5.8, 2.4, 1.9 Hz), 5.17 (1 H, ddd, $J$ = 5.8, 2.0, 1.0 Hz), 3.20 (1 H, br d, $J$ = 16 Hz), 2.58 (1 H, br d, $J$ = 16 Hz), 2.08 (3 H, s), 1.37 (3 H, s), 1.27 (3 H, s), and 0.84 (3 H, s); LRMS, $m/z$ (relative intensity) 296 (17), 294 ($M^+$, 16), 281 (6), 279 (6), 240 (5), 238 (5), 215 (22), 200 (41), 185 (22), 173 (100), 159 (20), 158 (12), 155 (8), 145 (8), 115 (8), 91 (9), and 77 (11).

**Cupalaurenol acetate (6):** $[\alpha]^{19}_D$ + 65.1° ($c$ 1.0, $CHCl_3$); UV (EtOH) $\lambda_{max}$ 205 (ε 21 000), 225 (sh) (10 000), and 280 nm (3000); IR ($CCl_4$) 3040, 2960, 2920, 2860, 1760, 1480, 1370, 1210, 1180, 1140, and 905 cm$^{-1}$; $^1$H NMR ($CCl_4$) δ 7.28 (1 H, s), 7.00 (1 H, s), 5.50 (1 H, br d, $J$ = 5.8 Hz), 5.25 (1 H, br d, $J$ = 5.8 Hz), 3.26 (1 H, br d, $J$ = 16 Hz), 2.69 (1 H, br d, $J$ = 16 Hz), 2.21 (3 H, s), 2.05 (3 H, s), 1.40 (3 H, s), 1.33 (3 H, s), and 0.87 (3 H, s); LRMS, $m/z$ (relative intensity) 338 (8), 336 (9), 279 (4), 257 (7), 240 (7), 238 (7), 215 (26), 200 (27), 185 (11), 173 (100), and 159 (15). Found: C, 60.57; H, 6.34; Br, 23.65. Calcd for $C_{17}H_{21}BrO_2$: C, 60.54; H, 6.28; Br, 23.69.

**Oxidation of 3 to Laurequinone (7).** To a solution of 34.7 mg of **3** in 80% acetic acid (1 mL) was added several drops of 1% chromium trioxide solution in acetic acid. The mixture was allowed to stand at 20 °C for 3 h and extracted with chloroform (3 × 5 mL) after addition of water (5 mL). The organic layer was separated by TLC (silica gel, 1:3 hexane–$CHCl_3$) to give 12.2 mg of **7** as a yellow oil, $[\alpha]^{18}_D$ −49.3° ($c$ 0.30, $CHCl_3$) [lit.[7] $[\alpha]^{24}_D$ −53.5° ($c$ 0.91, $CHCl_3$)]. The IR and $^1$H NMR spectra were virtually identical with those of an authentic sample.

**Conversion of 3 to 2.** A procedure developed by Musliner and Gates[8] was adapted. Thus, a mixture of 42.9 mg of **3**, 182 mg of anhydrous potassium carbonate, and 53.7 mg of 1-phenyl-5-chlorotetrazole in dry acetone (15 mL) was heated at reflux for 20 h. The reaction mixture was filtered to remove inorganic solid and separated by preparative TLC (silica gel, 1:3 hexane–$CHCl_3$) to give 64 mg of the tetrazoyl ether **8** as an oil: IR ($CCl_4$) 3060, 2960, 2930, 2860, 1505, 1430, 1295, 1145, 1130, 1110, and 1095 cm$^{-1}$; $^1$H NMR (60 MHz, $CDCl_3$) δ 7.92–7.40 (7 H, m), 2.13 (3 H, s), 1.52 (3 H, s), 1.26 (3 H, s), 0.53 (1 H, s), and 0.43 (1 H, br s). The ether **8** (64 mg) in ethanol (5 mL) was hydrogenated over 10% Pd/C (20 mg) for 32 h. After removing the catalyst by filtration, the reaction mixture was separated by preparative TLC (silica gel, 4:1 hexane–$CHCl_3$) to yield 26.8 mg of an oil. Further purification of the oil on a Lobar Si-60 column (5:1 hexane–$CHCl_3$) gave 16.2 mg of **2**; $[\alpha]^{20}_D$ −7.4° ($c$ 0.27, $CHCl_3$). The IR and $^1$H NMR spectra were identical with those of cyclolaurene isolated from *A. dactylomela*.

**Conversion of 5 to Cuparene (9).** A solution of **5** (44.2 mg) in acetone (25 mL) was similarly treated with 1-phenyl-5-chlorotetrazole (54.3 mg) and potassium carbonate (62 mg) to give 64 mg of the tetrazoyl ether of **5** as an oil: IR ($CCl_4$) 3050, 2970, 1600, 1505, 1455, 1360, 1300, 1145, and 1000 cm$^{-1}$; $^1$H NMR ($CDCl_3$) δ 8.0–7.4 (7 H, m), 5.62 (1 H, br d, $J$ = 6.1 Hz), 5.40 (1 H, br d, $J$ = 6.1 Hz), 3.35 (1 H, br d, $J$ = 15.6 Hz), 2.83 (1 H, br d, $J$ = 15.6 Hz), 2.17 (3 H, s), 1.45 (3 H, s), 1.33 (3 H, s), and 0.92 (3 H, s). Hydrogenolysis of the ether in the same manner gave, after TLC separation, 18.7 mg of cuparene (**9**) as an oil: $[\alpha]^{20}_D$ +66.8° ($c$ 0.37, $CHCl_3$); IR ($CCl_4$) 2960, 1520, 1465, 1380, 1200, 1125, and 815 cm$^{-1}$; $^1$H NMR ($CDCl_3$) δ 7.25 (2 H, d, $J$ = 8.4 Hz), 7.10 (2 H, d, $J$ = 8.4 Hz), 2.23 (3 H, s), 1.63 (6 H, m), 1.23 (3 H, s), 1.01 (3 H, s), and 0.55 (3 H, s).

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# *Notes*

## A Two-Dimensional $^1$H NMR Investigation of the Ring A Conformation in 3-Keto Triterpenoids: Observation of an Unusually Large Vicinal Coupling Constant

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The potential of two-dimensional (2D) NMR experiments such as $J$-resolved spectroscopy (2D-$J$) and $J$-correlated spectroscopy (COSY) in the structural and stereochemical analysis of proteins,[1] polysaccharides,[2] and nucleic acids,[3] where the spectra contain many overlapping but isolated spin systems, is now well documented. However, their applications to complex natural products containing extended spin systems such as steroids and triterpenoids have been limited.[4] In the present communication, we record the first application of homonuclear 2D-$J$ and COSY experiments to determine the ring A conformation of a 3-keto triterpenoid, viz., 3-ketours-12-en-24-oic acid methyl ester (**1**) (Chart I), a derivative of biologically active β-bosewellic acid.[5]

(1) For a review, see: Wider, G.; Macura, S.; Kumar Anil; Ernst, R. R.; Wüthrich, K. *J. Magn. Reson.* **1984**, *56*, 207.

(2) (a) Hall, L. D.; Morris, G. A.; Sukumar, S. *J. Am. Chem. Soc.* **1980**, *102*, 1745. (b) Bruch, R. C.; Bruch, M. D. *J. Biol. Chem.* **1982**, *257*, 3409. (c) Gagnaire, D. Y.; Taravel, F. R.; Vignon, M. R. *Macromolecules* **1982**, *15*, 126. (d) Bernstein, M. A.; Hall, L. D. *J. Am. Chem. Soc.* **1982**, *104*, 5553. (e) Prestegard, J. H.; Koerner, T. A. W., Jr.; Demou, P. C.; Yu, R. K. *J. Am. Chem. Soc.* **1982**, *104*, 4993. (f) Schraml, J.; Hirch, J.; Petrakova, E.; Krahe, E.; Bliefert, C. *Collect. Czech. Chem. Commun.* **1984**, *49*, 1605.

(3) (a) Feigon, J.; Wright, J. M.; Leupin, W.; Denny, W. A.; Kearns, D. R. *J. Am. Chem. Soc.* **1982**, *104*, 5540. (b) Haasnoot, C. A. G.; Westerink, H. P.; Van der Marel, G. A.; Van Boom, J. H. *J. Biomol. Struct. Dyn.* **1983**, *1*, 131. (c) Pardi, A.; Walker, R.; Rapoport, H.; Wider, G.; Wüthrich, K. *J. Am. Chem. Soc.* **1983**, *105*, 1652. (d) Frechet, D.; Cheng, D. M.; Kan, L. S.; Ts'O, P. O. P. *Biochemistry* **1983**, *22*, 5194. (e) Scheek, R. M.; Russo, N.; Boelens, R.; Kaptein, R.; Van Boom, J. H. *J. Am. Chem. Soc.* **1983**, *105*, 2914. (f) Lown, J. W.; Hanstock, C. C.; Bleakley, R. C.; Imback, J.-L.; Rayner, B.; Vasseur, J. J. *Nucleic Acids Res.* **1984**, *12*, 2517.

(4) (a) Hall, L. D.; Sanders, J. K. M. *J. Am. Chem. Soc.* **1980**, *102*, 5703. (b) Hall, L. D.; Sanders, J. K. M. *J. Org. Chem.* **1981**, *46*, 1132. (c) Barrett, M. W.; Farrant, R. D.; Kirk, D. N.; Mersh, J. D.; Sanders, J. K. M.; Duax, W. L. *J. Chem. Soc., Perkin Trans. 2* **1982**, 105. (d) Liebfritz, D.; Haipt, E.; Feigel, M.; Hull, W. E.; Weber, W. D. *Liebigs Ann. Chem.* **1982**, 1971. (e) Sedee, A. G. J.; Beijersbergen van Henegouwen, G. M. J.; Guijt, W.; Haasnoot, C. A. G. *J. Chem. Soc., Perkin Trans. 2* **1984**, 1755. (f) Steffens, J. C.; Roark, J. L.; Lynn, D. G.; Riopel, J. L. *J. Am. Chem. Soc.* **1983**, *105*, 1669.

(5) The potent antiinflammatory and antiarthritic activity of the Indian Ayurvedic drug obtained from *Boswellia serrata* has been shown to be due to β-boswellic acid and related triterpene acids present in it.[11]

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