Pergamon

Tetrahedron Letters 43 (2002) 3341–3345

TETRAHEDRON LETTERS

The total synthesis of (±)-arisugacin A†

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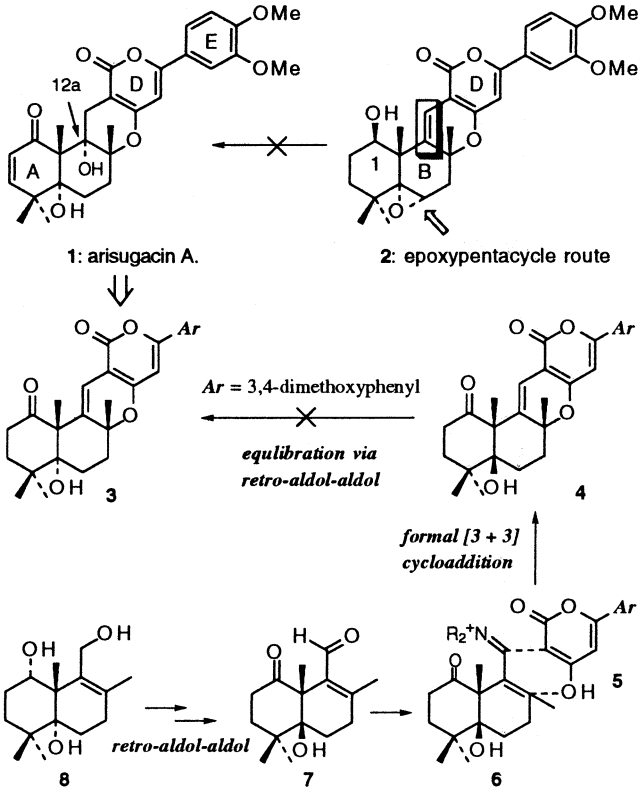
Received 25 February 2002; revised 11 March 2002; accepted 14 March 2002

Abstract—A 20-step total synthesis of (±)-arisugacin A with an overall yield of 2.1% is described here. This synthesis features highly convergent formal [3+3] cycloaddition and a strategic dihydroxylation–deoxygenation protocol leading to the desired angular C12a-OH.

In the preceding paper,[1] we reported our efforts towards synthesis of arisugacin A (**1**)[2] via a highly efficient formal [3+3] cycloaddition reaction approach.[3–5] The synthetic route[5a] using the epoxy pentacycle **2** proved to be futile due to difficulties in oxidation of the C-ring olefin despite success in our model studies[6] and the ring-opening of the B-ring epoxide. An alternative approach involving construction of the pentacycle **3** starting from the triol **8** appeared to be more feasible (Scheme 1). However, it was met with an



Scheme 1.

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† This paper is dedicated to Professor Gilbert Stork on the occasion of his 80th birthday.

‡ A recipient of 2001 Camille Dreyfus Teacher-Scholar and 2001–2003 McKnight New Faculty Awards.

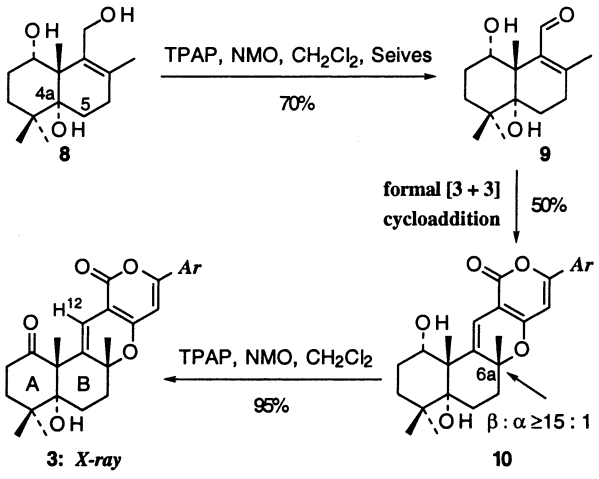
0040-4039/02/$ - see front matter
PII: S0040-4039(02)00551-8

unexpected retro-aldol–aldol process that occurred during the construction of the keto enal **7**. Although the pentacycle **3** with the *trans* fusion at the AB-ring is more stable ($\Delta E \sim 1.0$ kcal mol^{-1}) than the pentacycle **4** containing a *cis* fused AB-ring, equilibration via the retro-aldol–aldol process was not successful.

In spite of these difficulties, these efforts in the preceding paper provided several critical points that allowed us to eventually achieve our total synthesis of (±)-arisugacin A. First, the pentacycle **3** still possessed an inherent advantage over **2** because it circumvents the issue of opening the B-ring epoxide. Secondly, success and failures in transforming the C-ring olefin to C12a hydroxyl group pointed us to the potential significance of the stereochemistry of the C1-OH (being β or α). Thirdly, *retro-aldol–aldol* in the AB-ring indeed can occur and may further lead to other complications; this is an intriguing feature with respect to this family of natural products. We communicate here our success in a total synthesis of (±)-arisugacin A.

To avoid the *retro-aldol–aldol* predicament, synthesis of the desired pentacycle **3** was achieved via another route. As shown in Scheme 2, the triol **8** was oxidized, without protecting either the C1- or C4a-hydroxyl group, using Ley's TPAP oxidation to give the enal **9**[7] in 70% yield devoid of lactolization. In contrast, oxidations of the allylic alcohol to enal using the C4a-C5 epoxy equivalent of **8** without protecting the secondary C1-OH led to complex mixtures and partial lactolization. This finding significantly shortened the synthetic sequence.[8]

Reaction of **9** with **5** under the standard [3+3] conditions led to the desired pentacyle **10** with an improved and consistent 50% yield, and more importantly, high diastereoselectivity. Subsequent TPAP oxidation of **10** led to the pentacycle **3** in 95% yield. The relative stereochemistry was unambiguously confirmed using X-ray analysis.[8] The X-ray structure of **3** also explains the unusually downfield shifted olefinic H^{12} in the C-ring (7.43 ppm), whereas the same olefinic H^{12} in **3** is at the expected region (6.09 ppm). The H^{12} in **3** experiences a diamagnetic anisotropic effect due to its close proximity to the A-ring carbonyl oxygen.

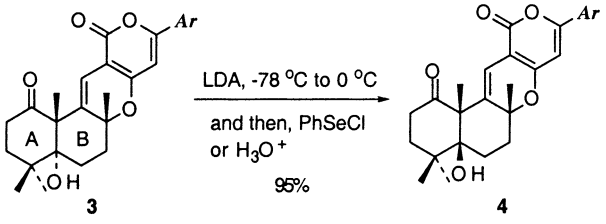


Scheme 2.

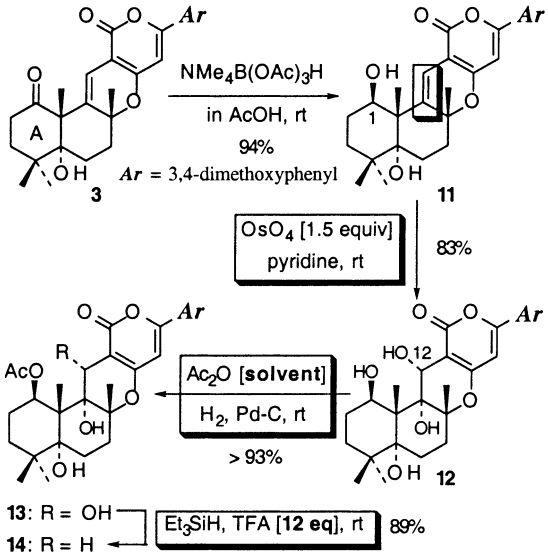
Surprisingly, when **3** was treated with 2.0 equiv. of LDA, in an attempt to pursue selenation for installing the A-ring olefin, **3** was found to quantitatively isomerize to the kinetic pentacycle **4** presumably via a *retro-aldol–aldol* sequence (Scheme 3). Given the inability to thermodynamically epimerize **4** back to **3**, the pentacycle **4** appears to be a 'locked' structure. Such epimerization has not been previously observed among the arisugacins. We are currently exploring its relevance to the biological activity of this family of natural products.

Preparations of advanced pentacycles **3** and **10** provided a useful route to an eventual total synthesis of (±)-arisugacin A. All attempts at oxidizing the C-ring olefin in **10** via hydroboration, epoxidation, and dihydroxylation failed. These failures led us to speculate the impact of the C1-OH on such an oxidative process. Given our earlier success in epoxidizing the epoxy pentacycle having the β-C1-OH,[1] **3** was subjected to directed reduction using $NMe_4B(OAc)_3H$ in AcOH/MeOH to give exclusively **11** in 94% yield with β-C1-OH (Scheme 4). Unlike the reductions of **6**, the Dibal-H or $NaBH_4$ reduction of **3** gave much inferior C1-α:β ratios.

Dihydroxylation[9] of **11** in pyridine using stoichiometric amount of OsO_4, a protocol used for our model studies,[6] successfully gave the desired tetraol **12** in 83% yield



Scheme 3.

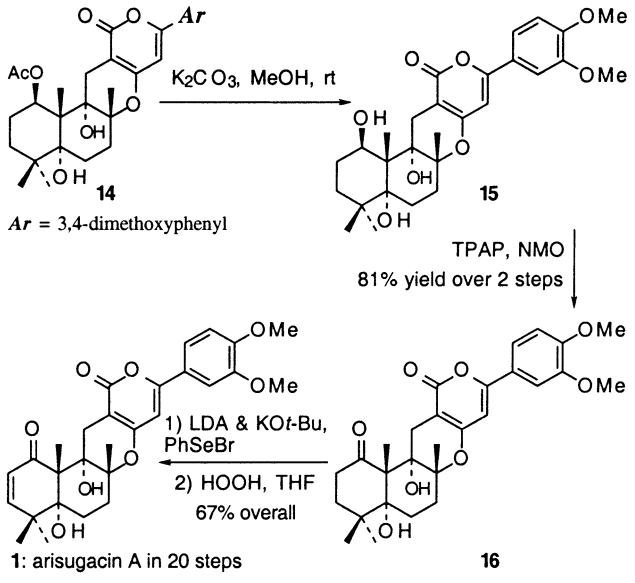


Scheme 4.

as a single diastereomer (Scheme 4). The removal of the C12-OH in **12** initially using the Et_3SiH protocol[6] led to a tentatively assigned hexacycle[10] as we had observed in the work related to the epoxy pentacycle **2**.[1] On the other hand, the hydrogenation protocol using Ac_2O as solvent[6] led to **13** (in >93% isolated yield) with selective acylation of the C1-OH in addition to a very small amount of **14** indicating that the removal of the C12-OH was slow. It is also noteworthy that subjecting the tetraol **12** to standard acylation conditions (Ac_2O, DMAP in pyridine/CH_2Cl_2 at rt) provided **13** quantitatively, thereby selectively acylating the β-C1-OH. Subsequent removal of the C12-OH in **13** using Et_3SiH and 12 equiv. of TFA gave **14** in 89% yield.[6]

Deacylation of **14** followed by TPAP oxidation of the triol **15** gave the pentacycle **16** in 81% overall yield (Scheme 5). To prevent the unwanted isomerization via *retro-aldol–aldol* that was observed earlier for **3**, different protocols such as DDQ or IBX[11] (gave **1** in low yields plus some isomerization) were examined to install the double bond in the A-ring. However, presumably due to the counter cation effect, Schlosser's base was effective in the selenation. A subsequent oxidative elimination of the selenide using H_2O_2 afforded in 67% overall yield (±)-arisugacin A (**1**) that matched spectroscopically (co-spectra of ^1H NMR in pyridine-d_5) and analytically (TLC: in 2:1 EtOAc:hexane; 2:1 ether:hexane; 1:9 acetone:$CHCl_3$] with the natural sample.

We have described here a 20-step total synthesis of (±)-arisugacin A with an overall yield of 2.1%. This synthesis features a useful and highly stereoselective formal [3+3] cycloaddition and a strategic dihydroxylation-deoxygenation protocol leading to the desired angular C12a-OH.



Scheme 5.

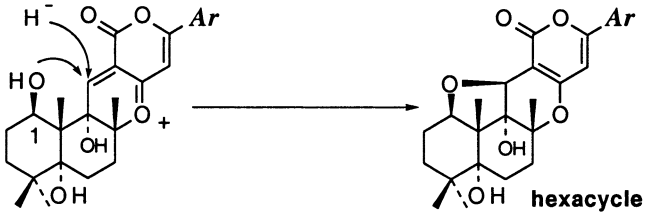
Acknowledgements

R.P.H. thanks National Institutes of Health [NS38049] and American Chemical Society PRF-Type-G for financial support. Authors also thank Dr. Neil R. Brooks for providing the X-ray structural analysis. We thank Professor S. Õmura for a generous sample of (+)-arisugacin A.

References

1. Wang, J.; Cole, K. P.; Wei, L.-L.; Zehnder, L. R.; Hsung, R. P. *Tetrahedron Lett.* **2002**, *43*, 3337.
2. (a) Õmura, S.; Kuno, F.; Otoguro, K.; Sunazuka, T.; Shiomi, K.; Masuma, R.; Iwai, Y. *J. Antibiotics* **1995**, *48*, 745. For biological activities of arisugacin see: (b) Kuno, F.; Otoguro, K.; Shiomi, K.; Iwai, Y.; Õmura, S. *J. Antibiotics* **1996**, *49*, 742; (c) Otoguro, K.; Kuno, F.; Õmura, S. *Pharmacol. Ther.* **1997**, *76*, 45; (d) Otoguro, K.; Shiomi, K.; Yamaguchi, Y.; Arai, N.; Sunazuka, T.; Masuma, R.; Iwai, Y.; Õmura, S. *J. Antibiotics* **2000**, *53*, 50.
3. For a review see: Hsung, R. P.; Wei, L.-L.; Sklenicka, H. M.; Shen, H. C.; McLaughlin, M. J.; Zehnder, L. R. *Trends in Heterocyclic Chemistry*; 2001; Vol. 7, pp. 1–24.
4. (a) Hsung, R. P.; Shen, H. C.; Douglas, C. J.; Morgan, C. D.; Degen, S. J.; Yao, L. J. *J. Org. Chem.* **1999**, *64*, 690; (b) Hsung, R. P.; Wei, L.-L.; Sklenicka, H. M.; Douglas, C. J.; McLaughlin, M. J.; Mulder, J. A.; Yao, L. J. *Org. Lett.* **1999**, *1*, 509; (c) Wei, L.-L.; Sklenicka, H. M.; Gerasyuto, A. I.; Hsung, R. P. *Angew. Chem., Int. Ed.* **2001**, *40*, 1516; (d) Sklenicka, H. M.; Hsung, R. P.; Wei, L.-L.; McLaughlin, M. J.; Gerasyuto, A. I.; Degen, S. J.; Mulder, J. A. *Org. Lett.* **2000**, *2*, 1161.
5. For our formal [3+3] cycloaddition approach arisugacin see: (a) Zehnder, L. R.; Hsung, R. P.; Wang, J.-S.; Golding, G. M. *Angew. Chem., Int. Ed.* **2000**, *39*, 3876. Also see: (b) Handa, M.; Sunazuka, T.; Nagai, K.; Kimura, R.; Shirahata, T.; Tian, Z. M.; Otoguro, K.; Harigaya, Y.; Õmura, S. *J. Antibiotics* **2001**, *54*, 382.
6. (a) Zehnder, L. R.; Wei, L.-L.; Hsung, R. P.; Cole, K. P.; McLaughlin, M. J.; Shen, H. C.; Sklenicka, H. M.; Wang, J.; Zificsak, C. A. *Org. Lett.* **2001**, *3*, 2141. (b) For a preliminary communication, see: Zehnder, L. R.; Hsung, R. P.; Wang, J. Abstract No. ORGN-51, *220th ACS National Meeting*, Washington D.C., Spring, 2000.
7. All new compounds are characterized by ^1H NMR, IR, ^{13}C NMR, and MS. See selected characterizations below in Ref. 12.
8. For a preliminary presentation on these results, see: Cole, K. P.; Zehnder, L. T.; Wei, L.-L., Wang, J.; Hsung, R. P. Abstract No. ORGN-178, *222nd ACS National Meeting*, Chicago, IL, Fall, 2001.
9. We tried epoxidizing **29** using various peroxyacids, but the best result gave the tentatively assigned hexacycle as the major product[10] in 28% yield with the desired product in only 21% yield.
10. The hexacycle was likely a result of intramolecular trapping of the incipient oxocarbenium intermediate by the C1-OH. Such facile trapping by oxygen nucleophiles agrees well with our previous experience in the model

studies and with the hexacycle that at this point is not useful for the arisugacin synthesis.



See: Hexacycle: R_f=0.18 (2:1 EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.88 (s, 3H), 0.95 (s, 3H), 1.24 (td, 1H, J=3.0, 13.5 Hz), 1.28 (s, 3H), 1.65 (s, 3H), 1.68 (m, 1H), 1.73–1.87 (m, 4H), 2.00–2.07 (m, 2H), 2.42 (br, 1H), 3.63 (br, 1H), 3.93 (s, 3H), 3.94 (s, 3H), 4.60 (dd, 1H, J=5.0, 12.0 Hz), 4.90 (s, 1H), 6.30 (s, 1H), 6.89 (d, 1H, J=8.5 Hz), 7.27 (d, 1H, J=2.0 Hz), 7.38 (dd, 1H, J=2.0, 8.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.7, 23.8, 24.4, 26.1, 26.5, 26.6, 30.7, 35.7, 36.5, 50.2, 56.2, 56.4, 71.2, 73.6, 80.1, 84.2, 88.7, 96.4, 98.5, 108.6, 111.2, 119.4, 124.2, 149.4, 151.7, 160.9, 163.8, 164.2; IR (film) cm^{-1} 3390 br, 2943 m, 1694 s, 1632 m, 1572 s, 1516 vs; mass spectrum (EI): m/e (%relative intensity) 497 (M–H)$^-$ (100), 291 (1); m/e [CI] calcd for $C_{28}H_{34}O_8$: 498.2248; found: 498.2252.

11. Nicolaou, K. C.; Zhong, Y.-L.; Baran, P. S. *J. Am. Chem. Soc.* **2000**, *122*, 7596.

12. Selected characterizations: **10**: mp 163–165°C; R_f=0.24 (50% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.02 (s, 3H), 1.04 (s, 3H), 1.31 (s, 3H), 1.53 (s, 3H), 1.76 (ddd, 1H, J=2.5, 4.0, 12.0 Hz), 1.82–1.87 (m, 2H), 1.94 (ddd, 1H, J=3.0, 4.5, 13.0 Hz), 2.07 (ddd, 1H, J=3.5, 14.0, 14.0), 2.19 (m, 1H), 2.56 (dddd, 1H, J=1.0, 5.5, 6.0, 6.0), 2.96 (brd, 1H, J=14.5 Hz), 3.94 (s, 3H), 3.95 (s, 3H), 4.36 (d, 1H, J=3.0 Hz), 4.55 (brd, 1H, J=6.5 Hz), 6.42 (s, 1H), 6.45 (s, 1H), 6.91 (d, 1H, J=8.5 Hz), 7.28 (d, 1H, J=1.5 Hz), 7.41 (dd, 1H, J=2.0, 9.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.0, 24.3, 25.1, 27.8, 27.9, 28.1, 30.6, 31.1, 34.5, 38.5, 47.5, 56.2, 56.3, 72.1, 80.7, 96.7, 100.8, 108.2, 111.2, 111.3, 119.2, 124.2, 142.4, 149.3, 151.5, 160.0, 162.4, 162.8; IR (film) cm^{-1} 3378 br, 3087 mw, 2930 s, 1693 s, 1682 s; mass spectrum (CI): m/e (%relative intensity) 483 (M+H)$^+$ (9), 466 (7), 465 (M+H-H_2O)$^+$ (43), 101 (17), 87 (100), 74 (20), 73 (35), 65 (40); m/e calcd for $C_{28}H_{34}O_7$: 482.2299; found: 482.2306. **3**: R_f=0.14 (50% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.09 (s, 3H), 1.20 (s, 3H), 1.55 (s, 3H), 1.66 (s, 3H), 1.71 (ddd, 1H, J=6.0, 7.5, 14.0 Hz), 1.84 (ddd, 1H, J=3.0, 5.0, 14.5 Hz), 1.98 (ddd, 1H, J=4.0, 14.0, 14.0 Hz), 2.03 (m, 1H), 2.08 (ddd, 1H, J=5.0, 10.0, 15.0 Hz), 2.33 (ddd, 1H, J=5.0, 14.0, 14.0 Hz), 2.63 (ddd, 1H, J=5.5, 6.5, 14.0 Hz), 2.83 (ddd, 1H, J=5.5, 10.0, 14.5 Hz), 3.95 (s, 3H), 3.96 (s, 3H), 6.38 (s, 1H), 6.92 (d, 1H, J=8.5 Hz), 7.32 (d, 1H, J=2.0 Hz), 7.42 (dd, 1H, J=2.0, 8.0 Hz), 7.47 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.6, 26.0, 26.9, 27.6, 28.2, 33.9, 36.6, 37.3, 37.9, 56.2, 56.3, 57.3, 79.3, 79.7, 96.3, 101.0, 108.4, 111.2, 119.3, 119.6, 124.3, 134.1, 149.4, 151.6, 160.6, 161.9, 162.7, 211.3; IR (film) cm^{-1} 2926 m, 1711 vs, 1602 m, 1514 vs; mass spectrum (EI): m/e (%relative intensity) 481 (M+H)$^+$ (100), 463 (M+H$^+$-H_2O)$^+$ (10), 87 (55), 84 (43), 74 (67), 73 (22); m/e calcd for $C_{28}H_{32}O_7$: 480.2143; found: 480.2155. **11**: R_f=0.29 (2:1 EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.96 (s, 3H), 1.02 (s, 3H), 1.19 (td, 1H, J=3.0, 14 Hz), 1.34 (s, 3H), 1.58 (s, 3H), 1.65 (s, 1H), 1.71 br, 1H), 1.72–1.82 (m, 3H), 1.93–2.00 (m, 2H), 2.08 (ddd, 1H, J=2, 5, 13.5 Hz), 2.34 (dt, 1H, J=5.5, 13.5 Hz), 3.93 (s, 3H), 3.95 (s, 3H), 4.37 (dd, 1H, J=6, 9.5 Hz), 6.34 (s, 1H), 6.90 (d, 1H, J=8.5 Hz), 7.02 (s, 1H), 7.29 (d, 1H, J=2.0 Hz), 7.39 (dd, 1H, J=2, 8.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2, 23.6, 24.6, 27.1, 28.2, 28.9, 34.6, 35.6, 37.9, 49.9, 56.0, 56.2, 71.7, 80.9, 81.2, 96.2, 99.7, 108.2, 111.0, 114.8, 119.0, 124.2, 140.5, 149.2, 151.4, 160.0, 161.9, 162.5; IR (film) cm^{-1} 3496 br, 2936 m, 1694 s, 1611 m, 1534 s, 1515 vs; mass spectrum (CI): m/e (%relative intensity) 483 (M+H)$^+$ (100), 465 (M+H-H_2O)$^+$ (18), 447 (M+H-2H_2O)$^+$ (4), 181 (7), 65 (4); m/e calcd for $C_{28}H_{34}O_7$: 482.2299; found: 482.2311. **12**: R_f=0.10 (2:1 EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.94 (s, 3H), 1.03 (s, 3H), 1.12 (ddd, 1H, J=3.0, 4.5, 13.5 Hz), 1.14 (s, 3H), 1.46 (s, 3H), 1.70–1.85 (m, 4H), 1.88 (dt, 1H, J=4.0, 14.5 Hz), 2.07 (dt, 1H, J=4.5, 13.5 Hz), 2.55 (dt, 1H, J=4.5, 14.0 Hz), 3.94 (s, 3H), 3.95 (s, 3H), 4.37 (dq, 1H, J=5.5, 11.0 Hz), 4.82 (brs, 1H, –OH), 5.15 (s, 1H), 5.76 (brs, 1H, –OH), 6.39 (s, 1H), 6.92 (d, 1H, J=8.5 Hz), 7.27 (d, 1H, J=2.3 Hz), 7.41 (dd, 1H, J=2.3, 8.5 Hz); mass spectrum (CI): m/e (%relative intensity) 516.2 M^+ (26), 515.2 (M–H)$^+$ (100), 497 (M+H-H_2O)$^+$ (12), 275 (10). **14**: R_f=0.37 (2:1 EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.95 (s, 3H), 1.09 (s, 3H), 1.21 (m, 1H), 1.30 (s, 3H), 1.45 (s, 1H), 1.72–1.82 (m, 4H), 1.89 (dt, 1H, J=4.5, 15.0 Hz), 1.96 (ddd, 1H, J=5, 8, 12.5 Hz), 2.09 (dt, 1H, J=5.0, 13.5 Hz), 2.18 (s, 3H), 2.41 (dt, 1H, J=4.0, 13.5 Hz), 2.44 (d, 1H, J=17.5 Hz), 2.91 (d, 1H, J=18.0 Hz), 3.92 (s, 3H), 3.93 (s, 3H), 4.11 (s, 1H), 4.63 (s, 1H), 5.79 (dd, 1H, J=5.5, 11.5 Hz), 6.33 (s, 1H), 6.91 (d, 1H, J=8.0 Hz), 7.28 (d, 1H, J=2.0 Hz), 7.37 (dd, 1H, J=2.0, 8.0 Hz); ^{13}C NMR (1245 MHz, $CDCl_3$) δ 17.0, 22.0, 24.2, 24.6, 24.7, 25.5, 27.2, 29.1, 29.4, 34.5, 39.0, 47.7, 56.0, 56.1, 73.0, 77.4, 81.0, 81.7, 96.5, 97.5, 108.2, 111.1, 118.8, 124.2, 149.2, 151.2, 158.8, 162.5, 164.4, 171.1; IR (film) cm^{-1} 3375 br, 2952 m, 2927 m, 1737 vs, 1677 vs, 1574 m, 1516 vs; mass spectrum (CI): m/e (%relative intensity) 543 (M+H)$^+$ (24), 525 (M+H-H_2O)$^+$ (100), 507 (M+H-2H_2O)$^+$ (16), 483 (M+H-AcOH)$^+$ (66), 465 (M+H-H_2O-AcOH)$^+$ (37), 447 (M+H-2H_2O-AcOH)$^+$ (11), 289 (12), 261 (21); m/e calcd for $C_{30}H_{39}O_9$: 543.2594; found: 543.2610. **16**: R_f=0.33 (2:1 EtOAc in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.06 (s, 3H), 1.25 (s, 3H), 1.43 (s, 3H), 1.51 (s, 3H), 1.68–1.97 (m, 4H), 2.21 (ddd, 1H, J=6.0, 10.2, 20.0 Hz), 2.35–2.48 (m, 2H), 2.84 (d, 1H, J=17.7 Hz), 2.89 (ddd, 1H, J=6.9, 10.2, 15.9 Hz), 3.24 (d, 1H, J=17.7 Hz), 3.93 (s, 3H), 3.94 (s, 3H), 4.12 (s, 1H), 6.05 (s, 1H), 6.36 (s, 1H), 6.91 (d, 1H, J=8.4 Hz), 7.29 (d, 1H, J=2.1 Hz), 7.39 (dd, 1H, J=2.1, 8.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.5, 24.0, 25.9, 26.4, 27.1, 27.9, 28.7, 35.4, 37.4, 38.7, 56.0, 56.1, 57.9, 74.1, 77.2, 79.8, 81.8, 83.2, 96.7, 108.2, 111.1, 118.8, 124.3, 149.2, 155.5, 158.8, 164.6, 216.0; IR (film) cm^{-1} 3495 br, 3377 br, 2964 m, 1713 s, 1694 s, 1640 m, 1578 s, 1519 vs; mass spectrum (CI): m/e (%relative intensity) 497 (M–H)$^-$ (100), 479 (M–H-H_2O)$^-$ (8); m/e calcd for $C_{28}H_{34}O_8$: 498.2248; found: 498.2239. **(±)-Arisugacin A (1):** R_f=0.27 (2:1 EtOAc in hexanes); ^{1}H NMR (500 MHz, pyridine-d_5) δ 1.19 (s, 3H), 1.30 (s, 3H), 1.46 (s,

3H), 1.50 (s, 3H), 1.86–1.98 (m, 3H), 2.90 (dt, 1H, $J=4.5$, 13.5 Hz), 3.17 (d, 1H, $J=17.5$ Hz), 3.77 (s, 3H), 3.78 (s, 3H), 4.35 (d, 1H, $J=17.5$ Hz), 5.95 (d, 1H, $J=10.5$ Hz), 6.28 (d, 1H, $J=10.0$ Hz), 6.79 (s, 1H), 7.00 (d, 1H, $J=9.0$ Hz), 7.48 (d, 1H, $J=2.0$ Hz), 7.59 (m, 1H), 7.69 (s, 1H), 8.95 (s, 1H); ^{13}C NMR (75 MHz, pyridine-d_5) δ 22.4, 23.9, 24.2, 26.2, 26.5, 27.9, 29.9, 43.2, 56.3 (2C), 56.9, 76.6, 79.5, 81.8, 97.7, 98.3, 109.5, 112.6, 119.5, 124.6, 125.3, 150.0, 152.4, 153.5, 159.0, 163.6, 164.4, 202.6; IR (film) cm^{-1} 3357 brs, 2198 m, 1683 s, 1638 s, 1575 s, 1518 vs; mass spectrum (CI): m/e (%relative intensity) 495 (M–H)$^-$ (100), 477 (M–H-H_2O)$^-$ (7), 381 (95), 366 (4); m/e calcd for $C_{28}H_{33}O_8$: 497.2170; found: 497.2181. The synthetic sample has an identical R_f value with the natural sample in three different solvent systems: (a) 2:1 EtOAc:hexane: $R_f=0.27$; (b) 2:1 ether:hexane: $R_f=0.09$; (c) 1:9 acetone:$CHCl_3$: $R_f=0.24$. In addition, the ^{1}H NMR of the synthetic sample was unchanged by addition of (+)-arisugacin.