Available online at www.sciencedirect.com
SCIENCE DIRECT®
Tetrahedron Letters 47 (2006) 5409–5413
Tetrahedron Letters

Convergent route to the purpuromycin bisphenolic spiroketal: hydrogen bonding control of spiroketalization stereochemistry

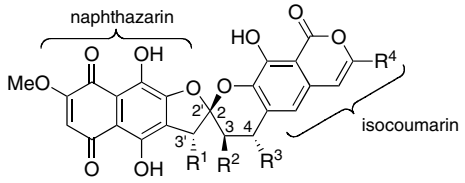
Stephen P. Waters, Michael W. Fennie and Marisa C. Kozlowski*

Department of Chemistry, Roy and Diana Vagelos Laboratories, University of Pennsylvania, Philadelphia, PA 19104-6323, United States

Received 11 April 2006; revised 3 May 2006; accepted 8 May 2006
Available online 9 June 2006

Abstract—A mild and efficient [3+2] nitrile oxide/olefin cycloaddition provided a rapid and convergent entry into precursors of bisphenolic spiroketals, a structural type unique to the rubromycin family of natural products. In addition, implementation of the premise that a hydrogen bond from the C4-OH controls the stereochemistry of the purpuromycin core resulted in moderate diastereocontrol in the spiroketalization. Spectroscopic and X-ray data of these systems have provided the first assignment of the relative configuration of purpuromycin.

Purpuromycin (**1**),[1] γ-rubromycin (**2**),[2] heliquinomycin (**3**),[3] and the griseorhodins (**4**–**5**)[4] are a set of structurally related polyketides consisting of highly functionalized naphthazarin and isocoumarin ring systems linked through a bisbenzannulated 5,6-spiroketal (Fig. 1). Our particular interest in purpuromycin (**1**), isolated from the soil bacterium *A. ianthinogenes*, followed reports of its potent antimicrobial[5] and human telomerase inhibitory properties.[6] Moreover, its unique ability to bind with high affinity to all tRNAs, thereby inhibiting their acceptor capacity and disrupting further protein synthesis, represents a novel mode of activity.[7]



Purpuromycin (**1**, R^1=H, R^2=H, R^3=OH, R^4 = CO_2Me)
γ-Rubromycin (**2**, R^1=H, R^2=H, R^3=H, R^4 = CO_2Me)
Heliquinomycin (**3**, R^1=cymarose, R^2=OH, R^3=H, R^4 = CO_2Me)
Griseorhodin C (**4**, R^1=OH, R^2=OH, R^3 = OH, R^4 = Me)
Griseorhodin G (**5**, R^1=OH, R^2=OH, R^3 = H, R^4 = Me)

Figure 1. The rubromycin family of natural products.

While a formidable array of oxidation is present within the hexacyclic ring system, the most striking feature is the highly unusual 5,6-bisbenzannulated spiroketal core. Indeed, the only reported synthesis of a natural product featuring this linkage is that of heliquinomycin aglycone by Danishefsky and co-workers, which was realized through coupling of a lithiated naphthofuran with an arylacetaldehyde and Mitsunobu-like ring closure to form the spiroketal.[8] In early model studies toward the rubromycins by de Koning, Henry condensation of two aryl moieties furnished a nitroalkene which, after a Nef reaction revealed the ketone function, standard acid-catalyzed spirocyclization formed the core bisbenzannulated spiroketal.[9] Later model studies by Brimble employed a similar spiroketalization after uniting a lithiated arylacetylene with an arylacetaldehyde.[10] None of these programs addressed substitution at C4 nor the controlled assembly of defined spiroketal diastereomers.

In this letter, we disclose a rapid, convergent strategy as a general means for construction of the C4-functionalized bisphenolic spiroketal array found in purpuromycin and congeners (Fig. 2). A key feature is the [3+2] cycloaddition[11] strategy to unite different left hand and right hand fragments. In addition to enabling rapid model studies, such an approach is amenable to the synthesis

* Corresponding author. Tel.: +1 215 898 3048; fax: +1 215 573 7165; e-mail: marisa@sas.upenn.edu

0040-4039/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2006.05.044

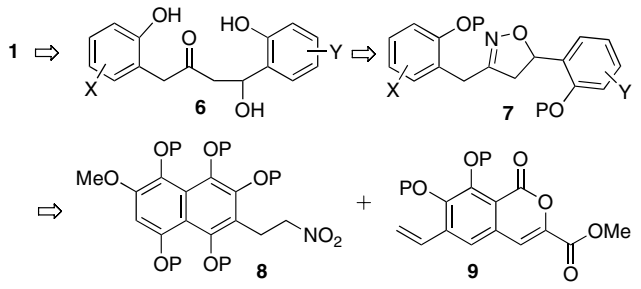


Figure 2. Retrosynthesis of purpuromycin.

of multiple analogs from a few fragments. The mild conditions afforded by this method are highly desirable due to the sensitive functional arrays present including the β-hydroxyketone, the electron rich naphthalene (**8**), and the electrophilic isocoumarin (**9**). Finally, we report that hydrogen bonding is key to setting the spiroketal stereochemistry.

As a first step in defining the stereochemistry of the purpuromycin spiroketal, we recorded the NMR spectra from a sample of natural purpuromycin[12] in $CDCl_3$ at 500 MHz (Fig. 3). Together with computational models, this information permitted a tentative assignment of the relative configuration and conformation of the spiroketal core. Specifically, coupling of C3-H^b with C4-H^a ($J = 1.1$ Hz) is consistent with an equatorial–equatorial arrangement whereas the coupling of C3-H^a with C4-H^a ($J = 5.3$ Hz) is consistent with an axial–equatorial arrangement. Thus, the C4-OH group occupies a pseudo-axial position within the pyran ring which occupies a twist boat form due to the aromatic ring of the isocoumarin (Fig. 3).

Further, an anomeric effect is proposed to cause O1′ to occupy a pseudo-axial position in purpuromycin leading to a *syn* relationship between O1′ and C4-OH.[13] We propose that this form is stabilized by an intramolecular hydrogen bond between C4-OH and O1′.[14] Unfortunately, direct evidence for this hydrogen bond could not be obtained since the alcohol proton signal was not distinct. However, calculations provide strong support for the stabilizing nature of this interaction (Fig. 4).[15] The **10ax** form was more stable even when a continuum water solvent model was employed.

Assuming that thermodynamic control operates during the spiroketalization, then protection of the C4-OH is

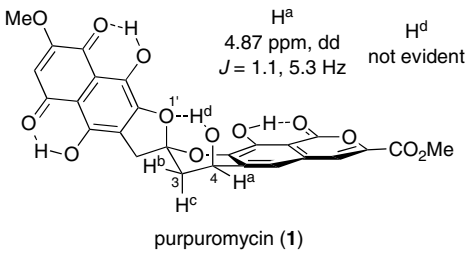


Figure 3. Proposed relative configuration and conformation of purpuromycin (**1**).

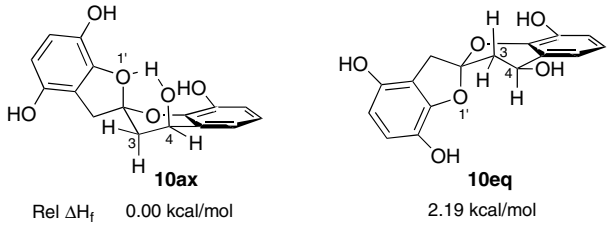
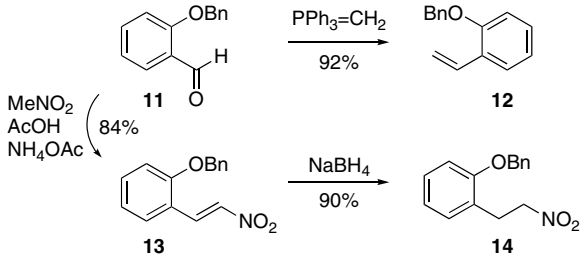


Figure 4. Calculated energies (AM1) of the model spiroketal diastereomers.



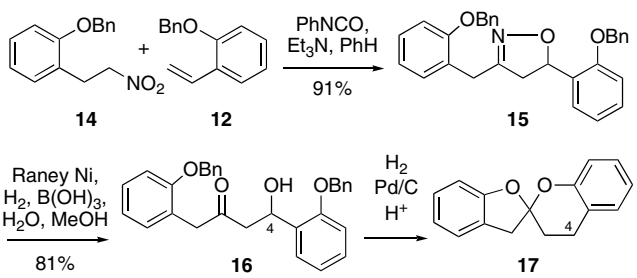
Scheme 1. Synthesis of [3+2] coupling substrates.

undesirable during spiroketalization of **6** as the free hydroxyl is needed. For example, the equatorial form **10eq** would predominate with a silyl group on the C4-OH.

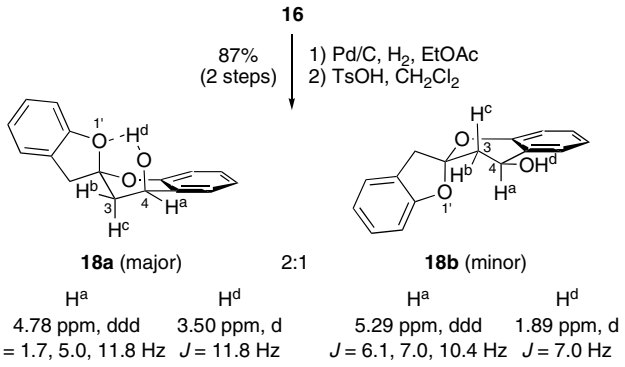
We thus commenced studies with model substrates that would allow formation of precursors with the free C4-OH. Both required precursors could be prepared from the benzyl ether **11**[16] obtained from salicylaldehyde (Scheme 1). Olefination of **11** by Wittig homologation[17] produced styrene derivative **12** in 92% yield. Alternately, treatment with nitromethane and catalytic NH_4OAc effected Henry condensation[18] to give nitrostyrene **13** in 84% yield. Conjugate reduction with $NaBH_4$[19] then provided nitroalkane **14** in 90% yield.

Styrene **12** and nitroalkane **14** underwent smooth [3+2] cycloaddition in the presence of PhNCO and catalytic Et_3N to afford isoxazoline **15** in 91% yield (Scheme 2). Hydrogenolysis of the isoxazoline using the conditions described by Curran (catalytic Raney Ni, $B(OH)_3$, aqueous MeOH) gave the keto-alcohol **16** in 81% yield.[11]

At this point, an attempt was made to combine the benzyl ether hydrogenolyses and the spirocyclization. When this protocol was applied to **16**, hydrogenolysis of the



Scheme 2. [3+2] Cycloaddition and spirocyclization.



Scheme 3. Spiroketal diastereomers **18a** and **18b**.

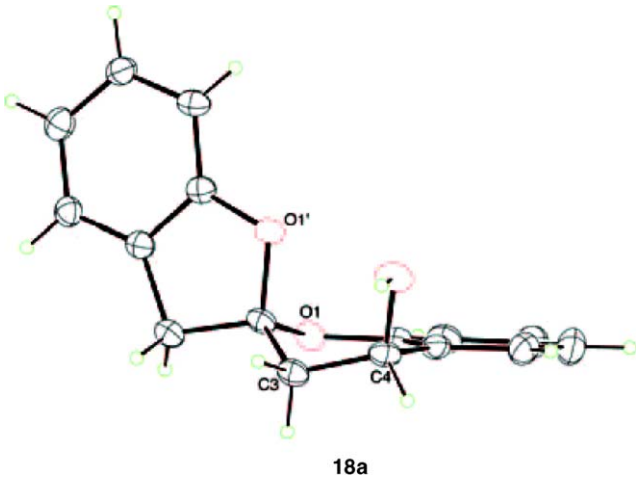
crucial C4-OH was observed yielding **17** in analogy to prior reports from de Koning.[9]

To circumvent this problem, sequential hydrogenolysis and acid induced spirocyclization was undertaken. Diastereomeric spiroketals **18a** and **18b** were produced as a 2:1 mixture in a combined yield of 87% over the two steps (Scheme 3). Assignment of the relative configurations and conformations of spiroketals **18a** and **18b** was possible by examination of their respective ^{1}H NMR spectra ($CDCl_3$, 500 MHz). For the major diastereomer (**18a**), coupling between C4-H^a and the diastereotopic C3-H^b and C3-H^c protons gave J values of 1.7 and 5.0 Hz. As expected from our prior analysis (see above), these values indicate that, within the pyran ring of **18a**, the C4-OH occupies a pseudo-axial position (Scheme 3). For the minor diastereomer (**18b**), coupling between C4-H^a and the diastereotopic C3-H^b and C3-H^c gave J values of 6.1 and 10.4 Hz. These values support that, within the pyran ring of **18b**, the C4-OH now occupies a pseudo-equatorial position. Due to an anomeric effect, O1′ was reasoned to be pseudo-axial position in both spiroketal diastereomers.

The relatively high C4-OH chemical shift at 3.50 ppm in **18a** indicates an intramolecular hydrogen bond which further supports the pseudo-axial C4-OH orientation (Scheme 3).[20] In comparison, the 1.89 ppm shift for the pseudo-equatorial C4-OH of minor diastereomer **18b**, indicates an absence of hydrogen bonding.

An X-ray crystal analysis of major diastereomer **18a** secured unambiguous proof for these structural assignments (Fig. 5).[21] The pyran ring was found to adopt a flattened conformation best characterized as a twist-boat. The C4-OH and O1′ occupy pseudo-axial positions within the pyran ring, leading to a *syn* relationship.

This data provided further support for the original stereochemical assignment of purpuromycin (Fig. 2). The chemical shifts and coupling constants obtained from purpuromycin were in excellent agreement with those from major spiroketal **18a** while differing substantially with those from minor diastereomer **18b**. Interestingly, similar yields and diastereomeric ratios were observed with aprotic ($TsOH/CH_2Cl_2$) and protic (HCl/EtOH, and PPTS/MeOH) spiroketalization conditions providing considerable promise for control of this stereochemical element in syntheses of the natural products.



18a

Figure 5. X-ray structure of spiroketal **18a**.

In conclusion, a convergent method for the construction of bisbenzannulated 5,6-spiroketals is reported consisting of [3+2] cycloaddition of nitrile oxides with olefins, reduction of the resultant isoxazolines to β-keto alcohols, and subsequent spirocyclization.[22] In addition, implementation of our premise that a hydrogen bond from the C4-OH controls the stereochemistry of the purpuromycin core resulted in moderate stereocontrol in the spiroketalization.[14] This premise may also be useful for other members of this class of compounds. Structural analysis of the resultant diastereomeric 5,6-spiroketals provided a definitive assignment of the purpuromycin conformation and stereochemistry.

Acknowledgements

Support for this work was provided by the American Cancer Society (RSG-02-137-01-CDD) and by a Sloan Foundation Research Fellowship (MCK). We thank Dr. Patrick Carroll for the X-ray crystal analysis. We thank Biosearch Italia SpA for a sample of purpuromycin.

References and notes

1. (a) Coronelli, C.; Pagani, H.; Bardone, M. R.; Lancini, G. C. *J. Antibiot.* **1974**, *27*, 161–168; (b) Bardone, M. R.; Martinelli, E.; Zerilli, E. F.; Coronelli, C. *Tetrahedron* **1974**, *30*, 2747.
2. Brockmann, H.; Zeeck, A. *Chem. Ber.* **1970**, *103*, 1709.
3. (a) Chino, M.; Nishikawa, K.; Umekita, M.; Hayashi, C.; Yamazaki, T.; Tsuchida, T.; Sawa, R.; Hamada, M.; Takeuchi, T. *J. Antibiot.* **1996**, *49*, 752; (b) Chino, M.; Nishikawa, K.; Tsuchida, T.; Sawa, R.; Nakamura, H.; Nakamura, K. T.; Muraoka, M. Y.; Ikeda, D.; Naganawa, H.; Sawa, T.; Takeuchi, T. *J. Antibiot.* **1997**, *50*, 143.
4. (a) Yang, J.; Fan, S.; Pei, H.; Zhu, B.; Xu, W.; Naganawa, H.; Hamada, M.; Takeuchi, T. *J. Antibiot.* **1991**, *44*, 1277;

(b) Panzone, G.; Trani, A.; Ferrari, P.; Gastaldo, L.; Colombo, L. *J. Antibiot.* **1997**, *50*, 665.
5. (a) Trani, A.; Dallanoce, C.; Ferarri, P.; Goldstein, B. P.; Ripamonti, F.; Ciabatti, R. *Il Farmaco* **1996**, *51*, 503; (b) Trani, A.; Kettenring, J.; Ripamonti, F.; Goldstein, B.; Ciabatti, R. *Il Farmaco* **1993**, *48*, 637.
6. Ueno, T.; Takahashi, H.; Oda, M.; Mizunuma, M.; Yokoyama, A.; Goto, Y.; Mizushina, Y.; Sakaguchi, K.; Hayashi, H. *Biochemistry* **2000**, *39*, 5995.
7. Krillov, S.; Vitali, L. A.; Goldstein, B. P.; Monti, F.; Semenkov, Y.; Makhno, V.; Ripa, S.; Pon, C. L.; Gualerzi, C. O. *RNA* **1997**, *3*, 905.
8. (a) Qin, D.; Ren, R. X.; Siu, T.; Zheng, C.; Danishefsky, S. J. *Angew. Chem., Int. Ed.* **2001**, *40*, 4709; (b) Siu, T.; Qin, D.; Danishefsky, S. J. *Angew. Chem., Int. Ed.* **2001**, *40*, 4713.
9. (a) Capecchi, T.; de Koning, C. B.; Michael, J. P. *Tetrahedron Lett.* **1998**, *39*, 5429; (b) Capecchi, T.; de Koning, C. B.; Michael, J. P. *J. Chem. Soc., Perkin Trans. 1* **2000**, 2681.
10. Tsang, K. T.; Brimble, M. A.; Bremner, J. B. *Org. Lett.* **2003**, *5*, 4425.
11. (a) Curran, D. P. *J. Am. Chem. Soc.* **1983**, *105*, 5826; (b) Curran, D. P. *J. Am. Chem. Soc.* **1982**, *104*, 4024.
12. Obtained from Biosearch Italia SpA.
13. For reviews, see: (a) *Anomeric Effects*; Szarek, W. A., Horton, D., Eds. ACS Symposium Series 87; American Chemical Society: Washington, DC, 1979; (b) Kirby, A. J. *The Anomeric Effect and Related Stereoelectronic Effects at Oxygen*; Springer: Berlin, 1983.
14. For a review of spiroketals including examples controlled by hydrogen bonding, see: (a) Perron, F.; Albizati, K. F. *Chem. Rev.* **1989**, *89*, 1617–1661; For a specific example of hydrogen bonding being used to control spiroketal configuration, see: (b) Ireland, R. E.; Habich, D.; Norbeck, D. W. *J. Am. Chem. Soc.* **1985**, *107*, 3271–3278.
15. Spartan '02 Windows, Wavefunction, Inc., 2001.
16. Harris, T. D.; Roth, G. P. *J. Org. Chem.* **1979**, *44*, 2004.
17. Wei, X.; Taylor, R. J. K. *Tetrahedron Lett.* **1996**, *37*, 4209.
18. (a) Kita, Y.; Takada, T.; Ibaraki, M.; Gyoten, M.; Mihara, S.; Fujita, S.; Tohma, H. *J. Org. Chem.* **1996**, *61*, 223; (b) Dauzonne, D.; Royer, R. *Synthesis* **1984**, 1054.
19. Sinhababu, A. K.; Borchardt, R. T. *Tetrahedron Lett.* **1983**, *24*, 227.
20. Kumar, G. A.; McAllister, M. A. *J. Org. Chem.* **1998**, *63*, 6968–6972.
21. Crystallographic data (excluding structure factors) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 604209. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44 (0)1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].
22. **4-(2-Benzyloxy-benzyl)-6-(2-benzyloxy-phenyl)-5,6-dihydro-2*H*-[1,3] oxazine (15)**. To a solution of nitroalkane **14** (257 mg, 1.00 mmol) and styrene **12** (210 mg, 1.00 mmol) in PhH (10 mL) at rt were added PhNCO (435 μL, 4.00 mmol) and Et_3N (28 μL, 0.20 mmol). After 24 h, the reaction mixture was filtered and the solvent removed. Purification by flash chromatography (20% EtOAc/hexanes) afforded isoxazoline **15** (418 mg, 93% yield) as a clear colorless oil: IR (neat) 1602, 1494, 1243, 1015 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.32 (d, $J = 7.5$ Hz, 1H), 7.27–7.19 (m, 10H), 7.11 (t, $J = 7.5$ Hz, 1H), 7.08 (d, $J = 7.5$ Hz, 1H), 7.05 (d, $J = 7.5$ Hz, 1H), 6.83 (t, $J = 7.5$ Hz, 1H), 6.80–6.77 (m, 3H), 5.69 (dd, $J = 7.8$, 11.0 Hz, 1H), 4.93 (d, $J = 11.9$ Hz, 1H), 4.92 (d, $J = 11.2$ Hz, 1H), 4.90 (d, $J = 11.2$ Hz, 1H), 4.89 (d, $J = 11.9$ Hz, 1H), 3.64 (d, $J = 15.1$ Hz, 1H), 3.58 (d, $J = 15.1$ Hz, 1H), 3.15 (dd, $J = 11.0$, 17.3 Hz, 1H), 2.64 (dd, $J = 7.8$, 17.3 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.7, 156.4, 155.1, 136.9, 136.8, 130.4, 130.1, 128.6, 128.5 (2C), 128.2, 127.8 (2C), 127.1 (2C), 126.3, 124.7, 121.0, 120.9, 111.8, 111.5, 77.2, 70.0, 69.9, 44.3, 28.1; HRMS (ESI) *m/z* calcd for $C_{30}H_{27}NO_3Na$ (MNa^+) 472.1889, found 472.1880.

1,4-Bis-(2-benzyloxy-phenyl)-4-hydroxy-butan-2-one (16). To a solution of isoxazoline **15** (418 mg, 0.93 mmol) in MeOH (50 mL) and H_2O (5 mL) were added boric acid (172 mg, 2.79 mmol) and Raney Ni (10 drops, 50% slurry in H_2O). After stirring under H_2 (1 atm) for 5 h at rt, the reaction mixture was filtered, poured into H_2O (50 mL), and extracted with CH_2Cl_2 (2×50 mL). The combined organic layers were washed with brine (100 mL), dried (Na_2SO_4), and concentrated. Purification of the residue by flash chromatography (33% EtOAc/hexanes) afforded keto-alcohol **16** (339 mg, 81% yield) as a clear colorless oil: IR (neat) 3501 (br), 1710, 1602, 1015 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.41 (dd, $J = 1.6$, 7.5 Hz, 1H), 7.33–7.24 (m, 10H), 7.19 (dd, $J = 1.6$, 7.4 Hz, 1H), 7.16 (dd, $J = 1.6$, 7.5 Hz, 1H), 7.03 (dd, $J = 1.6$, 7.4 Hz, 1H), 6.94 (t, $J = 7.4$ Hz, 1H), 6.88 (t, $J = 7.4$ Hz, 1H), 6.85 (t, $J = 7.5$ Hz, 1H), 6.83 (t, $J = 7.5$ Hz, 1H), 5.42 (dd, $J = 2.7$, 9.0 Hz, 1H), 4.98 (s, 2H), 4.95 (s, 2H), 3.66 (d, $J = 16.1$ Hz, 1H), 3.62 (d, $J = 16.1$ Hz, 1H), 3.53 (br s, 1H), 2.96 (dd, $J = 2.7$, 17.3 Hz, 1H), 2.72 (dd, $J = 9.0$, 17.3 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.6, 156.4, 154.8, 136.8 (2C), 131.3 (2C), 128.6, 128.5 (2C), 128.1, 127.9, 127.8, 127.2, 127.0, 126.6, 123.3, 121.1, 121.0, 111.8, 111.5, 70.0, 69.9, 65.6, 48.6, 45.5; HRMS (ESI) *m/z* calcd for $C_{30}H_{28}O_4Na$ (MNa^+) 475.1885, found 475.1874.

Spiroketal (17). To a solution of ketone **16** (200 mg, 0.442 mmol) in EtOH (10 mL) were added HCl (1 drop, 12 M) and Pd/C (40 mg, 10% Pd). After stirring under H_2 (1 atm) for 12 h at rt, the reaction mixture was filtered and concentrated. Purification of the residue by flash chromatography (33% EtOAc/hexanes) afforded spiroketal **17** (82 mg, 78% yield) as a clear colorless oil: IR (neat) 3042, 2934, 1586 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.25 (d, $J = 7.5$ Hz. 1H), 7.16 (m, 3H), 6.94 (t, $J = 7.5$ Hz, 2H), 6.82 (d, $J = 8.1$ Hz, 2H), 3.49 (d, $J = 16.5$ Hz, 1H), 3.32 (d, $J = 16.5$ Hz, 1H), 3.28 (ddd, $J = 6.2$, 13.1, 16.8 Hz, 1H), 2.85 (ddd, $J = 3.1$, 6.2, 16.2 Hz, 1H), 2.35 (ddd, $J = 2.5$, 6.2, 13.1 Hz, 1H), 2.24 (ddd, 6.2, 13.1, 13.1 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.8, 152.3, 129.0, 128.1, 127.4, 125.3, 124.8, 121.3, 121.1, 121.0, 117.1, 109.8, 108.9, 41.8, 30.4, 21.9; HRMS (CI) *m/z* calcd for $C_{16}H_{14}O_2$ (M^+) 238.0994, found 238.0997.

Spiroketals 18a and 18b. A suspension of keto-alcohol **16** (168 mg, 0.37 mmol) and 10% Pd/C (50 mg) in EtOAc (10 mL) at rt was stirred under H_2 (1 atm) overnight. The reaction mixture was filtered through Celite and the solvent removed. The residue was then dissolved in CH_2Cl_2 (10 mL), and to this solution was added TsOH (21 mg, 0.11 mmol). After stirring at rt for 45 min, the reaction mixture was concentrated, and the residue purified by flash chromatography (25% EtOAc/hexanes) to afford first spiroketal **18a** (57 mg), followed by spiroketal **18b** (25 mg) in 87% combined yield. **Major diastereomer 18a**: white solid; mp 126–127 °C; IR (film) 3489 (br), 1586, 1212, 1065 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.49 (dd, $J = 1.9$, 7.5 Hz, 1H), 7.28 (d, $J = 7.5$ Hz, 1H), 7.24 (td, $J = 1.9$, 7.5 Hz, 1H), 7.16 (t, $J = 7.5$ Hz, 1H), 7.06 (td, $J = 1.3$, 7.5 Hz, 1H), 6.97 (td, $J = 1.3$, 7.5 Hz, 1H), 6.83 (d, $J = 7.5$ Hz, 1H), 6.77 (d, $J = 7.5$ Hz, 1H), 4.78 (ddd, $J = 1.7$, 5.0, 11.8 Hz, 1H), 3.53 (d, $J = 16.4$ Hz, 1H), 3.50 (d, $J = 11.8$ Hz, 1H, OH), 3.38 (d, $J = 16.4$ Hz, 1H), 2.67

(dd, $J = 1.7$, 14.5 Hz, 1H), 2.53 (dd, $J = 5.0$, 14.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.3, 151.0, 130.6, 129.8, 128.2, 124.9, 124.6, 123.8, 122.1, 121.7, 117.5, 110.1, 109.4, 63.5, 42.2, 38.5; HRMS (CI) m/z calcd for $C_{16}H_{14}O_3$ (M^+) 254.0943, found 254.0953. **Minor diastereomer 18b**: white solid; mp 85–86 °C; IR (film) 3350 (br), 1586, 1204, 1038 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, $J = 7.5$ Hz, 1H), 7.25 (d, $J = 7.5$ Hz, 1H), 7.21 (td, $J =$ 1.9, 7.5 Hz, 1H), 7.16 (t, $J = 7.5$ Hz, 1H), 7.04 (td, $J = 1.3$, 7.5 Hz, 1H), 6.94 (t, $J = 7.5$ Hz, 1H), 6.80 (d, $J = 8.0$ Hz, 1H), 6.79 (d, $J = 8.0$ Hz, 1H), 5.29 (ddd, $J = 6.1$, 7.0, 10.4 Hz, 1H), 3.48 (d, $J = 16.6$ Hz, 1H), 3.36 (d, $J = 16.6$ Hz, 1H), 2.68 (dd, $J = 6.1$, 13.0 Hz, 1H), 2.28 (dd, $J = 10.4$, 13.0 Hz, 1H), 1.89 (d, $J = 7.0$ Hz, 1H, OH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.7, 151.4, 129.2, 128.2, 126.5, 125.1, 125.0, 124.9, 121.8, 121.4, 116.9, 110.0, 109.9, 63.4, 41.9, 39.9; HRMS (CI) m/z calcd for $C_{16}H_{12}O_2$ ($[M-OH]^+$) 236.0837, found 236.0827.