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1,2-Dioxines Containing Tethered Hydroxyl Functionality as Convenient Precursors for Pyran Syntheses

Thomas D. Avery,[†] Daniela Caiazza,[†] Julie A. Culbert,[†] Dennis K. Taylor,*[,†] and Edward R. T. Tiekink[‡]

Department of Chemistry, The University of Adelaide, South Australia 5005, Australia, and School of Science, Griffith University, Nathan, Queensland 4111, Australia

dennis.taylor@adelaide.edu.au

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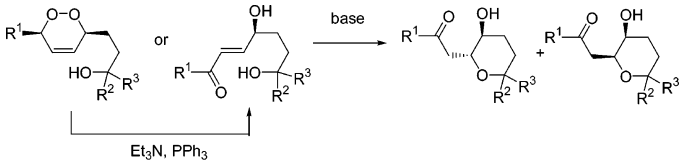

A new method for the construction of tetrahydropyrans derived from readily available 1,2-dioxines containing a tethered hydroxyl moiety is described. The reaction proceeds via a base-catalyzed rearrangement of the 1,2-dioxines to either the isomeric *cis* or *trans* γ-hydroxy enones followed by intramolecular oxa-Michael addition of the tethered hydroxyl group.

Introduction

Pyrans represent an important structural motif in many significant biologically active compounds with many groups tackling their sytheses.[1] Examples include simple pyrans, represented by (+)-decarestrictine L, an inhibitor of cholesterol biosynthesis,[2] and the relatively complex antimitotic macrolide spongistatin 1,[3] Figure 1.

Primarily, our research group has focused on the chemistry of monocyclic 1,2-dioxines **1** and the rearrangements that this class of compounds undergo. One important base-catalyzed rearrangement, which is known as the Kornblum−De La Mare reaction, converts 1,2-dioxines **1** into *cis* γ-hydroxy enones **2** through removal of the most acidic proton adjacent the O−O linkage, Scheme 1.[4] We have found that these enones are exceptional conjugate acceptors. They undergo facially selective

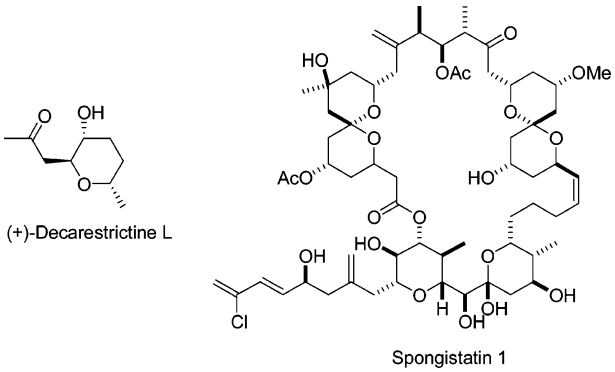

FIGURE 1. Examples of pyran-containing natural products.

1,4-addition with both carbon-centered nucleophiles such as stabilized ylides,[5] phosphonates,[6] malonates[7] and also oxygen-centered nucleophiles when catalyzed by a suitable base.[8] *cis*-γ-Hydroxy enones are, however, sus-

* To whom correspondence should be addressed. Phone: (+61) 8 8303 5494. Fax: (+61) 8 83034358.

[†] The University of Adelaide.

[‡] Griffith University.

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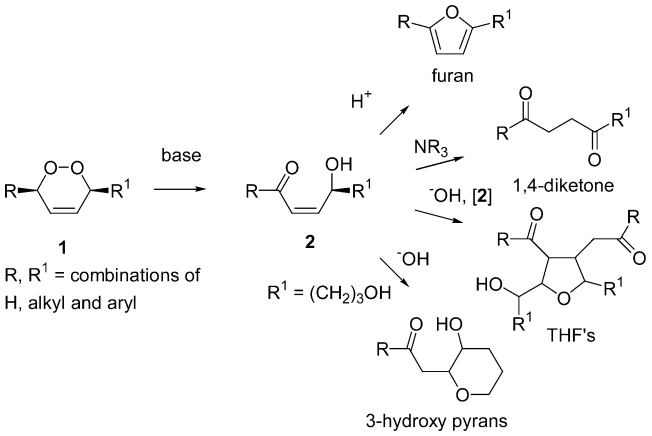
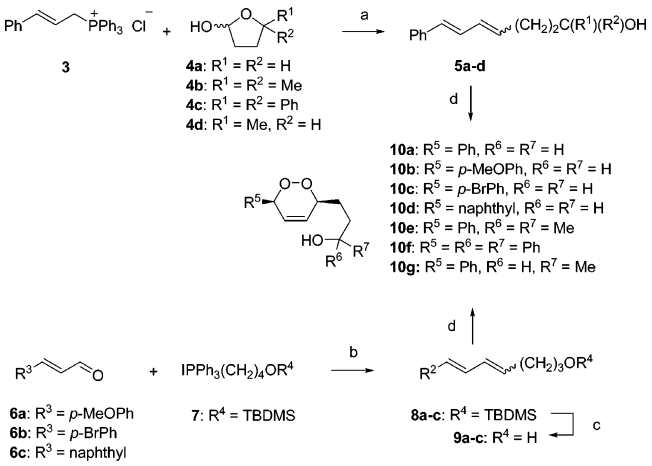
SCHEME 1



SCHEME 2



ceptible to further rearrangement to furans under acidic and neutral conditions and 1,4-diketones when amine bases are employed. In the presence of hydroxide, self-condensation occurs to form THFs with no competing 1,4-diketone formation, Scheme 1.[8]

Thus, the ubiquity of pyrans in nature and these previous discoveries moved us to examine whether, by tethering a hydroxyl grouping to 1,2-dioxines, functionalized oxygen containing heterocycles such as 3-hydroxy pyrans could potentially be generated in a stereospecific manner, Scheme 1. This report describes the synthesis of the precursor hydroxyl containing 1,2-dioxines and a domino Kornblum–De La Mare/intramolecular oxa-Michael ring closure (OMIRC) reaction for the generation of 3-hydroxypyrans.

Results and Discussion

To investigate this approach and to evaluate the effect of substituents about the hydroxyl terminus a series of 1,2-dioxines **10a**–**g** were synthesized, Scheme 2. Thus, Wittig reaction of the phosphorane, generated from the phosphonium salt **3** using potassium *tert*-butoxide with hemiacetals **4**, yielded the requisite 1,3-dienes **5** in moderate yields, 52–64%. 1,3-Dienes **8** were synthesized in good overall yields (70–86%) through Wittig reaction of phosphorane, generated from phosphonium salt **7**[9] using *n*-BuLi, with aldehydes **6**. Deprotection with TBAF gave the free alcohols **9** in excellent yield. The resultant 1,3-dienes **5** and **9** were subjected to photooxidation in the presence of rose bengal bis(triethylammonium) salt to yield the 1,2-dioxines **10a**–**g** in yields ranging from 23 to 70%, Scheme 2.[10]

When **10a** was allowed to react with an equimolar amount of lithium hydroxide in THF, pyrans **12a** and **13a** were formed in 51% and 21% isolated yield, respectively, Scheme 3, thus verifying the hypothesis. None of the 1,4-diketone **14a** was detectible under these conditions, which is consistent with our previous observations that mild amine bases effectively catalyze the rearrangement of *cis* γ-hydroxy enones into 1,4-diketones[5c] while hydroxide and alkoxide bases promote dimerization of *cis* γ-hydroxy enones into THFs if no tethered hydroxyl grouping is present.[8]

The structure and stereochemistry of **12a** and **13a** were unambiguously elucidated through a combination of ^{1}H, ^{13}C, gCOSY, gHMBC, gHSQC, and ROESY NMR experiments and further confirmed through the X-ray crystal structure of **12a**. Pyran **13a** was acid sensitive and underwent quantitative rearrangement to give furan **18a** when dissolved in $CDCl_3$. Pyran **12a** was also transformed into furan **18a** when allowed to react with *p*-toluenesulfonic acid. Pyran **12a** was found not to interconvert to **13a** or decompose over the reaction time period when resubjected to the reaction conditions.

To avoid this furanization of the pyran products, the hydroxyl groups within **12a** and **13a** were acetylated in excellent yield, Scheme 3, and the resultant pyran acetates **15a** and **16a** were found to be stable to acid, which indicated the importance of the hydroxyl group in the rearrangement to furan. Mechanistically, furanization proceeds through isomeric hemiacetal formation, which is prevented by acetylation. Elimination of water followed by aromatization yields the 2,5-disubstituted furan **18a**. This mechanism also explains the greater reactivity of the *cis*-substituted pyran (**13a**) toward furanization.

To extend and investigate the cyclization reaction further, 1,2-dioxines **10b**–**f** were also allowed to react with LiOH and the products acetylated to furnish pyrans **15** and **16**, Table 1, entries 2–6, Scheme 3. In nearly all cases, lithium hydroxide favored the formation of the *trans* pyrans **15**. Of note was the lack of pronounced influence that the substitution of the tethered hydroxyl moiety had on the reaction outcome, compare entries 1 and 5. Moreover, switching to the use of NaOH had little effect on product outcome, entries 1 and 7.

To further examine the influence of different bases on reaction outcome, 1,2-dioxines **10a**–**f** were allowed to react with a catalytic amount of DABCO and the products acetylated, Table 2. When catalyzed by DABCO, significant amounts of 1,4-diketone **17** were observed in the reaction mixtures and the major product was now found to be the *cis* pyrans **16**, which is in direct contrast to when LiOH was employed above. Pyran formation was maximized and 1,4-diketone minimized when chloroform was used as the reaction solvent. Pyran **12a** was found not

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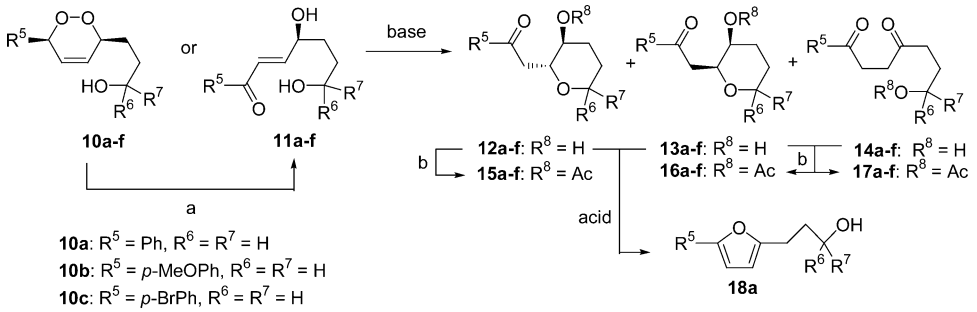
SCHEME 3



[a]Key: (a) Et_3N, PPh_3; (b) pyridine, $(CH_3CO)_2$, DMAP

TABLE 1. Formation of Pyrans 15 and 16 from 1,2-Dioxines 10 and LiOH

entry	1,2-dioxine	product ratio **15**:**16**[a] (% isolated yield)
1[b]	**10a**	64 (46):36 (18)
2[b]	**10b**	71 (41):29 (11)
3[b]	**10c**	73 (55):27 (21)
4[b]	**10d**	36 (17):64 (40)
5[b]	**10e**	74 (38):26 (14)
6[b]	**10f**	40:60
7[c]	**10a**	75:25

[a] Ratio determined by ^{1}H NMR spectra (300 MHz) of the crude reaction mixtures. [b] Reactions performed in THF using 1 equiv of LiOH with a concentration of 0.1 M with respect to **10**. [c] Reactions performed in THF using 1 equiv of NaOH with a concentration of 0.1 M with respect to **10**.

TABLE 2. Formation of Pyrans 15 and 16 from 1,2-Dioxines 10 and DABCO

entry	1,2-dioxine	solvent	product ratio **15**:**16**:**17**[a] (% isolated yield)[b]
1	**10a**	$CHCl_3$	6:56:38
2	**10b**	$CHCl_3$	2 (1):55 (22):43 (25)
3	**10c**	$CHCl_3$	4 (3): 67 (39):29 (17)
4	**10d**	$CHCl_3$	<1:63 (47):37 (24)
5	**10e**	$CHCl_3$	0:6:94
6	**10f**	$CHCl_3$	0:19:81
7	**10a**	THF	6:15:79
8	**10a**	acetone	30:24:46

[a] Ratio determined by ^{1}H NMR spectra (300 MHz) of the crude reaction mixtures. [b] Reactions performed using 0.4 equiv of DABCO with a concentration of 0.1 M with respect to **10**.

to interconvert to **13a** or decompose over the reaction time when subjected to DABCO in chloroform. The use of DABCO with the tertiary alcohols **10e** and **10f** led to significant 1,4-diketone formation. This can be attributed to the lesser nucleophilicity/basicity of the tertiary alcohol relative to the primary alcohols.

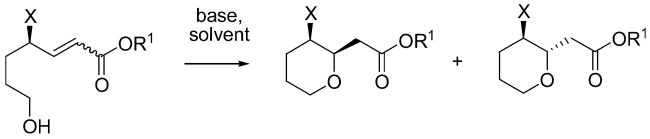
cis-γ-Hydroxy enones may be catalytically isomerized to the *trans* isomer by treatment with triphenylphosphine.[11] Consequently, we also had the opportunity to investigate pyran outcome when starting from the isomeric *trans* γ-hydroxy enones **11a**−**f**. The use of *trans*-γ-hydroxy enones **11a**−**f** as alternative starting materials generated pyrans **15** and **16** in virtually identical ratios from each substrate (**10a**−**f**) using LiOH in THF, Table 3.

TABLE 3. Formation of Pyrans 15 and 16 from *trans*-γ-Hydroxy Enones 11 and LiOH

entry	*trans* γ-hydroxy enone	product ratio **15**:**16**[a] (% isolated yield)[b]
1	**11a**	82:18
2	**11b**	86 (66):14 (10)
3	**11c**	81 (54):19 (15)
4	**11d**	80 (46):20 (7)
5	**11e**	79:21
6	**11f**	80:20

[a] Ratio determined by ^{1}H NMR spectra (300 MHz) of the crude reaction mixtures. [b] Reactions performed in THF using 1 equiv of LiOH with a concentration of 0.1 M with respect to **11**.

SCHEME 4



Examination of pyran formation from the base-catalyzed cyclization of hydroxyl-tethered *trans* γ-substituted α,β-unsaturated esters by Gung et al.[12] and Martín et al.[13] (Scheme 4) has provided us with a basis on which to build a rationalization of our results.

Gung et al. have found that the nature of the protecting group on the γ-hydroxyl moiety influences which is the most stable ground state (GS) conformer and, therefore, dictates the preferred transition state for kinetically controlled cyclization to *cis* and/or *trans* pyrans, Scheme 4 and Figure 2. Additionally, through variation of solvent and the cation associated with the base, they found that one can override the GS conformers contribution resulting in an altered *cis*/*trans* pyran ratio. Consequently, they have proposed that the use of tighter binding (smaller) cations and nonpolar solvents (in the presence of a cation) increase the activation energy required for cyclization by

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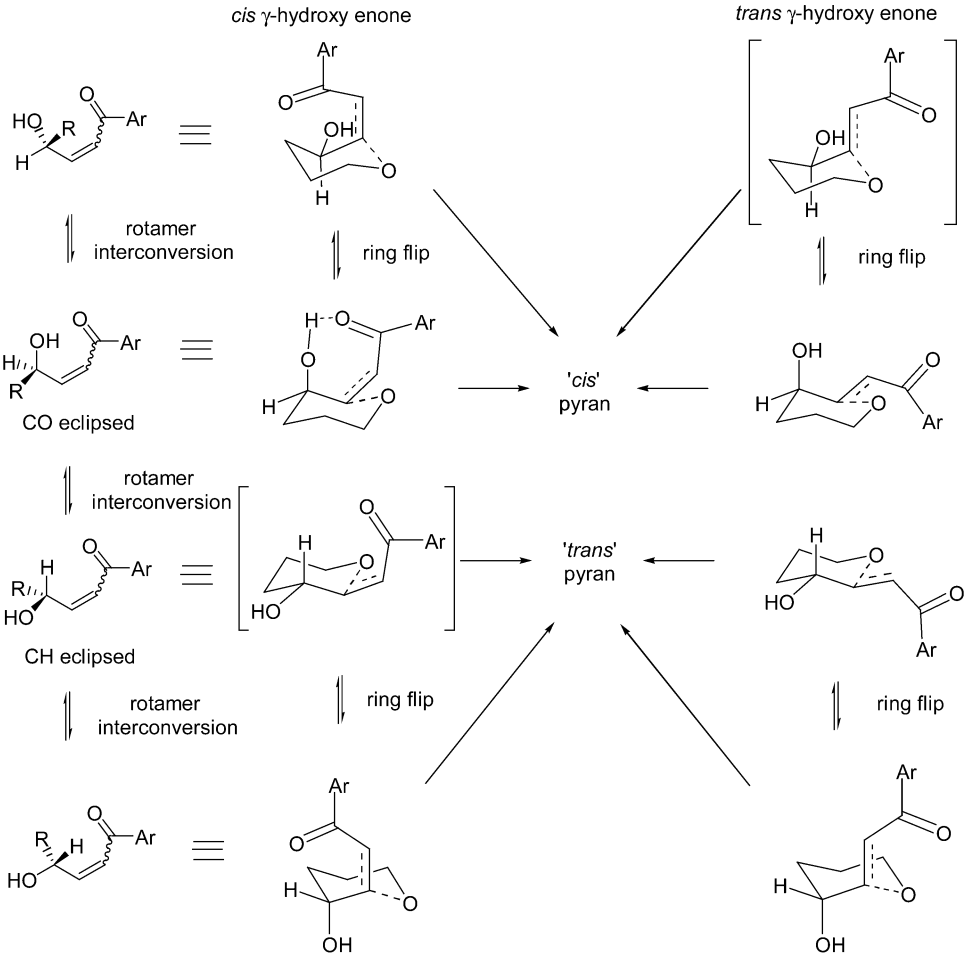

FIGURE 2. Transition states contributing to pyran formation.

lowering the HOMO of the nucleophile through coordination, thus rendering the GS conformational preferences insignificant due to the activation energy being higher than that required for rotamer interconversion, Figure 2. Martín et al. expanded on these findings with their work on related systems depicted within Scheme 4, for which they used computational techniques to justify their findings. Instead of considering only the CH- and CX-eclipsed rotamers as potential GS conformations as Gung et al.,[12a] did Martín et al.[13] reasoned and subsequently demonstrated that cation coordination could in fact favor the noneclipsed rotamers, Figure 2.

It has been proposed that for *trans* γ-hydroxy α,β-unsaturated esters the CO eclipsed rotamer is preferred.[14] Consequently, we suggest that this finding may be extrapolated to our *cis*/*trans* γ-hydroxy enone systems due to similarity in electronics. Therefore, if the CO eclipsed rotamer of our *cis*/*trans* γ-hydroxy enones predomines, then we would expect the "*cis*" pyrans to dominate in the absence of small tightly coordinating cations, Figure 2. Indeed, we observe in all cases "*cis*" pyran formation dominating when cyclization was carried out in the presence of DABCO in chloroform, Table 2. Exploration of more polar solvents resulted in a gradual increase in the proportion of "*trans*" pyran with increased solvent polarity.

When utilizing LiOH as the base, which has the tightly coordinating lithium cation, we observe a shift to "*trans*" pyran dominance, Table 1. This result is in agreement with the findings of Martín et al. and suggest that the *cis* γ-hydroxy enone is formed primarily from the base induced ring-opening of 1,2-dioxines **10**.[4] Predominance of the "*cis*" pyran in entries 4 and 6, Table 1, may be a result of the increased steric bulk or changes in the electronics of the systems. It is unlikely to be a result of increased *trans* γ-hydroxy enone formation as the *trans* γ-hydroxy enones favor formation of the "*trans*" pyrans, Table 3. The "*trans*" pyran dominance seen when starting from the *trans* γ-hydroxy enones, where the ratio in all cases was 4:1 (Table 3), is in contradiction to the Martín et al. model which was validated for a range of X substituents, Scheme 4. Our findings are further complicated by a number of currently unquantified factors. First, it is difficult to quantify the amount of pyran generated from *cis* γ-hydroxy enone when starting from 1,2-dioxines; it is clear that it has an effect on the pyran ratio (compare Table 1 to 3). When using 1,2-dioxine **10** as a starting material, *cis* γ-hydroxy enone is generated primarily with *trans* γ-hydroxy enone forming through

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SCHEME 5

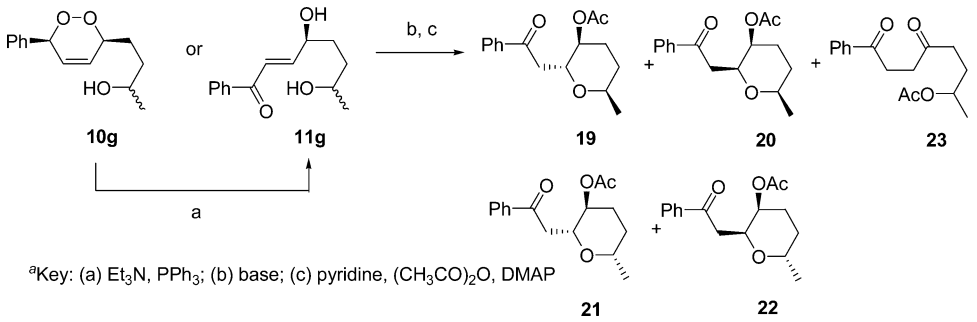

TABLE 4. Formation of Pyrans 19−22

entry	starting material	base/solvent	product ratio **19**:**20**:**21**:**22**:**23**[a] (% isolated yield)
1[b]	**10g**	LiOH/THF	9 (8):52 (42):37 (29):2 (1):(0)
2[c]	**10g**	DABCO/$CHCl_3$	[23:68:8:1] (24):(34)
3[b]	**11g**	LiOH/THF	13:54:28:5:0
4[d]	**10g**	LiOH/THF	4:51:40:5:0

[a] Ratio determined by ^{1}H NMR spectra (300 MHz) of the crude reaction mixtures. [b] Reactions performed in THF using 1 equiv of LiOH with a concentration of 0.1 M with respect to **10g** or **11g**. [c] Reactions performed in chloroform using 0.4 equiv of DABCO with a concentration of 0.1 M with respect to **10g** or **11g**. [d] Pyrans not isolated prior to acetylation.

reversible Michael addition of hydroxide.[8] Second, the *cis* and *trans* γ-hydroxy enones have a free OH grouping in the γ position, which is able to, in both its protonated and deprotonated forms, coordinate cations. Finally, our assumption that the similarities in electronic structure when comparing our keto systems with the ester systems of Gung et al. and Martín et al. is insignificant may not be entirely true. Importantly, while a full mechanistic rationale is yet to be determined, the synthetic utility of this new reaction has clearly been demonstrated.

1,2-Dioxine **10g** was also synthesized in order to investigate further the influence of substitution on pyran formation and because this system is also of interest as it generates pyrans closely resembling (+)-decarestrictine L. 1,2-Dioxine **10g** was generated as a diastereomeric pair through a similar sequence described in Scheme 2 from phosphonium salt **3** and 5-methyltetrahydro-2-furanol **4d** derived from γ-valerolactone.[15] Treatment of **10g** and isomeric **11g** with base followed by acetylation generated pyrans **19**−**22** in a variety of yields, Scheme 5, Table 4. Pyrans **19** and **20** arise from one of the diastereomers of 1,2-dioxine **10g** or *trans* γ-hydroxy enone **11g** and pyrans **21** and **22** from the other diastereomer. Therefore, one would expect their combined ratio (**19** + **20**):(**21** + **22**) to be almost equal; however, this was found not to be the case, Table 4. There are several possible reasons for this: (i) the comparative stability of each hydroxy pyran isomer (prior to acetylation) in the reaction mixture and during purification by column chromatography, (ii) the comparative decomposition rate of 1,2-dioxine/*trans* γ-hydroxy enone diastereomers into 1,4-diketone, or (iii) the rate of pyran cyclization. To address the first case, an experiment identical to that shown in entry 1, Table 4, was conducted with the exception that the resulting hydroxy pyrans were not isolated by column chromatography, rather were directly acetylated in the crude reaction mixture still containing LiOH, entry 4 Table 4. This alternative approach was not found to effect the ratios of the resulting pyrans, compare entries 1 and 4, Table 4. Thus, the stability of the pyrans in the crude reaction mixture prior to acetylation and subsequently on silica during the purification by column chromatography, was not likely to result in the discrepancies in the overall pyran ratios observed. The second explanation was found not to be plausible by monitoring the DABCO-catalyzed decomposition of 1,2-dioxine **10g** to 1,4-diketone by ^{1}H NMR with both diastereomers showing equal rates of decomposition. The third explanation is more plausible as greater variation in pyran ratio is observed in the reactions where decomposition to 1,4-diketone predominates, entry 2, Table 4. In these cases, unequal amounts of the diastereomers of 1,2-dioxine/*trans* γ-hydroxy enone are being competitively drawn off to 1,4-diketone as the rates of pyran formation differ considerably with solvent and base. The discrepancy in the ratio of pyrans observed in entry 3, Table 4, could also be a function of the formation of *trans* γ-hydroxy enone as its synthesis too involves the formation of 1,4-diketone and to a small extent pyran. The ratio of *cis*:*trans*-substituted pyrans (with respect to acetate and keto side chains) resulting from each diastereomer of **10g** or **11g** give a clear pattern where the dominating pyran arises from the transition state in which the stereogenic methyl group is equatorial, overriding any coordinating effects. This effect was also observed by Martín et al.[13a]

To expand the methodology and introduce another stereogenic center to the pyran synthesis it was realized that pyran formation would still occur if the 1,2-dioxine was initially epoxidized.[16] Pyran formation would lead to the introduction of a hydroxyl moiety stereoselectively, adjacent the aromatic ketone, Scheme 6. Using parent 1,2-dioxine **10a**, epoxidation proceeded in excellent yield using *m*-CPBA, with only a trace of cyclization product **26** observed.[17] Cyclization proceeded in moderate yield in the presence of PTSA (unoptimized conditions) to give 1,2-dioxine **26**, followed by regioselective ring opening of the peroxide bond in the presence of triethylamine and protection of the diol afforded diacetate **27** in good yield.

This latter variation may represent a novel alternative for the preparation of exotic perhydrofuro[3,2-*b*]pyran

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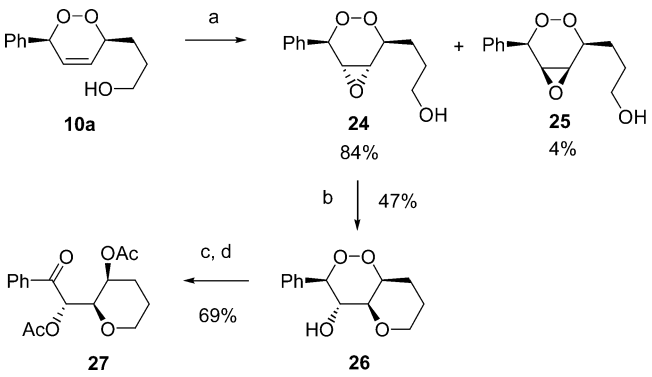
SCHEME 6



skeletons such as those found within herbicidin B and G and aureonuclemycin.[18]

Conclusion

Herein, we have presented a novel synthesis of 3-hydroxypyrans utilizing 1,2-dioxines with tethered hydroxyl functionality as masked *cis*/*trans* γ-hydroxy enones. There is a clear preference for "*trans*" pyran formation when utilizing LiOH as the base while amine bases such as DABCO favor "*cis*" pyran formation. Importantly, while a full mechanistic rationale is yet to be determined, the synthetic utility of this new reaction has clearly been demonstrated.

Experimental Section

General Procedure for LiOH-Mediated Pyran Synthesis. To a 0.1 M solution of 1,2-dioxine or *trans* γ-hydroxy enone in THF was added lithium hydroxide (1 equiv) and the mixture stirred for 2−4 days. The volatiles were removed in vacuo, and the crude pyrans were then purified by column chromatography. Pyridine (15 equiv), acetic anhydride (9 equiv), and DMAP (0.2 equiv) were then added to the combined pyrans, and the solution was stirred overnight. Dichloromethane was then added, the solution was extracted with water, the organic layer was dried ($MgSO_4$) and filtered, and the volatiles were removed in vacuo. The crude pyrans were purified by column chromatography.

General Procedure for DABCO-Mediated Pyran Synthesis. To a 0.1 M solution of 1,2-dioxine or *trans* γ-hydroxy enone in chloroform was added DABCO (0.4 equiv) and the mixture stirred overnight. The volatiles were removed in vacuo, and the crude pyrans were then purified by column chromatography. Pyridine (15 equiv), acetic anhydride (9 equiv), and DMAP (0.2 equiv) were then added to the combined pyrans, and the solution was stirred overnight. Dichloromethane was then added, the solution was extracted with water, the organic layer was dried ($MgSO_4$) and filtered, and the volatiles were removed in vacuo. The crude pyrans were purified by column chromatography.

(±)-(2*S*,3*R*)-2-(2-Oxo-2-phenylethyl)tetrahydro-2*H*-3-pyranyl acetate (15a): colorless oil; R_f 0.25 (1:3 ethyl acetate/hexanes); IR (neat) 1732, 1683, 1598, 1581, 1449, 1374, 1239, 1097, 1039 cm^{-1}; ^1H NMR (600 MHz) δ 1.52 (dddd, J = 12.6, 10.8, 10.8, 4.2 Hz, 1H), 1.67−1.71 (m, 1H), 1.73−1.81 (m, 1H), 1.96 (s, 3H), 2.17−2.24 (m, 1H), 3.03 (dd, J = 16.2, 3.6 Hz, 1H), 3.19 (dd, J = 16.2, 8.4 Hz, 1H), 3.42 (ddd, J = 12.0, 12.0, 2.4 Hz, 1H), 3.86−3.90 (m, 1H), 3.99 (ddd, J = 9.6, 8.4, 3.6 Hz, 1H), 4.64 (ddd, J = 10.8, 9.6, 4.8 Hz, 1H), 7.44−7.48 (m, 2H), 7.54−7.57 (m, 1H), 7.95−7.97, (m, 2H); ^{13}C NMR (150 MHz) δ 21.1, 25.2, 29.4, 41.5, 67.8, 72.0, 76.3, 128.3, 128.6, 133.1, 137.2, 170.3, 197.8; EIMS *m/z* 263 ($[M + H]^+$, 27), 202 (12), 174 (1), 105 (100), 77 (27), 71 (11), 43 (46). Anal. Calcd for $C_{15}H_{18}O_4$: C, 68.68; H, 6.91. Found: C, 68.04; H, 6.71.

(±)-(2*S*,3*S*)-2-(2-Oxo-2-phenylethyl)tetrahydro-2*H*-3-pyranyl acetate (16a): colorless oil; R_f 0.38 (1:3 ethyl acetate/hexanes); IR (neat) 1732, 1682, 1598, 1581, 1449, 1372, 1243, 1090, 1020 cm^{-1}; ^1H NMR (600 MHz) δ 1.42−1.46 (m, 1H), 1.78−1.84 (m, 1H), 1.87−1.95 (m, 1H), 2.02−2.09 (m, 1H), 2.13 (s, 3H), 2.97 (dd, J = 16.8, 5.4 Hz, 1H), 3.29 (dd, J = 16.8, 7.2 Hz, 1H), 3.57 (ddd, J = 12.6, 11.4, 2.4 Hz, 1H), 3.99−4.02 (m, 1H), 4.19 (ddd, J = 7.2, 5.4, 1.8 Hz, 1H), 4.96−4.98 (m, 1H), 7.44−7.47 (m, 2H), 7.54−7.57 (m, 1H), 7.93−7.95 (m, 2H); ^{13}C NMR (150 MHz) δ 20.5, 21.1, 27.8, 40.6, 68.2, 69.2, 74.4, 128.1, 128.5, 133.2, 137.0, 170.6, 197.3; EIMS *m/z* 263 ($[M + H]^+$, 71), 202 (52), 174 (5), 105 (71), 77 (51), 71 (34), 43 (100). Anal. Calcd for $C_{15}H_{18}O_4$: C, 68.68; H, 6.91. Found: C, 68.43; H, 7.02.

(±)-(2*S*,3*R*)-2-[2-(4-Methoxyphenyl)-2-oxoethyl]tetrahydro-2*H*-3-pyranyl acetate (15b): colorless oil; R_f 0.30 (1:3 ethyl acetate/hexanes); IR (neat) 1732, 1682, 1601, 1576, 1512, 1239, 1172, 1198, 1037 cm^{-1}; ^1H NMR (300 MHz) δ 1.45−1.58 (m, 1H), 1.65−1.85 (m, 2H), 1.96 (s, 3H), 2.16−2.25 (m, 1H), 2.97 (dd, J = 15.6, 3.6 Hz, 1H), 3.15 (dd, J = 15.6, 8.4 Hz, 1H), 3.42 (ddd, J = 11.4, 11.4, 3.0 Hz, 1H), 3.85−3.91 (m, 1H), 3.87 (s, 3H), 3.98 (ddd, J = 9.6, 8.4, 3.6 Hz, 1H), 4.64 (ddd, J = 10.8, 9.6, 4.5 Hz, 1H), 6.90−6.96 (m, 2H), 7.92−7.97 (m, 2H); ^{13}C NMR (75 MHz) δ 21.0, 25.1, 29.4, 41.1, 55.4, 67.7, 72.0, 76.4, 113.7, 130.4, 130.6, 163.5, 170.2, 196.3; EIMS *m/z* 292 (M^+, 9), 256 (7), 232 (12), 135 (100), 92 (7), 77 (13), 55 (5), 43 (100); HRMS (EI) calcd for $C_{16}H_{20}O_5$ 292.1311, found 292.1307.

(±)-(2*S*,3*S*)-2-[2-(4-Methoxyphenyl)-2-oxoethyl]tetrahydro-2*H*-3-pyranyl acetate (16b): colorless solid; mp 74−75 °C; R_f 0.15 (1:3 ethyl acetate/hexanes); IR (Nujol) 1725, 1681, 1601, 1578, 1515, 1239, 1216, 1090, 1023 cm^{-1}; ^1H NMR (300 MHz) δ 1.42−1.47 (m, 1H), 1.75−1.99 (m, 2H), 2.03−2.12 (m, 1H), 2.14 (s, 3H), 2.92 (dd, J = 16.5, 5.4 Hz, 1H), 3.25 (dd, J = 16.5, 6.9 Hz, 1H), 3.58 (ddd, J = 11.7, 11.7, 2.1 Hz, 1H), 3.87 (s, 3H), 3.98−4.04 (m, 1H), 4.18 (ddd, J = 6.9, 5.4, 1.5 Hz, 1H), 4.96−4.98 (m, 1H), 6.90−6.95 (m, 2H), 7.91−7.96 (m, 2H); ^{13}C NMR (75 MHz) δ 20.5, 21.1, 27.8, 40.2, 55.4, 68.3, 69.4, 74.7, 113.7, 130.2, 130.5, 163.6, 170.6, 195.8; EIMS *m/z* 292 (M^+, 2), 279 (1), 256 (3), 232 (51), 204 (4), 179 (2), 163 (5), 135 (100), 121 (1), 92 (7), 77 (10), 55 (4), 43 (43). Anal. Calcd for $C_{16}H_{20}O_5$: C, 65.74; H, 6.89: Found: C, 65.69; H, 6.80.

(±)-(2*S*,3*R*)-2-[2-(4-Bromophenyl)-2-oxoethyl]tetrahydro-2*H*-3-pyranyl acetate (15c): colorless oil; R_f 0.44 (1:3 ethyl acetate/hexanes); IR (neat) 1732, 1682, 1597, 1586, 1571, 1244, 1097, 1039, 1007 cm^{-1}; ^1H NMR (300 MHz) δ 1.45−1.58 (m, 1H), 1.67−1.83 (m, 2H), 1.99 (s, 3H), 2.17−2.26 (m, 1H), 2.96 (dd, J = 15.9, 3.3 Hz, 1H), 3.17 (dd, J = 15.9, 8.4 Hz, 1H), 3.40 (ddd, J = 11.4, 11.4, 3.3 Hz, 1H), 3.84−3.90 (m, 1H), 3.95 (ddd, J = 9.6, 8.4, 3.3 Hz, 1H), 4.63 (ddd, J = 10.8, 9.6, 4.5 Hz, 1H), 7.58−7.62 (m, 2H), 7.80−7.84 (m, 2H); ^{13}C NMR (75 MHz) δ 21.1, 25.1, 29.4, 41.4, 67.8, 71.9, 76.3, 128.3, 129.9, 131.9, 136.0, 170.2, 197.0; EIMS *m/z* 342 ($[M + H]^+$, 3), 340 (3), 282 (15), 280 (16), 185 (61), 183 (58), 157 (6), 142 (7), 97 (11), 71 (15), 50 (4), 43 (100); HRMS (EI) calcd for $C_{15}H_{17}O_4Br$ 341.0389, found 341.0389.

(±)-(2*S*,3*S*)-2-[2-(4-Bromophenyl)-2-oxoethyl]tetrahydro-2*H*-3-pyranyl acetate (16c): colorless oil; R_f 0.32 (1:3 ethyl acetate/hexanes); IR (neat) 1732, 1688, 1586, 1568, 1373, 1243, 1090, 733 cm^{-1}; ^1H NMR (300 MHz) δ 1.42−1.47 (m, 1H), 1.75−1.95 (m, 2H), 2.03−2.10 (m, 1H), 2.14 (s, 3H), 2.90 (dd, J = 16.8, 5.1 Hz, 1H), 3.26 (dd, J = 16.8, 7.5 Hz, 1H), 3.56 (ddd, J = 11.7, 11.7, 2.1 Hz, 1H), 3.97−4.02 (m, 1H), 4.16 (ddd, J = 7.5, 5.1, 1.2 Hz, 1H), 4.94−4.98 (m, 1H), 7.57−7.62 (m, 2H), 7.78−7.82 (m, 2H); ^{13}C NMR (75 MHz) δ 20.4, 21.1, 27.8, 40.6, 68.2, 69.1, 74.4, 128.3, 129.6, 131.8, 135. 7, 170.5, 196.3; EIMS *m/z* 341 (M^+, 65), 283 (53), 282 (59), 281 (56), 280 (54), 185 (100), 183 (100), 169 (7), 143 (26), 104 (4), 97

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(10), 71 (18), 43 (40); HRMS (EI) calcd for $C_{15}H_{17}O_4Br$ 341.0389, found 341.0393.

(±)-(2*S*,3*R*)-2-[2-(2-Naphthyl)-2-oxoethyl]tetrahydro-2*H*-3-pyranyl acetate (15d): pale yellow oil; R_f 0.28 (1:4 ethyl acetate/hexanes); IR (neat) 1732, 1682, 1628, 1596, 1578, 1507, 1469, 1375, 1238, 1038, 867, 817 cm^{-1}; ^{1}H NMR (600 MHz) δ 1.54 (dddd, J = 12.6, 10.8, 10.8, 4.2 Hz, 1H), 1.67−1.72 (m, 1H), 1.74−1.82 (m, 1H), 1.98 (s, 3H), 2.21−2.25 (m, 1H), 3.13 (dd, J = 15.6, 3.6 Hz, 1H), 3.35 (dd, J = 15.6, 8.4 Hz, 1H), 3.43 (ddd, J = 11.4, 11.4, 2.4 Hz, 1H), 3.86−3.91 (m, 1H), 4.05 (ddd, J = 9.6, 8.4, 3.6 Hz, 1H), 4.70 (ddd, J = 10.8, 9.6, 4.2 Hz, 1H), 7.53−7.56 (m, 1H), 7.57−7.60 (m, 1H), 7.86 (dd, J = 7.8, 0.6 Hz, 1H), 7.88 (d, J = 9.0 Hz, 1H), 7.97 (dd, J = 7.8, 0.6 Hz, 1H), 8.04 (dd, J = 9.0, 1.8 Hz, 1H), 8.46 (d, J = 1.2 Hz, 1H); ^{13}C NMR (75 MHz) δ 21.1, 25.1, 29.4, 41.4, 67.8, 72.0, 76.3, 123.9, 126.7, 127.7, 128.4, 128.4, 129.6, 130.1, 132.4, 134.5, 135.5, 170.2, 197.7; EIMS *m/z* 313 ([M + H]$^+$, 74), 253 (40), 155 (100), 127 (11), 43 (12). Anal. Calcd for $C_{19}H_{20}O_4$: C, 73.06; H, 6.45. Found: C, 72.54; H, 6.60.

(±)-(2*S*,3*S*)-2-[2-(2-Naphthyl)-2-oxoethyl]tetrahydro-2*H*-3-pyranyl acetate (16d): colorless solid; mp 75−76.5 °C; R_f 0.35 (1:3 ethyl acetate/hexanes); IR (Nujol) 1726, 1677, 1628, 1597, 1578, 1242, 1090 cm^{-1};^{1}H NMR (600 MHz) δ 1.44−1.47 (m, 1H), 1.80−1.86 (m, 1H), 1.89−1.97 (m, 1H), 2.07−2.11 (m, 1H), 2.15 (s, 3H), 3.09 (dd, J = 16.8, 5.4 Hz, 1H), 3.43 (dd, J = 16.8, 7.2 Hz, 1H), 3.59 (ddd, J = 12.6, 12.0, 3.0 Hz, 1H), 4.00−4.04 (m, 1H), 4.24 (ddd, J = 7.2, 5.4, 1.8 Hz, 1H), 5.01−5.03 (m, 1H), 7.53−7.56 (m, 1H), 7.58−7.61 (m, 1H), 7.87 (dd, J = 7.8, 0.6 Hz, 1H), 7.88 (d, J = 9.0 Hz, 1H), 7.96 (dd, J = 7.8, 0.6 Hz, 1H), 8.01 (dd, J = 9.0, 1.8 Hz, 1H), 8.45 (d, J = 1.2 Hz, 1H); ^{13}C NMR (75 MHz) δ 20.5, 21.2, 27.8, 40.7, 68.3, 69.3, 74.6, 123.8, 126.7, 127.7, 128.4, 128.5, 129.6, 129.9, 132.5, 134.4, 135.6, 170.6, 197.3; EIMS *m/z* 312 (M$^+$, 4), 252 (6), 155 (100), 127 (26), 43 (23). Anal. Calcd for $C_{19}H_{20}O_4$: C, 73.06; H, 6.45. Found: C, 73.11; H, 6.50.

(±)-(2*S*,3*R*)-6,6-Dimethyl-2-(2-oxo-2-phenylethyl)tetrahydro-2*H*-3-pyranyl acetate (15e): colorless oil; R_f 0.33 (3:17 ethyl acetate/hexanes); IR (neat) 1740, 1690, 1598, 1581, 1449, 1368, 1232, 1093 cm^{-1}; ^{1}H NMR (600 MHz) δ 1.16 (s, 3H), 1.26 (s, 3H), 1.57−1.74 (m, 3H), 1.94 (s, 3H), 2.00−2.04 (m, 1H), 2.98 (dd, J = 15.6, 3.6 Hz, 1H), 3.12 (dd, J = 15.6, 7.8 Hz, 1H), 4.26 (ddd, J = 10.2, 7.8, 3.6 Hz, 1H), 4.57 (ddd, J = 10.2, 10.2, 4.8 Hz, 1H), 7.43−7.47 (m, 2H), 7.53−7.56 (m, 1H), 7.94−7.96 (m, 2H); ^{13}C NMR (150 MHz) δ 21.1, 21.5, 26.0, 30.7, 35.4, 42.2, 69.2, 72.2, 72.9, 128.3, 128.5, 132.9, 137.5, 170.4, 198.1; EIMS *m/z* 291 (M$^+$, 23), 230 (60), 175 (15), 157 (20), 149 (16), 120 (11), 105 (100). Anal. Calcd for $C_{17}H_{22}O_4$: C, 70.32; H, 7.64. Found: C, 70.40; H, 7.44.

(±)-(2*S*,3*S*)-6,6-Dimethyl-2-(2-oxo-2-phenylethyl)tetrahydro-2*H*-3-pyranyl acetate (16e): colorless oil; R_f 0.21 (3:17 ethyl acetate/hexanes); IR (neat) 1736, 1687, 1598, 1581, 1449, 1366, 1243, 1042 cm^{-1}; ^{1}H NMR (600 MHz) δ 1.23 (s, 3H), 1.26 (s, 3H), 1.34 (ddd, J = 13.2, 7.2, 1.2 Hz, 1H), 1.73 (ddd, J = 13.2, 13.2, 5.4 Hz, 1H), 1.90−1.99 (m, 2H), 2.09 (s, 3H), 3.04 (dd, J = 16.8, 6.0 Hz, 1H), 3.21 (dd, J = 16.8, 6.0 Hz, 1H), 4.41 (ddd, J = 6.0, 6.0, 1.2 Hz, 1H), 4.90−4.92 (m, 1H), 7.43−7.46 (m, 2H), 7.53−7.56 (m, 1H), 7.93−7.96 (m, 2H); ^{13}C NMR (150 MHz) δ 21.2, 21.3, 24.7, 30.6, 31.2, 40.9, 67.7, 68.5, 72.4, 128.1, 128.5, 133.1, 137.1, 170.8, 197.7; EIMS *m/z* 291 (M$^+$, 84), 273 (4), 231 (84), 213 (75), 175 (18), 157 (56), 147 (13), 110 (27), 105 (100), 77(67), 43 (96). Anal. Calcd for $C_{17}H_{22}O_4$: C, 70.32; H, 7.64. Found: C, 70.06; H, 7.87.

2-(2-Oxo-2-phenylethyl)-6,6-diphenyltetrahydro-2*H*-3-pyranyl Acetate (15f and 16f). *Cis* (**16f**)[a] and *trans* (**15f**)[b] isomers were inseparable by column chromatography and were obtained as a 3:2 mixture, respectively: pale yellow solid; mp 45−50 °C; R_f 0.55 (3:7 ethyl acetate/hexanes); IR (Nujol) 1734, 1683, 1597, 1580 cm^{-1}; ^{1}H NMR (300 MHz) δ 1.92 (s, 3H),[a] 2.12 (s, 3H),[b] 1.66−2.21 (m, 6H),[a,b] 2.57 (ddd, J = 14.1, 3.3, 3.3 Hz, 1H),[b] 2.84 (ddd, J = 14.1, 3.6, 3.6 Hz, 1H),[a] 3.01 (dd, J = 16.2, 5.1 Hz, 1H),[b] 3.08 (dd, J = 14.7, 3.6 Hz, 1H),[a] 3.41 (dd, J = 14.7, 8.7 Hz, 1H),[a] 3.52 (dd, J = 16.2, 8.1 Hz, 1H),[b] 4.15 (ddd, J = 9.6, 8.7, 3.6 Hz, 1H),[a] 4.26 (ddd, J = 8.1, 5.1, 1.5 Hz, 1H),[b] 4.81 (ddd, J = 10.5, 9.6, 4.8 Hz, 1H),[a] 4.83−4.86 (m, 1H),[b] 7.31−7.58 (m, 26H),[a,b] 8.00−8.05 (m, 4H);[a,b] ^{13}C NMR (75 MHz) δ 20.9,[a] 21.1,[b] 25.5,[b] 26.5,[a] 28.6,[b] 33.8,[a] 40.9,[b] 42.1,[a] 68.5,[b] 69.5,[a] 70.8,[a] 72.6,[b] 80.2,[a] 80.4,[b] 124.6, 124.7, 126.3, 127.1, 127.1, 127.2, 127.8, 128.2, 128.4, 128.5, 128.5, 128.6, 132.9, 133.0, 137.3, 137.5, 141.3, 147.5, 148.3, 170.1,[a] 170.5,[b] 197.8,[b] 198.1;[a] EIMS *m/z* 414 (M$^+$, 17), 373 (40), 354 (6), 180 (44), 157 (19), 105 (84), 77 (39), 43 (100). Anal. Calcd for $C_{27}H_{26}O_4$: C, 78.24; H, 6.32. Found: C, 77.96; H, 6.43.

(±)-(2*R*,3*S*,6*R*)-6-Methyl-2-(2-oxo-2-phenylethyl)tetrahydro-2*H*-3-pyranyl acetate (19): yield 60 mg, 8%; colorless oil; R_f = 0.35 (1:4 ethyl acetate/hexane); IR (neat) 1738, 1687, 1597, 1581, 1449, 1374, 1240, 1042 cm^{-1}; ^{1}H NMR (600 MHz) δ 1.23 (d, J = 6.0 Hz, 3H), 1.34 (dddd, J = 13.2, 6.0, 3.6, 3.6 Hz, 1H), 1.83 (dddd, J = 13.2, 7.2, 3.6, 3.6 Hz, 1H), 1.92−2.01 (m, 2H), 2.02 (s, 3H), 3.15 (dd, J = 16.2, 6.0 Hz, 1H), 3,24 (dd, J = 16.2, 6.6 Hz, 1H), 4.02 (ddq, J = 7.2, 6.0, 6.0 Hz, 1H), 4.61 (ddd, J = 6.6, 6.0, 3.6 Hz, 1H), 4.99 (ddd, J = 7.2, 3.6, 3.6 Hz, 1H), 7.45−7.48 (m, 2H), 7.55−7.58 (m, 1H), 7.93−7.95 (m, 2H); ^{13}C NMR (150 MHz) δ 18.3, 21.1, 23.5, 27.3, 38.7, 67.6, 67.9, 69.4, 128.1, 128.6, 133.1, 137.1, 170.3, 197.6; EIMS *m/z*: 277 ([M + H]$^+$, 5), 216 (24), 105 (100), 77 (21), 43 (42); HRMS (ESI) calcd for $C_{16}H_{20}O_4$ + Na 299.1259, found 299.1263.

(±)-(2*S*,3*S*,6*R*)-6-Methyl-2-(2-oxo-2-phenylethyl)tetrahydro-2*H*-3-pyranyl acetate (20): yield 326 mg, 42%; colorless oil; R_f = 0.40 (1:4 ethyl acetate/hexane); IR (neat) 1732, 1688, 1597, 1580, 1449, 1244, 1082 cm^{-1}; ^{1}H NMR (600 MHz) δ 1.20 (d, J = 6.6 Hz, 3H) 1.48 (dddd, J = 13.8, 5.4, 3.0, 3.0 Hz, 1H), 1.54 (dddd, J = 13.8, 13.8, 10.8, 3.0 Hz, 1H), 1.82 (dddd, J = 14.4, 13.8, 5.4, 3.0 Hz, 1H), 2.05 (dddd, J = 14.4, 3.0, 3.0, 3.0 Hz, 1H), 2.11 (s, 3H), 3.05 (dd, J = 16.8, 6.0 Hz, 1H), 3.28 (dd, J = 16.8, 6.0 Hz, 1H), 3.60 (ddq, J = 10.8, 6.6, 3.0 Hz, 1H), 4.22 (ddd, J = 6.0, 6.0, 1.2 Hz, 1H), 4.94 (ddd, J = 3.0, 3.0, 1.2 Hz, 1H), 7.44−7.47 (m, 2H), 7.54−7.57 (m, 1H), 7.93−7.95 (m, 2H); ^{13}C NMR (150 MHz) δ 21.2, 21.8, 27.7, 28.1, 40.7, 68.5, 74.2, 74.4, 128.1, 128.5, 133.1, 137.1, 170.7, 197.4; EIMS *m/z* 277 ([M + H]$^+$, 27), 216 (25), 105 (100), 77 (22), 43 (55). Anal. Calcd for $C_{16}H_{20}O_4$: C, 69.54; H, 7.29. Found: C, 69.23; H, 7.41.

(±)-(2*R*,3*S*,6*S*)-6-Methyl-2-(2-oxo-2-phenylethyl)tetrahydro-2*H*-3-pyranyl acetate (21): yield 232 mg, 29%; colorless oil; R_f = 0.60 (1:4 ethyl acetate/hexane); IR (neat) 1738, 1690, 1597, 1580, 1449, 1239, 1088, 1039 cm^{-1}; ^{1}H NMR (600 MHz) δ 1.12 (d, J = 6.6 Hz, 3H), 1.44 (dddd, J = 13.8, 13.2, 10.8, 4.8 Hz, 1H), 1.55 (dddd, J = 13.2, 12.0, 10.2, 2.4 Hz, 1H), 1.73 (dddd, J = 13.8, 4.8, 2.4, 2.4 Hz, 1H), 1.92 (s, 3H), 2.17 (dddd, J = 12.0, 4.8, 4.8, 4.8 Hz, 1H), 3.02 (dd, J = 15.6, 4.2 Hz, 1H), 3.18 (dd, J = 15.6, 7.8 Hz, 1H), 3.54 (ddq, J = 10.8, 6.6, 2.4 Hz, 1H), 4.05 (ddd, J = 9.6, 7.8, 4.2 Hz, 1H), 4.60 (ddd, J = 10.2, 9.6, 4.8 Hz, 1H), 7.44−7.47 (m, 2H), 7.54−7.57 (m, 1H), 7.95−7.97 (m, 2H); ^{13}C NMR (150 MHz) δ 21.0, 21.2, 29.5, 32.4, 41.8, 72.2, 73.8, 75.8, 128.3, 128.5, 133.0, 137.3, 170.4, 197.9; EIMS *m/z* 277 ([M + H]$^+$, 33), 216 (65), 105 (100), 77 (25), 43 (68). Anal. Calcd for $C_{16}H_{20}O_4$: C, 69.54; H, 7.29. Found: C, 69.35; H, 7.39.

(±)-(2*S*,3*S*,6*S*)-6-Methyl-2-(2-oxo-2-phenylethyl)tetrahydro-2*H*-3-pyranyl acetate (22): yield 11 mg, 1%; colorless oil; R_f = 0.37 (1:4 ethyl acetate/hexane); IR (neat) 1731, 1681, 1597, 1580, 1449, 1243, 754 cm^{-1}; ^{1}H NMR (600 MHz) δ 1.22 (d, J = 6.6 Hz, 3H), 1.57 (dddd, J = 13.8, 7.2, 6.6, 4.2 Hz, 1H), 1.73 (dddd, J = 13.8, 4.2, 4.2, 4.2 Hz, 1H), 1.83 (dddd, J = 13.8, 7.2, 6.6, 4.2 Hz, 1H), 1.97 (dddd, J = 13.8, 4.2, 4.2, 4.2 Hz, 1H), 2.03 (s, 3H), 3.10 (dd, J = 15.6, 5.4 Hz, 1H), 3.23 (dd, J = 15.6, 7.8 Hz, 1H), 3.96 (ddq, J = 6.6, 6.6, 4.2 Hz, 1H), 4.43 (ddd, J = 7.8, 5.4, 5.4 Hz, 1H), 4.70 (ddd, J = 6.6, 5.4, 4.2 Hz, 1H), 7.44−7.48 (m, 2H), 7.54−7.57 (m, 1H), 7.93−7.95 (m, 2H); ^{13}C NMR (150 MHz) δ 18.9, 21.2, 24.0, 28.1, 40.4, 67.3, 70.1, 70.8, 128.2, 128.6, 133.1, 136.9, 170.4, 197.5; EIMS *m/z* 277 ([M + H]$^+$, 27), 258 (26), 233 (26), 216 (45), 105 (100), 77 (24), 43 (39); HRMS (ESI) calcd for $C_{16}H_{20}O_4$ + Na 299.1259, found 299.1263.

(±)-3-[(1a*R*,2*S*,5*R*,5a*S*)-5-Phenylperhydrooxireno[2,3-*d*][1,2]dioxin-2-yl]-1-propanol (24).[10] To a solution of 1,2-dioxine **10a** (366 mg, 1.66 mmol) in dichloromethane (15 mL) was added 70% 3-chloroperbenzoic acid (1.229 g, 4.98 mol) and the solution stirred for 3 days at ambient temperature. Dichloromethane (10 mL) was then added and the solution extracted with satd $Na_2S_2O_3$ (20 mL) followed by $NaHCO_3$ (20 mL). The organic layer was dried over $MgSO_4$ and filtered, and the volatiles were removed in vacuo. The crude epoxides were purified by column chromatography to yield major epoxide **24** (347 mg, 84%) as a colorless oil: $R_f = 0.50$ (3:2 ethyl acetate/hexane); IR (neat) 3392, 1597, 1580, 1493, 1455, 1049 cm^{-1}; ^1H NMR (300 MHz) δ 1.66−1.87 (m, 3H), 1.93−2.06 (m, 2H), 3.35 (d, $J = 4.5$ Hz, 1H), 3.55 (d, $J = 4.5$ Hz, 1H), 3.68 (dd, $J = 6.3$, 6.3 Hz, 2H), 4.37 (dd, $J = 9.6$, 3.9 Hz, 1H), 5.31 (bs, 1H), 7.38−7.41 (m, 5H); ^{13}C NMR (75 MHz) δ 26.5, 28.4, 52.1, 52.8, 62.0, 77.9, 80.4, 128.0, 128.7, 129.1, 135.8; EIMS *m/z* 236 (M^+, 3), 204 (11), 131 (27), 120 (100), 105 (78), 77 (94), 71 (74). Anal. Calcd for $C_{13}H_{16}O_4$: C, 66.09; H, 6.83. Found: C, 65.90; H, 6.75.

(±)-3-[(1a*S*,2*S*,5*R*,5a*R*)-5-Phenylperhydrooxireno[2,3-*d*][1,2]dioxin-2-yl]-1-propanol (25): (17 mg, 4%) as a colorless oil; $R_f = 0.47$ (3:2 ethyl acetate/hexane); IR (neat) 3368, 1661, 1495, 1455, 1050 cm^{-1}; ^1H NMR (300 MHz) δ 1.64−2.13 (m, 6H), 3.57 (dd, $J = 4.2$, 1.2 Hz, 1H), 3.62 (dd, $J = 4.2$, 4.2 Hz, 1H), 3.73 (dd, $J = 6.3$, 6.3 Hz, 2H), 4.36 (ddd, $J = 9.0$, 5.1, 4.2 Hz, 1H), 5.32 (d, $J = 1.2$ Hz, 1H), 7.36−7.43 (m, 3H), 7.51−7.54 (m, 2H); ^{13}C NMR (75 MHz) δ 25.6, 28.6, 51.8, 53.2, 62.7, 79.5 (masked carbon), 128.5, 128.6, 129.2, 135.1; EIMS *m/z* 236 (M^+, 1), 131 (40), 120 (81), 105 (100), 91 (71), 77 (75), 71 (56); HRMS (ESI) calcd for $C_{13}H_{16}O_4$ + Na 259.0946, found 259.0942.

(±)-(3*R*,4*S*,4a*S*,8a*S*)-3-Phenylperhydrpyrano[3,2-*c*][1,2]-dioxin-4-ol (26). To a solution of epoxide **24** (340 mg, 1.44 mmol) in dry dichoromethane (10 mL) was added *p*-toluenesulfonic acid (137 mg, 0.72 mmol) and the solution stirred overnight. After this time, the volatiles were removed in vacuo and the crude pyran purified by column chromatography to yield pyran **26** (160 mg, 47%) as a colorless oil: $R_f = 0.25$ (2:3 ethyl acetate/hexane); IR (neat) 3401, 1602, 1585, 1496, 1455, 1096 cm^{-1}; ^1H NMR (600 MHz) δ 1.69 (ddddd, $J = 13.8$, 11.4, 10.2, 4.2, 1.2 Hz, 1H), 1.81 (ddddd, $J = 13.8$, 4.2, 4.2, 4.2, 4.2 Hz, 1H), 2.01 (dddd, $J = 13.8$, 4.2, 4.2, 4.2 Hz, 1H) 2.23 (dddd, $J = 13.8$, 10.8, 10.2, 4.2 Hz, 1H), 2.29 (bs, 1H), 3.63 (ddd, $J = 11.4$, 4.2, 1.2 Hz, 1H), 3.68 (ddd, $J = 11.4$, 11.4, 4.2 Hz, 1H), 3.99 (dd, $J = 8.4$, 5.4 Hz, 1H), 4.38 (ddd, $J = 10.8$, 5.4, 4.2 Hz, 1H), 4.44 (dd, $J = 8.4$, 8.4 Hz, 1H), 4.91 (d, $J = 8.4$ Hz, 1H), 7.34−7.40 (m, 3H), 7.41−7.44 (m, 2H); ^{13}C NMR (150 MHz) δ 24.2, 24.6, 61.6, 65.6, 75.1, 77.7, 86.5, 127.6, 128.5, 128.9, 135.4; EIMS *m/z* 236 (M^+, 13), 105 (26), 71 (100), 60 (35), 43 (71); HRMS (ESI) calcd for $C_{13}H_{16}O_4$ + Na requires 259.0946, found 259.0942.

(±)-(2*R*,3*S*)-2-[(1*S*)-1-(Acetyloxy)-2-oxo-2-phenylethyl]-tetrahydro-2*H*-3-pyranyl Acetate (27). To a solution of pyran **26** (160 mg, 0.68 mmol) in dry dichloromethane (10 mL) was added triethylamine (10 drops) and the solution stirred overnight. The volatiles were then removed in vacuo, pyridine (0.82 mL, 10.16 mmol), acetic anhydride (0.68 mL, 6.78 mmol), and DMAP (33 mg, 0.27 mmol) were added, and the solution was stirred overnight. Dichloromethane (10 mL) was then added, the solution was extracted with water (10 mL), the organic layer was dried ($MgSO_4$) and filtered, and the volatiles were removed in vacuo. The crude pyran was purified by column chromatography to yield pyran **27** (150 mg, 69%) as a colorless solid: mp = 70−71 °C; $R_f = 0.36$ (2:3 ethyl acetate/hexane); IR (Nujol) 1739, 1729, 1687, 1597, 1580, 1234, 1092, 720 cm^{-1}; ^1H NMR (300 MHz) δ 1.39−1.42 (m, 1H), 1.63−1.68 (m, 1H), 1.81 (s, 3H), 1.83−1.91 (m, 1H), 1.99−2.04 (m, 1H), 2.12 (s, 3H), 3.53 (ddd, $J = 12.6$, 12.6, 2.4 Hz, 1H), 3.91 (dd, $J = 7.2$, 1.2 Hz, 1H), 4.09 (ddd, $J = 12.6$, 4.8, 2.4 Hz, 1H), 4.67 (bs, 1H), 6.02 (d, $J = 7.2$ Hz, 1H), 7.45−7.48 (m, 2H), 7.57−7.60 (m, 1H), 8.00−8.01 (m, 2H); ^{13}C NMR (75 MHz) δ 20.3, 20.6, 20.8, 27.3, 66.9, 68.5, 74.1, 77.8, 128.7, 128.9, 133.7, 135.8, 169.8, 170.4, 196.0; EIMS *m/z* 321 ($[M + H]^+$,18), 277 (35), 261 (39), 218 (45), 105 (100), 77 (14), 43 (30); HRMS (ESI) calcd for $C_{17}H_{20}O_6$ + Na 343.1157, found 343.1157.

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Supporting Information Available: Experimental details for compounds **5a**−**d**, **6a**−**c**, **7**, **8a**−**c**, **9a**−**c**, **10a**−**g**, **12a**, **13a**, **14a**, **17a**−**d**, **23**, **11a**−**g**, **30a**−**c**, and **31a**−**c**. ^{13}C NMR spectra for compounds **10a**−**g**, **12a**, **13a**, **14a**, **15a**−**e**, **16a**−**e**, **17a**,**c**−**d**, **18a**, and **19**−**27** and ^1H NMR spectra for compound **17b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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