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A Hetero Diels–Alder Approach to the Synthesis of Chromans (3,4-Dihydrobenzopyrans) Using Oxonium Ion Chemistry: The Oxa-Povarov Reaction

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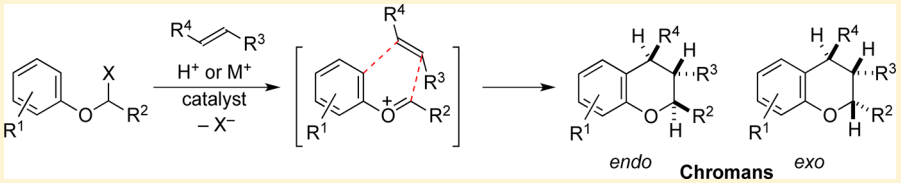
Supporting Information

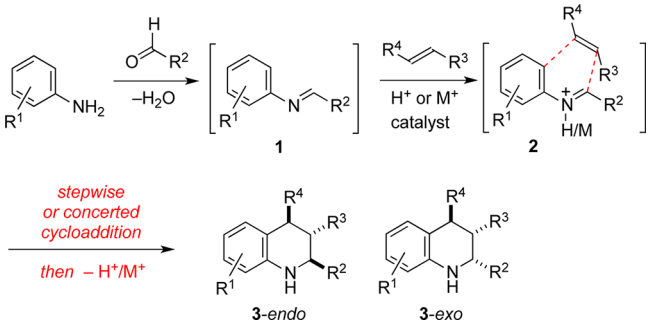


ABSTRACT: An oxa analogue of the well-known Povarov reaction has been developed for the synthesis of 3,4-dihydrobenzopyrans (chromans). The reaction involves the formal inverse electron demand [4 + 2] cycloaddition reaction of in situ-generated cationic aryl 2-oxadiene oxocarbenium ions with alkenes. The oxonium ion intermediates are generated through Lewis acid ($SnCl_4$)-promoted reactions of phenol-derived Rychnovsky-type mixed acetals. The yield and diastereoselectivity of the chroman products are found to depend upon the substitution pattern of the precursor alkene (i.e., monosubstituted, trans- or cis-disubstituted and cyclic alkenes). Generally, the reactions afford the endo-diastereomers as the major products, except for the reactions of *trans*-*β*-methylstyrene, which afford *exo*-chromans. A comparison of the product distributions from the reactions of *trans*- and *cis*-*β*-methylstyrene reveal that the reaction proceeds, at least in part, by a nonconcerted ionic pathway. Just as for the aza-Povarov reaction, there are two potential mechanisms for the reaction. The first mechanism involves a direct asynchronous [4 + 2] cycloaddition pathway, while the second occurs through the stepwise Prins addition of the alkene to the aryl 2-oxadiene oxonium ion, followed by an intramolecular aromatic substitution reaction of the resultant cation (i.e., a domino Prins/intramolecular Friedel–Crafts reaction).

INTRODUCTION

Hetero Diels–Alder reactions and their formal equivalents provide a powerful means for the rapid construction of heterocyclic scaffolds. Oxa- and aza-hetero Diels–Alder variants have been developed in which the dienophile and/or dienes can incorporate the heterocomponents.[1] One such aza-variant is the Povarov reaction,[2,3] originally developed 50 years ago, in which *N*-arylimines (2-azadienes) **1** react with electron-rich alkenes in a formal inverse electron demand [4 + 2] cycloaddition via **2** to furnish tetrahydroquinolines **3** (Scheme 1). Modern variants include multicomponent,[4] organocatalytic,[5] and solid-supported reactions.[6] The tetrahydroquinoline products can be oxidized to give quinolones,[7] and the reaction has been used both for the production of diverse chemical libraries[8] as well as in the synthesis of a number of natural products.[9]

Scheme 1. The Povarov Reaction



The key reaction intermediate in Povarov reactions are either protonated or Lewis acid-coordinated *N*-arylimines **2** or *N*-aryliminium ions. The cationic nature of these species increases their electrophilicity and reactivity as electron-deficient dienes. Given the considerable utility of the Povarov reaction, we were interested to establish whether an *O*-aryl oxonium species **5**, which is equivalent to a cationic 2-oxadiene intermediate, would undergo an analogous reaction to give 3,4-dihydrobenzopyrans (chromans) **6** (Scheme 2). Despite the extensive research on 2-azadienes,[10] and the importance of oxonium ions as intermediates in numerous reactions, the chemistry of *O*-aryl oxonium species **5**, or their corresponding precursors **4**,[11] including their cycloaddition chemistry remains virtually unexplored.[12,13] Such oxonium ion species would be expected to be more reactive than the corresponding iminium ions and capable of undergoing either direct hetero Diels–Alder reaction or the

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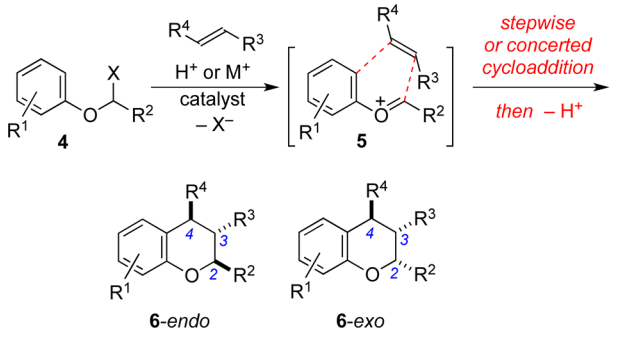
Scheme 2. Chroman Formation via the Oxa-Povarov (domino Prins/Friedel–Crafts) Reaction

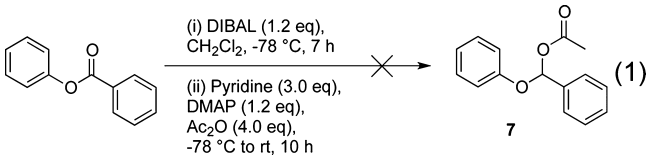


equivalent stepwise Prins addition/intramolecular electrophilic aromatic substitution reaction to give **6**.

The chroman skeleton appears in a number of natural products, including the tocopherols[14] and flavans.[15] They display a diverse array of biological activities, including antioxidant,[16] antiestrogen,[17] antiviral,[18] antihypertensive,[19] and anticancer[20] activity. Common approaches to the chroman skeleton[21] include hetero Diels–Alder reactions of *o*-quinone methides (1-oxadienes),[22] additions of *o*-hydroxy acetophenones,[23] and intramolecular nucleophilic substitution of phenols.[24] Alternative approaches to the chroman skeleton are of considerable interest for the formation of substituted chromans. Herein we describe the development of the oxa-Povarov reaction and its application to the diastereoselective synthesis of 2,3,4-substituted chromans.[25]

RESULTS AND DISCUSSION

Establishing conditions suitable for the formation of the *O*-aryl oxonium species **5** is perhaps the major challenge associated with the development of an oxa-Povarov reaction. In general, formation of **5** could be achieved by the selective ionization of ArOCHXR **4** using a Lewis acid. Selective ionization of the X^- group from **4** rather than the ArO^- group would be required under these conditions. Synthetic approaches to suitably substituted **4** are rather limited, but one approach investigated was the use of Rychnovsky's protocol for mixed acetal synthesis.[26] The Rychnovsky-type mixed acetals have found widespread application as oxonium ion precursors. According to the literature procedure, treatment of phenyl benzoate with DIBAL at −78 °C, followed by quenching with acetic anhydride, DMAP, and pyridine, afforded only phenyl acetate and benzyl alcohol and none of the desired mixed acetal **7** (eq 1). Attempts



to modify the reaction conditions with other hydride reducing agents were unsuccessful. The failure of this reaction must result from facile collapse of the tetrahedral alumino intermediate **8a** under the DIBAL conditions, leading to over-reduced products (Figure 1). The more facile collapse of **8a** is presumably due to faster loss of phenoxide ion from **8a** (pK_a of phenol is 9.95) relative to that of alkoxide loss (pK_a of aliphatic alcohols are approximately 15.5–17) from the standard Rychnovsky-type tetrahedral intermediate **8b**.[27] Indeed, to the best of our

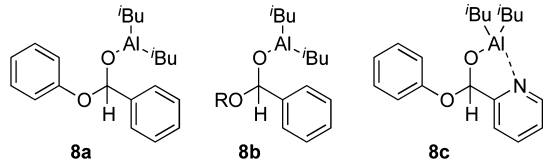
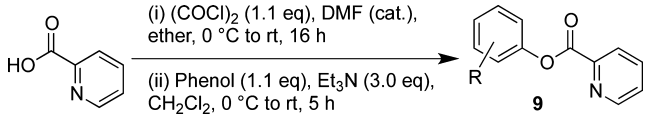


Figure 1. Tetrahedral intermediates formed using the Rychnovsky protocol.

knowledge there are no reported examples of reductive acetylation of phenyl or aryl esters using the Rychnovsky protocol.

To circumvent this problem, the formation of a more stable tetrahedral intermediate is necessary. Accordingly the introduction of an appropriately positioned heteroatom should sufficiently stabilize such an intermediate by chelation. The use of a picolinate ester was therefore considered, because it would lead to a tetrahedral intermediate **8c** stabilized by the pyridyl nitrogen in a five-membered ring chelate. The requisite aryl picolinate precursors **9** were synthesized in good yields by reaction of picolinic acid with oxalyl chloride/DMF, followed by treatment of the resultant acid chloride with phenol and triethylamine (Table 1). Reaction of phenyl picolinate **9a**

Table 1. Synthesis of Aryl Picolinates 9



entry	R	product	yield (%)
1	H	**9a**	86
2	*o*-Me	**9b**	80
3	*m*-Me	**9c**	82
4	*p*-Me	**9d**	76
5	*o*-Cl	**9e**	78
6	*m*-Cl	**9f**	63
7	*p*-Cl	**9g**	76
8	*o*-OMe	**9h**	80
9	*m*-OMe	**9i**	64
10	*p*-OMe	**9j**	79
11	3,5-di-OMe	**9k**	60
12	3,5-di-Me	**9l**	65
13	*m*-NO_2	**9m**	75
14	3,5-di-Cl	**9n**	35

according to the standard reductive acetylation conditions afforded the desired mixed acetal **10a** in 58% yield (Table 2, entry 1). A similar approach was utilized to synthesize other mixed acetals **10** (Table 2). The success of this procedure was sensitive to the pK_a of the phenolic component of the ester **9**. Higher yields were obtained for the more electron-rich esters such as **9b** and **9j** (phenol pK_a of 10.22 and 10.21, respectively), whereas a significant decline in yield was observed for electron-deficient esters, **9f** and **9g** (phenol pK_a of 9.08 and 9.38, respectively). Esters derived from phenols with a pK_a less than 8.50 (e.g., **9e**, **9k**, **9m**, and **9n**) afforded none of the desired mixed acetal.

Optimization studies on the reaction of **10a** with norbornene as a dienophile revealed that only stoichiometric amounts of either $SnCl_4$ or $TiCl_4$ would promote the reaction, although better diastereoselectivity was obtained with $SnCl_4$. Stoichiometric quantities of $Yb(OTf)_3$, $In(OTf)_3$, $InCl_3$, or $BF_3{\cdot}OEt_2$

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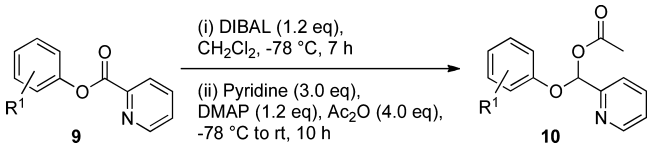
Table 2. Reductive Acetylation of Aryl Picolinates 9



entry	R	product	yield (%)	phenol pK_a
1	H	**10a**	58	9.97
2	*o*-Me	**10b**	67	10.22
3	*m*-Me	**10c**	62	10.10
4	*p*-Me	**10d**	66	10.19
5	*o*-Cl	**10e**	0	8.48
6	*m*-Cl	**10f**	13	9.08
7	*p*-Cl	**10g**	44	9.38
8	*o*-OMe	**10h**	55	9.98
9	*m*-OMe	**10i**	47	9.65
10	*p*-OMe	**10j**	71	10.21
11	3,5-di-OMe	**10k**	0	9.35
12	3,5-di-Me	**10l**	63	10.19
13	*m*-NO_2	**10m**	0	8.35
14	3,5-di-Cl	**10n**	0	8.19

afforded only recovered starting material. Furthermore, the reaction required at least 1.2 equiv of $SnCl_4$ to proceed, and the best results were obtained with 2.0 equiv. This likely arises from preferential complexation with the pyridine nitrogen over the acetate carbonyl group.[28] The reaction was further optimized, and the best conditions were determined to be the use of 2.0 equiv of $SnCl_4$ in dichloromethane at −15 °C for 24 h.

Reaction of the acetal **10** with a variety of electron-rich alkenes using the optimized conditions of $SnCl_4$ (2.0 equiv) and dienophile (1.2−4.0 equiv) in dichloromethane at −15 °C for 24 h afforded cycloadducts in moderate to good yields (Table 3). Reaction of **10a** with norbornene led to the formation of chroman **11a** in high yield and diastereoselectivity, favoring the exo-endo[29] diastereomer (Table 3, entry 1). Reactions of styrenes led to the formation of chromans **11b−d** with approximately 5:1 diastereomeric ratios favoring the cis-2,4-endo diastereoisomers (Table 3, entries 2−4). The reaction was intolerant of very electron-rich alkenes such as ethyl vinyl ether, endocyclic enecarbamates, cyclopentadiene, or dihydrofuran, species that can be used in the Povarov reaction. In these cases, the strong Lewis acidic conditions resulted in competitive polymerization of the alkenes. Less reactive cyclic alkenes such as cyclopentene and cyclohexene are only rarely encountered in the Povarov reaction but interestingly were capable of participating in the oxa-Povarov reaction, to give chromans **11e** and **11f**, respectively, albeit in lower yields than were obtained for the adducts of norbornene or styrene (Table 3, entries 5 and 6). Again the reactions were found to be diastereoselective favoring the endo-diastereoisomers. The more reactive substrates 1,3-cyclohexadiene and indene also underwent addition to give adducts **11g** and **11h**, respectively, in modest yields (Table 3, entries 7 and 8).

The stereochemistry of each adduct was determined by analysis of the ^{1}H NMR spectra of the products. The major diastereomers of the products derived from cyclic alkenes (**11a** and **11e−h**) could be identified on the basis of the peaks corresponding to the H2 protons. For example, the isolated norbornene adduct **11a**-*exo-endo* shows a doublet at 4.93 ppm for H2 with a coupling constant of 3.5 Hz, which is indicative of an axial−equatorial-like coupling. This is consistent with the syn relationship in the exo-endo diastereomer where the phenyl substituent adopts a pseudoequatorial orientation.[30] The identity of the major exo-endo diastereomer **11a** was confirmed by ^{1}H NMR and X-ray crystallographic analysis.[31] (see Supporting Information). The H2−H3 and H3−H4 coupling constants were observed to be 3.5 and 9.0 Hz, respectively, which are consistent with a pseudoaxial orientation of H2 and a pseudoequatorial orientation of H3. The X-ray crystal structure indicates that the chroman ring adopts a distorted half-chair conformation, with a syn relationship between the C2, C3, and C4 substituents. The H2/H3 and H3/H4 dihedral angles of 52.5° and 8.2°, respectively, correlate well with the coupling constants observed by ^{1}H NMR.

The major diastereomers of the chromans derived from the acyclic styrenes (**11b−d**) showed H2−H3 and H3−H4 vicinal coupling constants that are also consistent with the endo stereoisomers. As a representative example, the styrene adduct **11b**-*endo* shows a doublet of doublet at 5.33 ppm with coupling constants of 11.5 and 2.0 Hz, corresponding to H2, and a peak at 4.40 ppm with coupling constants of 12.0 and 5.5 Hz, corresponding to H4. The coupling constants for both sets of peaks are characteristic of an axial−axial and axial−equatorial relationship for both the H2−H3/H2−H3′ and H4−H3/H4−H3′ pairs. This is consistent with a half chairlike conformation of the chroman ring and a syn relationship of the H2 and H4 protons of **11b**-*endo*, such that both the pyridyl and phenyl substituents adopt pseudoequatorial orientations. The stereochemistry for **11b**-*endo* was also verified by X-ray crystallographic analysis. The observed dihedral angles of 63.8° and 177.5° for H2−C2−C3−H3/H3′ and 58.3° and 177.0° for H4−C4−C3−H3/H3′ are also consistent with the observed vicinal coupling constants.[32] In general, the most diagnostic peak to identify the exo-diastereoisomers was that for H4 which appears as an apparent triplet (with, for example, a coupling constant of J = 5.0 Hz for **11b**-*exo*).[33,34]

To examine stereoelectronic effects, ortho- and para-substituted acetyl esters **10** were allowed to react with both styrene (Table 4) and norbornene (Table 5) under the optimized conditions. Reaction of styrene as the dienophile with methyl-, methoxy-, and chloro-substituted compounds **10** occurred to give the chromans **12** as the major endo-isomers with moderate to good diastereomeric ratios (2.0−7.6:1) (Table 4). For reaction of the para-substituted compounds, the diastereomeric ratio showed a modest decrease with increasing electron-donating ability of the substituent (Cl > Me > MeO). Products from the reaction of the ortho-substituted compounds showed slightly increased selectivity relative to their para-substituted counterparts. The observed preference for the formation of the **12**-*endo* products parallels the results generally obtained for the preferential formation of *endo*-tetrahydroquinolines in the aza-Povarov reaction, although reactions of styrenes are known to occur with both endo and exo selectivity.[3]

In general, the cycloaddition reactions of norbornene were more effective than those for styrene (Table 5). The reactions of *ortho*- and *para*-methyl, -methoxy, and -chloro-substituted compounds **10** occurred to give the chromans **13**. As for the reactions with styrene the endo-products (i.e., **13**-*exo-endo*) were obtained as the major isomers with good to excellent diastereomeric ratios (10−30:1) (Table 5). The observed preference for the formation of the **13**-*exo-endo* products contrasts with the results for comparable standard aza-Povarov reactions.[35] In these cases, the product tetrahydroquinolines were obtained with high *exo-exo* selectivity, and the selectivity was attributed to reaction occurring via a concerted [4 + 2] mechanism.[36]

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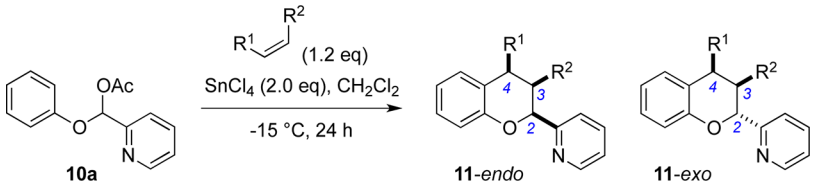
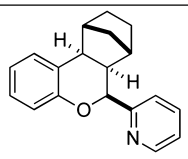
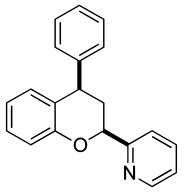
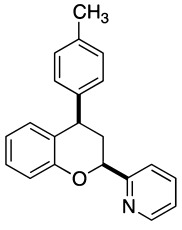
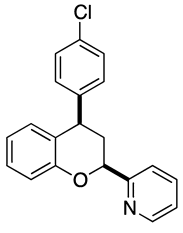
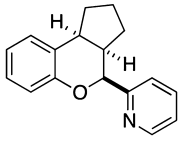
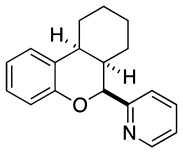
Table 3. Reaction of 10a with Various Alkenes



entry	alkene	product[a]	yield (%)	d.r.[b]
1	norbornene[c]	 **11a**[d]	77	20 : 1
2	styrene	 **11b**	64	4.8 : 1
3	4-Me-styrene	 **11c**	20	5 : 1
4	4-Cl-styrene	 **11d**	54	4.7 : 1
5	cyclopentene	 **11e**	42[e]	11 : 1
6	cyclohexene		25[e]	17 : 1

[a]Only the major (endo) product is shown. [b]**11**-*endo*:**11**-*exo* ratio determined by analysis of the ^{1}H NMR spectrum of the crude reaction mixture. [c]4.0 equiv of dienophile used. [d]Only the major (exo-endo) product is shown. [e]Reaction conducted at 0 °C for 24 h.

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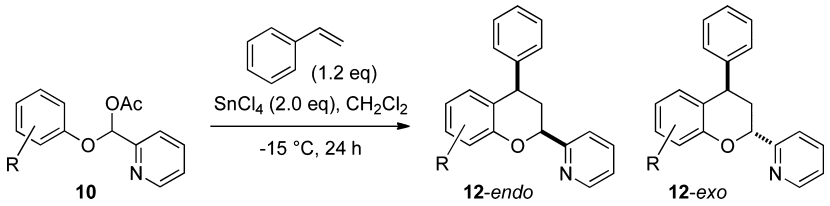
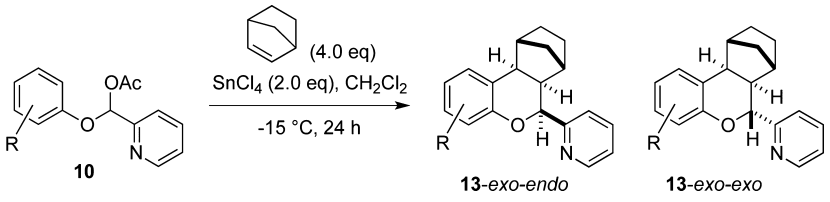
Table 4. Reaction of Styrene with Substituted Aryl Acetals 10



entry	precursor	R	product	yield (%)	dr[a]
1	**10a**	H	**11b**	64	4.8:1
2	**10b**	*o*-Me	**12b**	66	4.9:1
3	**10d**	*p*-Me	**12d**	59	4.0:1
4	**10g**	*p*-Cl	**12g**	28	7.6:1
5	**10h**	*o*-OMe	**12h**	45	6.0:1
6	**10j**	*p*-OMe	**12j**	58	2.0:1

[a]**12**-*endo*:**12**-*exo* ratio determined by analysis of the ^{1}H NMR spectrum of the crude reaction mixture.

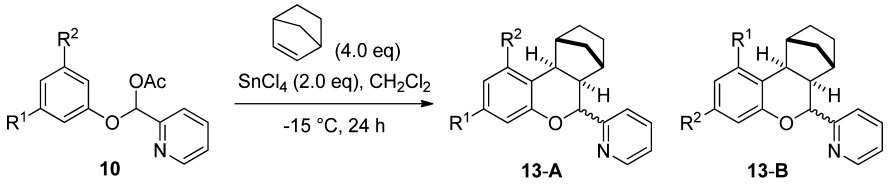
Table 5. Reaction of Norbornene with Substituted Acetals 10



entry	precrusor	R	product	isolated yield, %	dr[a]
1	**10a**	H	**11a**	80	20:1
2	**10b**	*o*-Me	**13b**	82	11:1
3	**10d**	*p*-Me	**13d**	79	20:1
4	**10g**	*p*-Cl	**13g**	58	18:1
5	**10h**	*o*-OMe	**13h**	68	30:1
6	**10j**	*p*-OMe	**13j**	65	10:1

[a]**13**-*exo-endo*:**13**-*exo-exo* ratio determined by analysis of the ^{1}H NMR spectrum of the crude reaction mixture.

Table 6. Reaction of Norbornene with Meta-Substituted Acetals 10



entry	R^1	R^2	product	isolated yield, %	ratio (**13-A**:**13-B**)[a]	dr[a,b]
1	Me	H	**13c**	81	1.7:1	20:1
2	Cl	H	**13f**	55	2.2:1	15:1
3	OMe	H	**13i**	57	2.1:1	15:1
4	Me	Me	**13l**	66	–	≥40:1

[a]Determined by analysis of the ^{1}H NMR spectrum of the crude reaction mixture. [b]**13**-*exo-endo*:**13**-*exo-exo* determined for **13-A**.

For the reactions of meta-substituted substrates **10**, issues of both regio- and diastereoselectivity arise. To examine these selectivity issues, norbornene was chosen as a model dienophile (Table 6). In all cases the products **13** were obtained favoring isomer **13-A** (with the substituent para to the norbornyl ring) over **13-B** (ortho) (1.7−2.2:1), and with high diastereomeric ratios favoring the exo-endo-diastereoisomers.[37]

■ MECHANISTIC STUDIES

When first reported, the aza-Povarov reaction was presumed to proceed via a concerted [4 + 2] cycloaddition mechanism, and the possible diastereomeric products were designated *endo* or *exo* in relation to the corresponding Diels−Alder reaction. More recent studies have demonstrated that a stepwise manifold is often operative,[3,38] with a Mannich-type addition of the alkene to the activated imine, followed by cyclization via intramolecular Friedel−Crafts reaction. In some instances, however, experimental results are better rationalized with a concerted mechanism.[3,39] An analogous mechanistic dichotomy is also possible for the oxa-Povarov reaction, with either stepwise or concerted [4 + 2] cycloaddition cationic pathways leading to the chroman products. The concerted [4 + 2] cycloaddition pathway proceeds via **14** to give cation **15**, which then loses a proton to give chroman **6** (Figure 2). The stepwise mechanism involves

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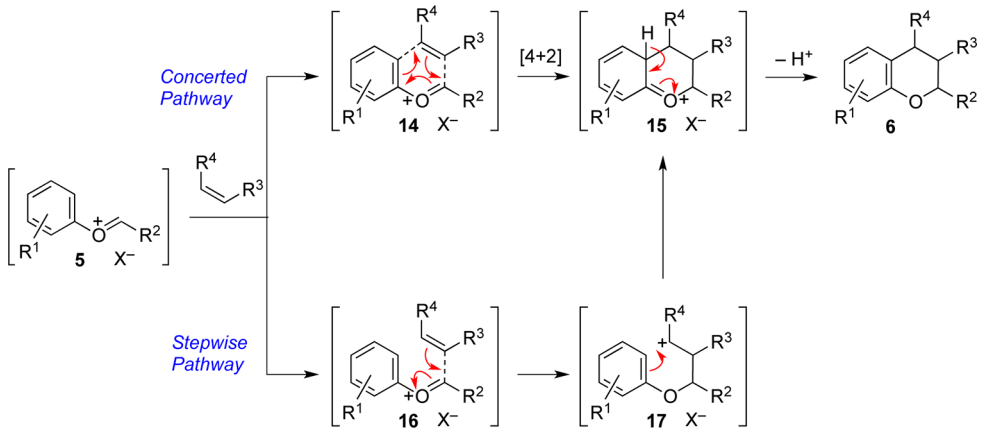
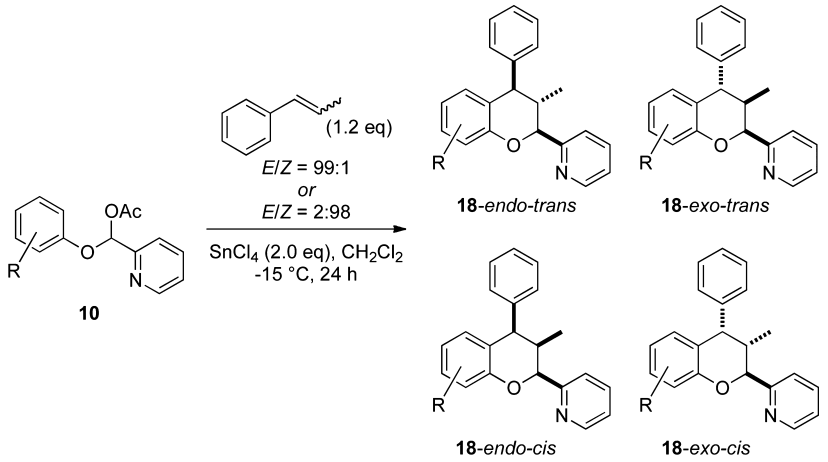


Figure 2. Concerted and stepwise reaction pathways for the Oxa-Povarov reaction.

Table 7. Reactions of *cis*- and *trans*-β-Methylstyrene with 10



entry	precursor styrene	precursor styrene	R	product	yield (%)	dr (endo:exo)[a]	dr (endo-trans:exo-trans:endo-cis:exo-cis)[a]
1	**10a**	trans	H	**18a**	29	1.0:6.3	1.0:6.3:–:–
2	**10d**	trans	*p*-Me	**18d**	46	1.0:3.7	1.0:3.7:–:–
3	**10j**	trans	*p*-OMe	**18j**	63	1.0:2.2	6.7:16.7:1.0:–
4	**10a**	cis	H	**18a**	28	8.1:1.0	25:3.0:7.5:1.0
5	**10d**	cis	*p*-Me	**18d**	34	7.8:1.0	14.3:2.1:10:1.0
6	**10j**	cis	*p*-OMe	**18j**	56	3.6:1.0	5.0:1.8:5.0:1.0

[a]Determined by analysis of the ^{1}H NMR spectrum of the crude reaction mixture.

initial Prins-type[40] addition of the alkene to the *E*-configured aryl oxocarbenium ion **5**[41] via **16**, followed by intramolecular Friedel–Crafts alkylation of the resultant cation **17** to give **15** and finally rearomatization to give **6**.[42,43]

One probe of whether a stepwise of concerted mechanism occurs is to examine the reactions of stereochemically defined trans- and cis-dienophiles, because the stereochemical relationship of the dienophile substituents should be retained in the case of a concerted [4 + 2] cycloaddition pathway (i.e., the reaction should be stereospecific with respect to alkene geometry), whereas reaction via a stepwise pathway can lead to stereochemical scrambling resulting from C3–C4 bond rotation of intermediate **17**. Reaction of **10** with either *cis*- or *trans*-β-methylstyrene under the standard conditions led to a mixture of diastereomeric products (Table 7). For example, the reaction of *trans*-β-methylstyrene and **10j** afforded **18j** as a mixture of the endo-trans, exo-trans, and endo-cis isomers in an 6.7:16.7:1.0 ratio. For the reactions of *cis*-β-methylstyrene, all four isomeric products were isolated in each case.

The stereochemistry of the cycloadducts **18** was determined by ^{1}H NMR analysis, in particular through a consideration of the H2 and H4 protons. An illustrative example is provided with selected NMR data for product **18j** (Table 8). The ^{1}H NMR spectrum of **18j**-*endo-trans* shows that both H2 and H4 have large vicinal couplings to H3 (J = 10.0 and 11.0 Hz), consistent with an axial–axial relationship between each of these protons and H3. 2D NOESY experiments show strong H2–H4 as well as methyl-H2 and methyl-H4 NOE enhancements, indicative of a syn relationship between H2, H4 and the methyl group. The exo-trans and endo-cis isomers were distinguished on the basis of observed NOE's for H2, H4 and the methyl group. The endo-cis isomer shows strong H2–H4, as well as H2–H3 and H3–H4 NOE enhancements, indicating a syn relationship between all three of these protons. The absence of NOE enhancements between either H2 or H4 and the methyl protons is also consistent with the endo-cis stereochemistry, given the anti relationship between both of these protons and the methyl group. The observed vicinal coupling constants of 1.0 Hz for

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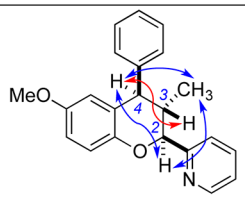
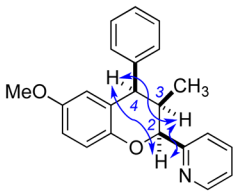
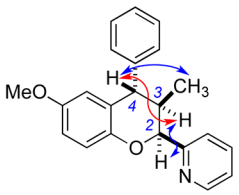
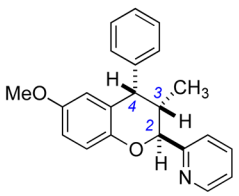
Table 8. Selected NMR Data for Diastereoisomers of 18j

R	Selected ^{1}H NMR Data	NOE[a]
18j-*endo-trans*	H2: 4.87 ppm, $J_{H2\text{-}H3}$ = 10.0 Hz H4: 3.82 ppm, $J_{H3\text{-}H4}$ = 11.0 Hz	
18j-*endo-cis*	H2: 5.39 ppm, $J_{H2\text{-}H3}$ = 1.0 Hz H4: 4.79 ppm, $J_{H3\text{-}H4}$ = 5.5 Hz	
18j-*exo-trans*	H2: 5.10 ppm, $J_{H2\text{-}H3}$ = 2.5 Hz H4: 4.00 ppm, $J_{H3\text{-}H4}$ = 1.5 Hz	
18j-*exo-cis*	H2: 5.04 ppm, $J_{H2\text{-}H3}$ = 9.0 Hz H4: 4.01 ppm $J_{H3\text{-}H4}$ = 5.5 Hz)	

[a]Strong interactions are shown in blue, and weak interactions are shown in red.

J_{H2-H3} and 5.5 Hz for J_{H3-H4} are also consistent with the axial−equatorial relationship between these pairs of protons. NOE data for the exo-trans isomer show methyl-H4 and H2−H3 NOE enhancements, indicating a syn relationship between these pairs, while the absence of an H2 and H4 NOE enhancement is consistent with an anti relationship between these protons. The ^{1}H NMR data of the exo-cis isomer[44] is consistent with a trans-diaxial relationship between H2 and H3, and an axial−equatorial relationship between H3 and H4.

Because the reaction is not stereospecific with respect to alkene geometry, and scrambling of alkene geometry does not occur in the absence of **10**, the oxa-Povarov reaction must proceed through a stepwise path (Figure 2),[45] at least for those cases where scrambling was observed (Table 7, entries 3−6). Initial stepwise Prins-type addition of the activated alkene to the oxonium generates carbocation intermediates **A**, **B**, and **C**, which can have endo/exo and trans/cis relative stereochemistry **19** (Figure 3). Intermediates **A** and **C** are formed through a synclinal approach of the oxonium ion to the alkene, whereas intermediate **B** is formed through an anticlinal approach. Intermediates **A** and **B** must undergo C2−C3 bond rotation to generate intermediate **C** from which Friedel−Crafts cyclization to the products occur. A concerted hetero Diels−Alder mechanism would proceed via a synclinal orientation analogous to **C**. For reactions of styrene, the favored products have endo stereochemistry (**19**, R = H), while for reactions of *trans*-*β*-methylstyrene, there is a reversal of selectivity in favor of the exo stereochemistry products (**19**, R = Me). However, for the reactions of *cis*-*β*-methylstyrene (R = Me), significant amounts of cis to trans scrambled products are observed (the endo-trans isomers are the major products), consistent with slow cyclization of the exo-cis intermediates relative to C3−C4 bond rotation. There is also partial scrambling of the endo-cis to the exo-trans intermediates. The overall product distributions for the reactions of *cis*-*β*-methylstyrene show that initial C2−C3 bond formation in the Prins step occurs with only modest selectivity (i.e., the product ratio of endo-trans + exo-cis:exo-trans + endo-cis).[46]

The relative C2/C3 stereochemistry should be set in the initial addition step of the oxonium ion for the reactions of both *cis* and *trans*-*β*-methylstyrene substrates, assuming that reaction occurs via an irreversible stepwise mechanism. The stereoselectivity of this C2−C3 bond formation can be compared to the additions of alkenes to oxonium ions, such as occur in carbonyl ene[47] and crotylsilylation reactions.[48] A combined experimental (using TMSOTf as a Lewis acid) and computational study (at the B3LYP/6-31+G(d) level of theory) revealed that reactions between unbranched aliphatic aldehydes and *E*-crotylsilanes occurred preferentially to give syn products, whereas *Z*-crotylsilanes react preferentially to give the corresponding anti products.[48] These observations were rationalized using the synclinal transition state model **20** and anticlinal transition state model **21**, respectively (Figure 4). The stereochemistry of TS **20** corresponds to the transition state *exo-trans*-**A** (Figure 3), and predicts the same relative stereochemistry for both reactions (i.e., the *syn*-crotylsilylation corresponds to the C2/C3 stereocontrol in the oxa-Povarov reaction). Similarly the analogous stereochemistry of TS **21** and TS *exo-cis*-**B** results in the same relative stereochemistry for the oxa Povarov and *Z*-crotylation products.

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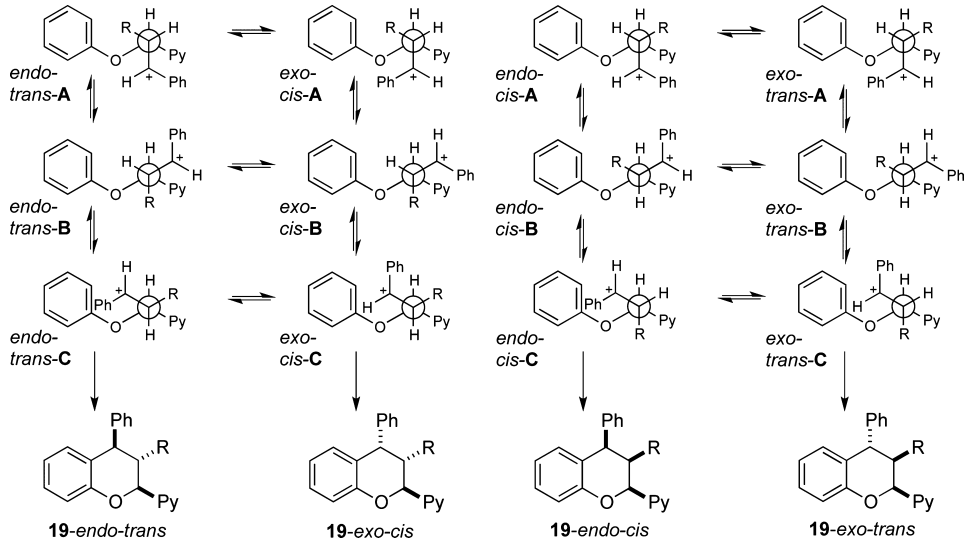

Figure 3. Rationale for the formation of scrambled products from **10** and β-methylstyrene showing reaction intermediates involved in a stepwise pathway.

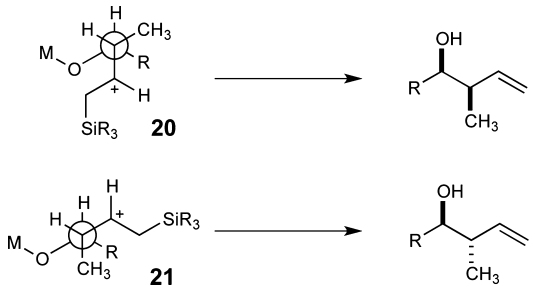

Figure 4. Calculated transition state model[48] for the reactions of oxonium ions with *E*- and *Z*-crotylsilanes (M = CH_3 and SiR_3 = SiH_3).

The higher selectivity obtained for the reactions of *trans*-β-methylstyrene compared to the cis isomer are also paralleled in the reactions of crotylsilanes. The similarity between these reactions may suggest that transition states *exo-trans*-**A** and *exo-cis*-**B** are relevant for the oxa-Povarov reaction.

Reactions with cyclic alkenes (i.e., also cis-configured alkenes) such as norbornene, cyclohexene, and indene proceed with high endo selectivity (≥10:1 for all cases studied). The C2/C3 relative stereochemistry of the products is thus opposite to that for the major isomers obtained from the reactions of *cis*-β-methylstyrene. Destabilization of the exo Prins transition states presumably occurs as a result of steric effects, particularly for transition states *exo-cyc-TS*-**A** and *exo-cyc-TS*-**B** (corresponding to *exo-cis*-**A** and **B**) (Figure 5). Similar destabilizing steric effects for *endo-cyc-TS*-**A** may suggest that reactions of cyclic alkenes occur through either the anticlinal transition state *endo-cyc-TS*-**B** or the Diels–Alder like synclinal transition state *endo-cyc-TS*-**C**.

The Povarov reaction using protic acid catalysis[49] has been shown to operate via a stepwise mechanism, although its cationic variant[50] has been shown to be stereospecific with respect to β-methylstyrene geometry, indicating a concerted mechanism. Related cycloaddition chemistry of α-thionium ion dienes to give the corresponding thiochromans, however, appears to operate by a stepwise mechanism.[51] The aza-Povarov reaction has been shown to be very sensitive to reaction conditions in terms of both yield and selectivity. For example, a complete reversal of endo/exo selectivity can be realized by changing from Lewis to protic acids in the case of reactions of cyclic enamide-type dienophiles.[52] For Povarov reactions using styrene as the dienophile, modest exo selectivity is generally observed under protic acid-catalyzed conditions;[53] however, endo selectivity is often observed with more reactive imine precursors.[54] Interestingly, Povarov reactions of *trans*-β-methylstyrenes occur with high levels of endo selectivity.[55] In contrast the oxa-Povarov reactions of *trans*-β-methylstyrene occur with exo selectivity, while the reactions of

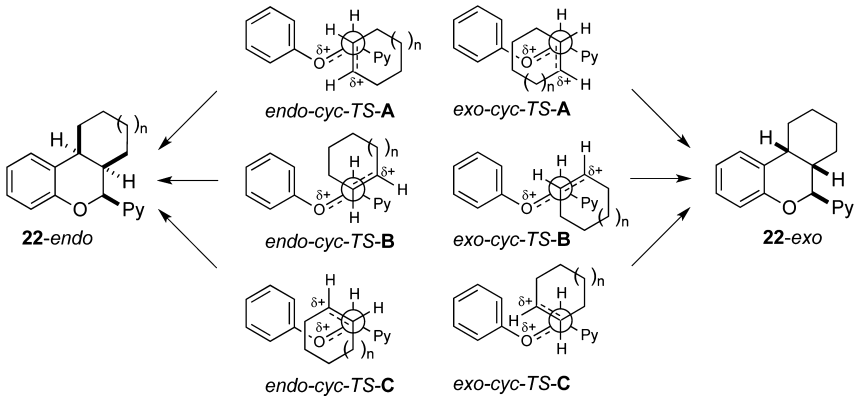

Figure 5. Prins transition states for the reactions of cyclic alkenes.

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styrene and *cis*-β-methylstyrene occur in an endo-selective fashion. A similar comparison can be made for the reactions of norbornene, for which *exo-exo* selectivity is observed in the aza-Povarov reactions,[35] but exo-endo selectivity in the oxa-Povarov reaction. A key difference between the intermediates for these reactions is the presence of the Lewis acid (bound to the imine nitrogen) in the Povarov reaction, compared to a vacant site at the *E*-configured oxocarbenium oxygen in the oxa-Povarov reaction. While there is no definitive transition state model for either the aza- or oxa-Povarov reactions, this difference and its effect on the mode of approach of the dienophile with the oxocarbenium ion relative to that obtained with an iminium ion is presumably a major factor underlying the opposite diastereoselectivities obtained in the oxa-Povarov versus the standard aza-Povarov reaction.

CONCLUSIONS

A hetero Diels–Alder approach to 2,3,4-substituted chromans has been developed. The reaction proceeds via a formal [4 + 2] cycloaddition between an electron-rich alkene and an extremely rare cationic 2-oxadiene intermediate. Aryl picolinate mixed acetals serve as precursors to these intermediates, such that chromans are formed on reaction with 2 equiv of $SnCl_4$ and electron-rich alkenes. Norbornene and styrene afforded moderate to good yields of chromans, whereas lower yields were obtained with other carbocyclic alkenes such as cyclohexene and cyclohexadiene. Endo-selective reactions occurred from the reactions of norbornene (≥10:1) and styrene (approximately 5:1 dr). Reactions of *trans*-β-methylstyrene occurred with exo selectivity, whereas the reactions of *cis*-β-methylstyrene occurred with endo selectivity. The reactions of *cis*-β-methylstyrene were also found to be nonstereospecific with respect to the styrene geometry, indicating that a sequential Prins/Friedel–Crafts-type mechanism occurs for the reactions of this substrate. The relative endo/exo stereochemistry observed in the oxa-Povarov reactions was generally found to be opposite to that observed for the comparable standard Povarov reactions.

Through the course of this study, the first example of a reductive acetylation procedure for the synthesis of phenol-substituted mixed acetals was also developed. The use of picolinate esters was essential to achieve selective DIBAL reduction. Further studies will be required to expand the scope of oxonium precursors and alkenes amenable to the reaction, as well as to provide additional mechanistic data to rationalize the observed selectivity differences for chroman formation.

EXPERIMENTAL SECTION

General Procedure. All reactions were performed under nitrogen or argon in flame-dried glassware. Ether was freshly distilled from sodium/benzophenone ketyl under nitrogen. Dichloromethane was freshly distilled from calcium hydride under nitrogen. All other solvents were obtained as ACS grade or better from commercial suppliers and used as received. All reagents were used as received from commercial suppliers. Flash chromatography on silica gel (60 Å, 230–400 mesh) was performed with reagent grade solvents. Analytical thin-layer chromatography (TLC) was performed on precoated silica gel plates, visualized with a UV_{254} lamp, and stained with vanillin. Solvent ratios for chromatography and R_f values are reported as v/v ratios. Melting points are uncorrected and obtained on compounds purified through flash chromatography with further recrystallization. ^1H and ^{13}C NMR spectra were obtained as solutions in deuterated solvents. Chemical shifts are reported in δ ppm values. Proton chemical shifts were internally referenced to tetramethylsilane (δ 0.00 ppm). Carbon chemical shifts were internally referenced to the solvent resonances in $CDCl_3$ (δ 77.00 ppm). Peak multiplicities are designated by the following abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad; *J*, coupling constant in hertz. Mass spectra were obtained on a TOF mass spectrometer.

General Procedure for Picolinate Ester Synthesis (9). A slurry of picolinic acid (4.0 mmol) in ether (30 mL) was cooled to 0 °C. Oxalyl chloride (4.4 mmol) was added, followed by DMF (50 μL). The reaction was stirred at 0 °C and warmed to room temperature over 16 h. The solvent was then evaporated with protection from moisture, and the resulting acid chloride was dissolved in CH_2Cl_2 (40 mL) and cooled to 0 °C. The appropriate phenol (4.4 mmol) was added, followed by triethylamine (12.0 mmol). The reaction was stirred at 0 °C and warmed to ambient temperature over 5 h. Saturated aqueous sodium bicarbonate (10 mL) and CH_2Cl_2 (20 mL) were added, and the reaction was stirred rapidly. The organic phase was collected and washed with saturated sodium bicarbonate, water, and brine. After being dried over Na_2SO_4, the reaction was concentrated under reduced pressure and purified by silica gel column chromatography to afford the picolinate ester.

Phenyl picolinate ***9a***. Flash chromatography (30% ethyl acetate/hexanes) gave **9a** as a white solid (0.685 g, 86% yield). R_f = 0.23 (30% ethyl acetate/hexanes); mp 78–79 °C (hexanes/ethyl acetate); IR (thin film, CH_2Cl_2) ν_{max} 3070, 1751, 1581, 1483, 1302, 1277, 1235, 1193, 1115, 1073, 924, 819, 749, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.86 (1H, ddd, *J* = 1.0, 1.5, 4.5 Hz), 8.31 (1H, ddd, *J* = 1.0, 1.0, 8.0 Hz), 7.93 (1H, ddd, *J* = 1.5, 7.5, 8.0 Hz), 7.57 (1H, ddd, *J* = 1.0, 4.5, 7.5 Hz), 7.45 (2H, dd, *J* = 8.0, 8.0 Hz), 7.26–7.33 (3H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9, 151.0, 150.2, 147.6, 137.3, 129.6, 127.5, 126.2, 125.9, 121.7; MS (EI) *m*/*z* 199 (16) $[M]^+$, 170 (4), 155 (100), 115 (4), 106 (31), 94 (8), 78 (64), 65 (17), 51 (8); HRMS (EI) calcd for $[M]^+$ $C_{12}H_9NO_2$ 199.0633; found 199.0633.

2-Methylphenyl picolinate ***9b***. Flash chromatography (30% ethyl acetate/hexanes) gave **9b** as a white solid (0.681 g, 80% yield). R_f = 0.21 (30% ethyl acetate/hexanes); mp 48–49 °C (hexanes/ethyl acetate); IR (thin film, CH_2Cl_2) ν_{max} 3057, 2926, 1736, 1582, 1491, 1304, 1290, 1244, 1174, 1117, 1078, 993, 768, 746, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.86 (1H, ddd, *J* = 0.5, 1.5, 4.5 Hz), 8.29 (1H, ddd, *J* = 0.5, 1.0, 8.0 Hz), 7.92 (1H, ddd, *J* = 1.5, 7.5, 8.0 Hz), 7.56 (1H, ddd, *J* = 1.0, 4.5, 7.5 Hz), 7.24–7.30 (2H, m), 7.15–7.22 (2H, m), 2.26 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5, 150.2, 149.6, 147.4, 137.3, 131.3, 130.2, 127.5, 127.1, 126.4, 125.8, 121.9, 16.3; MS (EI) *m*/*z* 213 (2, M^+), 184 (12), 169 (100), 156 (4), 129 (3), 106 (25), 91 (3), 78 (65), 51 (15); HRMS (EI) calcd for $[M]^+$ $C_{13}H_{11}NO_2$ 213.0790; found 213.0794.

3-Methylphenyl picolinate ***9c***. Flash chromatography (30% ethyl acetate/hexanes) gave **9c** as a white solid (0.597 g, 70% yield). R_f = 0.18 (30% ethyl acetate/hexanes); mp 51–52 °C (hexanes/ethyl acetate); IR (thin film, CH_2Cl_2) ν_{max} 3063, 2916, 2855, 1751, 1604, 1582, 1427, 1303, 1227, 1142, 1111, 1072, 1049, 995, 918, 787, 748, 687 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.84 (1H, dd, *J* = 1.0, 4.5 Hz), 8.27 (1H, dd, *J* = 0.5, 8.0 Hz), 7.90 (1H, ddd, *J* = 1.5, 7.5, 8.0 Hz), 7.54 (1H, dd, *J* = 4.5, 7.5 Hz), 7.31 (1H, dd, *J* = 7.5, 7.5 Hz), 7.02–7.11 (3H, m), 2.39 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0, 150.9, 150.2, 147.6, 139.7, 137.2, 129.3, 127.4, 127.0, 125.8, 122.3, 118.7, 21.4; MS (EI^+) *m*/*z* 213 (2, M^+), 184 (4), 169 (100), 156 (2), 129 (1), 106 (37), 91 (1), 78 (72), 51 (13); HRMS (EI) calcd for $[M]^+$ $C_{13}H_{11}NO_2$ 213.0790; found 213.0792.

4-Methylphenyl picolinate ***9d***. Flash chromatography (30% ethyl acetate/hexanes) gave **9d** as a white solid (0.648 g, 76% yield). R_f = 0.18 (30% ethyl acetate/hexanes); mp 85–86 °C (hexanes, ethyl acetate); IR (thin film, CH_2Cl_2) ν_{max} 3055, 2955, 2916, 2862, 1751, 1574, 1505, 1304, 1281, 1234, 1188, 1165, 1111, 1072, 995, 880, 802 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.84 (1H, ddd, *J* = 1.0, 1.5, 4.5 Hz), 8.27 (1H, dd, *J* = 1.0, 8.0 Hz), 7.90 (1H, ddd, *J* = 1.5, 7.5, 8.0 Hz), 7.55 (1H, ddd, *J* = 1.5, 4.5, 7.5 Hz), 7.23 (2H, d, *J* = 8.5 Hz), 7.14 (2H, d, *J* = 8.5 Hz), 2.37 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.2, 150.2, 148.8, 147.7, 137.3, 135.9, 130.2, 127.5, 125.9, 121.5, 21.0; MS (ESI^+) *m*/*z* 236 (36, $[M + Na]^+$), 214 (100, $[M + H]^+$), 124 (9), 106 (7), 96 (35); HRMS (ESI^+) calcd for $[M + H]^+$ $C_{13}H_{12}NO_2$ 214.0862; found 214.0872.

2-Chlorophenyl picolinate ***9e***. Flash chromatography (30% ethyl acetate/hexanes) gave **9e** as a white solid (0.730 g, 78% yield). R_f = 0.13 (30% ethyl acetate/hexanes); mp 80–81 °C (hexanes, ethyl acetate); IR

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(thin film, CH_2Cl_2) ν_{max} 3061, 3030, 3009, 1736, 1586, 1574, 1474, 1449, 1303, 1284, 1240, 1205, 1097, 1058, 1030, 995, 945, 882, 747 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.87 (1H, ddd, J = 1.0, 2.0, 4.5 Hz), 8.32 (1H, d, J = 8.0 Hz), 7.93 (1H, dd, J = 8.0, 8.5 Hz), 7.57 (1H, ddd, J = 1.0, 4.5, 8.5 Hz), 7.50 (1H, d, J = 1.5 Hz), 7.30−7.36 (2H, m), 6.97 (1H, dd, J = 7.0, 7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.9, 150.4, 147.3, 147.0, 137.4, 130.5, 128.0, 127.7, 127.5, 126.2, 123.8; MS (ESI^+) m/z 234 (90, $[M + H]^+$), 124 (100); HRMS (ESI^+) calcd for $C_{12}H_9ClNO_2$ $[M + H]^+$: 234.0322, found 234.0314.

3-Chlorophenyl picolinate ***9f***. Flash chromatography (30% ethyl acetate/hexanes) gave **9f** as a white solid (0.590 g, 63% yield). R_f = 0.13 (30% ethyl acetate/hexanes); mp 85−86 °C (hexanes, ethyl acetate); IR (thin film, CH_2Cl_2) ν_{max} 3065, 3036, 3014, 1755, 1591, 1478, 1431, 1304, 1279, 1234, 1204, 1115, 1069, 1047, 991, 912, 881, 756, 752, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.84 (1H, ddd, J = 1.0, 2.0, 5.0 Hz), 8.26 (1H, ddd, J = 1.0, 1.0, 8.0 Hz), 7.92 (1H, ddd, J = 1.5, 7.5, 8.0 Hz), 7.56 (1H, ddd, J = 1.0, 4.5, 7.5 Hz), 7.36 (1H, dd, J = 8.0, 8.0 Hz), 7.31 (1H, dd, J = 2.0, 2.0 Hz), 7.27 (1H, ddd, J = 1.0, 2.0, 8.0 Hz), 7.18 (1H, ddd, J = 1.0, 2.0, 7.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.7, 151.5, 150.4, 147.3, 137.4, 135.0, 130.4, 127.8, 126.7, 126.1, 122.6; MS (ESI^+) m/z 234 (100, $[M + H]^+$); HRMS (ESI^+) calcd for $[M + H]^+$ $C_{12}H_9ClNO_2$ 234.0322; found 234.0314.

4-Chlorophenyl picolinate ***9g***. Flash chromatography (30% ethyl acetate/hexanes) gave **9g** as a white solid (0.711 g, 76% yield). R_f = 0.13 (30% ethyl acetate/hexanes); mp 91−91 °C (hexanes, ethyl acetate); IR (thin film) ν_{max} 3092, 3051, 3036, 1759, 1582, 1485, 1437, 1404, 1304, 1283, 1244, 1198, 1157, 1117, 1078, 1012, 995, 889, 814, 746, 721, 698, 650, 621 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.85 (1H, ddd, J = 1.0, 1.5, 4.5 Hz), 8.27 (1H, ddd, J = 1.0, 1.0, 8.0 Hz), 7.92 (1H, ddd, J = 1.5, 8.0, 8.0 Hz), 7.57 (1H, ddd, J = 1.0, 4.5, 8.0 Hz), 7.40 (2H, ddd, J = 2.0, 2.0, 9.0 Hz), 7.21 (2H, ddd, J = 2.0, 2.0, 9.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9, 150.4, 149.6, 147.4, 137.4, 131.8, 129.8, 127.8, 126.1, 123.3; MS (ESI^+) m/z 356 (57, $[M + Na]^+$), 234 (100), 124 (18), 106 (24), 96 (77); HRMS (ESI^+) calcd for $[M + H]^+$ $C_{12}H_9NO_2Cl$ 234.0316; found 234.0322.

2-Methoxyphenyl picolinate ***9h***. Flash chromatography (30% ethyl acetate/hexanes) gave **9h** as a white solid (0.733 g, 80% yield). R_f = 0.11 (30% ethyl acetate/hexanes); mp 83−84 °C (hexanes, ethyl acetate); IR (thin film, CH_2Cl_2) ν_{max} 3071, 3021, 2974, 1748, 1609, 1505, 1462, 1377, 1303, 1281, 1257, 1234, 1195, 1123, 1042, 1026, 991, 821, 767, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.85 (1H, ddd, J = 1.0, 2.0, 4.5 Hz), 8.28 (1H, ddd, J = 1.0, 1.0, 8.0 Hz), 7.89 (1H, ddd, J = 2.0, 8.0, 8.0 Hz), 7.54 (1H, ddd, J = 1.0, 4.5, 8.0 Hz), 7.20−7.27 (2H, m), 6.97−7.03 (2H, m), 3.81 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.4, 151.3, 150.3, 147.6, 140.1, 137.3, 127.4, 127.3, 126.0, 123.0, 120.9, 112.6, 56.0; MS (EI) m/z 229 (2, M^+), 198 (8), 184 (86), 170 (7), 155 (12), 131 (4), 106 (41), 95 (6), 84 (34), 78 (100), 65 (5), 51 (13); HRMS (EI) calcd for $[M]^+$ $C_{13}H_{11}NO_3$ 229.0739; found 229.0736.

3-Methoxyphenyl picolinate ***9i***. Flash chromatography (30% ethyl acetate/hexanes) gave **9i** as a white solid (0.586 g, 64% yield). R_f = 0.21 (30% ethyl acetate/hexanes); mp 77−79 °C (hexanes, ethyl acetate); IR (thin film, CH_2Cl_2) ν_{max} 3022, 2843, 2855, 1747, 1582, 1504, 1431, 1304, 1279, 1260, 1196, 1119, 1074, 821, 748, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.81 (1H, ddd, J = 1.0, 1.5, 4.5 Hz), 8.25 (1H, ddd, J = 1.0, 1.0, 7.0 Hz), 7.87 (1H, ddd, J = 1.5, 7.0, 7.5 Hz), 7.51 (1H, ddd, J = 1.5, 4.5, 7.5 Hz), 7.17−7.24 (2H, m), 7.94−7.02 (2H, m), 3.78 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0, 150.9, 150.2, 147.6, 139.7, 137.2, 129.3, 127.4, 127.0, 125.8, 122.3, 118.7, 21.4; MS (ESI^+) m/z 230 (100, $[M + H]^+$); HRMS (ESI^+) calcd for $[M + H]^+$ $C_{13}H_{12}NO_3$ 230.0817; found 230.0871.

4-Methoxyphenyl picolinate ***9j***. Flash chromatography (30% ethyl acetate/hexanes) gave **9j** as a white solid (0.724 g, 79% yield). R_f = 0.11 (30% ethyl acetate/hexanes); mp 88−89 °C (hexanes, ethyl acetate); IR (thin film, CH_2Cl_2) ν_{max} 3065, 2952, 2855, 1751, 1579, 1508, 1440, 1304, 1290, 1236, 1194, 1114, 1074, 1028, 993, 874, 818, 754, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.85 (1H, ddd, J = 1.0, 2.0, 5.0 Hz), 8.28 (1H, ddd, J = 1.0, 1.0, 8.0 Hz), 7.91 (1H, ddd, J = 1.5, 7.5, 8.0 Hz), 7.55 (1H, ddd, J = 1.0, 5.0, 7.5 Hz), 7.18 (2H, d, J = 9.0 Hz), 6.94 (2H, d, J = 9.0 Hz), 3.81 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.3, 157.6, 150.2, 147.7, 144.5, 137.3, 127.5, 125.9, 122.5, 114.7, 55.7; MS (EI) m/z 229 (12, M^+), 185 (100), 170 (6), 158 (4), 130 (2), 106 (46), 95 (7), 78 (99), 65 (2), 51 (6); HRMS (EI) calcd for $[M]^+$ $C_{13}H_{11}NO_3$ 229.0739; found 229.0736.

3,5-Dimethoxyphenyl picolinate ***9k***. Flash chromatography (30% ethyl acetate/hexanes) gave **9k** as a white solid (0.622 g, 60% yield). R_f = 0.10 (30% ethyl acetate/hexanes); mp 73−74 °C (hexanes, ethyl acetate); IR (thin film, CH_2Cl_2) ν_{max} 3082, 3011, 2845, 1734, 1618, 1597, 1466, 1441, 1304, 1292, 1244, 1207, 1132, 1096, 1042, 991, 954, 922, 829, 745, 682, 646 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.84 (1H, ddd, J = 1.0, 2.0, 4.5 Hz), 8.27 (1H, ddd, J = 1.0, 2.0, 8.0 Hz), 7.90 (1H, ddd, J = 2.0, 8.0, 8.0 Hz), 7.56 (1H, ddd, J = 1.5, 4.5, 8.0 Hz), 6.44 (2H, d, J = 2.0), 6.39 (1H, d, J = 2.5), 3.80 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9, 161.4, 152.6, 150.3, 147.7, 137.4, 127.6, 126.0, 100.5, 98.9, 48.0; MS (ESI^+) m/z 260 (100, $[M + H]^+$); HRMS (ESI^+) calcd for $[M + H]^+$ $C_{14}H_{14}NO_4$ 260.0923; found 260.0919.

3,5-Dimethylphenyl picolinate ***9l***. Flash chromatography (30% ethyl acetate/hexanes) gave **9l** as a colorless oil (0.590 g, 65% yield). R_f = 0.15 (30% ethyl acetate/hexanes); IR (thin film, CH_2Cl_2) ν_{max} 3055, 3013, 2951, 1755, 1732, 1620, 1589, 1470, 1435, 1308, 1285, 1242, 1142, 1099, 1045, 995, 903, 868, 826, 745, 721, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.84 (1H, ddd, J = 1.0, 2.0, 4.5 Hz), 8.26 (1H, ddd, J = 1.0, 1.0, 8.0 Hz), 7.90 (1H, ddd, J = 2.0, 8.0, 8.0 Hz), 7.54 (1H, ddd, J = 1.0, 4.5, 8.0 Hz), 6.88 (1H, s), 6.87 (2H, s), 2.34 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.2, 150.5, 150.2, 147.8, 139.5, 137.3, 128.0, 127.4, 125.9, 119.3, 21.4; MS (ESI^+) m/z 228 (100, $[M + H]^+$); HRMS (ESI^+) calcd for $[M + H]^+$ $C_{14}H_{14}NO_2$ 228.1025; found 228.1021.

3-Nitrophenyl picolinate ***9m***. Flash chromatography (50% ethyl acetate/hexanes) gave **9m** as a white solid (0.735 g, 75% yield). R_f = 0.05 (40% ethyl acetate/hexanes); mp 115−116 °C (hexanes, ethyl acetate); IR (thin film, CH_2Cl_2) ν_{max} 3092, 3049, 1734, 1586, 1526, 1474, 1439, 1354, 1290, 1271, 1242, 1213, 1103, 1074, 991, 899, 814, 799, 739, 714, 696. 664 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.87 (1H, ddd, J = 1.0, 1.5, 4.5 Hz), 8.30 (1H, ddd, J = 1.0, 1.0, 8.0 Hz), 8.15−8.20 (2H, m), 7.96 (1H, ddd, J = 1.5, 7.5, 7.5 Hz), 7.60−7.68 (3H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5, 151.3, 150.4, 149.0, 146.7, 137.6, 130.3, 128.4, 128.1, 126.3, 121.3, 117.7; MS (ESI^+) m/z 245 (16, ([$M + H]^+$); HRMS (ESI^+) calcd for $[M + H]^+$ $C_{12}H_9N_2O_4$ 245.0562; found 245.0564.

3,5-Dichlorophenyl picolinate ***9n***. Flash chromatography (30% ethyl acetate/hexanes) gave **9n** as a white solid (0.482 g, 45% yield). R_f = 0.15 (30% ethyl acetate/hexanes); mp 88−89 °C (hexanes, ethyl acetate); IR (thin film, CH_2Cl_2) ν_{max} 3093, 3057, 1763, 1582, 1439, 1310, 1289, 1244, 1105, 1044, 997, 924, 891, 854, 839, 802, 744, 694, 664 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.81 (1H, ddd, J = 1.0, 2.0, 4.5 Hz), 8.22 (1H, ddd, J = 1.0, 1.0, 8.0 Hz), 7.90 (1H, ddd, J = 2.0, 8.0, 8.0 Hz), 7.54 (1H, ddd, J = 1.0, 4.5, 8.0 Hz), 7.27 (2H, dd, J = 2.0, 2.0 Hz), 7.20 (1H, d, J = 2.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3, 151.2, 150.4, 146.8, 137.5, 135.5, 127.09, 126.8, 126.2, 121.2; MS (ESI^+) m/z 268 (100, $[M + H]^+$), 124 (5); HRMS (ESI^+) calcd for $[M + H]^+$ $C_{12}H_8Cl_2NO_2$ 267.9932; found 267.9935.

General Procedure for *α*-Acetoxy Ester Synthesis (10). A solution of **9** (2.0 mmol) in CH_2Cl_2 (10 mL) was cooled to −78 °C. DIBAL (2.4 mmol, 1.0 M in hexanes) was added over 2 h, and the reaction was stirred until consumption of **9** was observed by TLC. Pyridine (6.0 mmol), DMAP (2.4 mmol, in 2 mL CH_2Cl_2), and Ac_2O (8.0 mmol) were added sequentially, and the reaction was stirred at −78 °C to room temperature for 10 h. Saturated sodium bicarbonate (5 mL) and saturated Rochelle's salt (10 mL) were added, and the reaction was stirred rapidly for 45 min. The crude mixture was extracted with dichloromethane, washed with cold 1 M sodium bisulfate (5 mL), sodium bicarbonate (5 mL), water, and brine. After being dried over Na_2SO_4, the reaction mixture was concentrated at reduced pressure. Purification by silica gel column chromatography afforded the desired product.

Phenoxy(pyridin-2-yl)methyl acetate ***10a***. Flash chromatography (25% ethyl acetate/hexanes) gave **10a** as a colorless oil (0.309 g, 58% yield). R_f = 0.25 (30% ethyl acetate/hexanes); IR (neat) ν_{max} 3065, 2955, 1751, 1589, 1493, 1439, 1371, 1240, 1206, 1105, 1071, 1013, 995, 962 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.67 (1H, ddd, J = 1.0, 1.5, 4.5 Hz), 7.78 (1H, ddd, J = 1.5, 7.5, 7.5 Hz), 7.70 (1H, ddd, J = 1.0, 1.0, 8.0 Hz), 7.39 (1H, s), 7.28−7.34 (3H, m), 7.94−7.12 (3H, m), 2.14 (3H, s);

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^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8, 156.1, 155.6, 149.7, 137.2, 129.0, 124.4, 123.2, 121.4, 117.1, 94.9, 21.2; MS (ESI$^+$) m/z 266 (9, [M + Na]$^+$), 266 (9), 184 (100), 156 (27), 108 (10); HRMS (ESI$^+$) calcd for [M + Na]$^+$ $C_{14}H_{13}NO_3Na$ 266.0787; found 266.0777.

(2-Methylphenoxy)(pyridin-2-yl)methyl acetate ***10b***. Flash chromatography (25% ethyl acetate/hexanes) gave **10b** as a colorless oil (0.345 g, 67% yield). R_f = 0.22 (30% ethyl acetate/hexanes); IR (neat) ν_{max} 3060, 3024, 2951, 1745, 1593, 1496, 1439, 1370, 1300, 1242, 1215, 1184, 1126, 1068, 995, 957, 752, 714 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (1H, ddd, J = 1.0, 1.5, 5.0 Hz), 7.77 (1H, ddd, J = 1.5, 7.5, 7.5 Hz), 7.72 (1H, ddd, J = 1.0, 1.0, 7.5 Hz), 7.36 (1H, s), 7.30 (1H, ddd, J = 1.5, 5.0, 7.5 Hz), 7.12−7.18 (2H, m), 7.06 (1H, d, J = 7.5 Hz), 6.97 (1H, ddd, J = 1.0, 7.5, 7.5 Hz), 2.29 (3H, s), 2.11 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.7, 155.9, 154.4, 149.6, 137.1, 131.2, 128.4, 127.1, 124.2, 123.1, 121.2, 115.4, 95.3, 21.2, 16.5; MS (ESI$^+$) m/z 280 (6, (M + Na)$^+$), 198 (100), 183 (10), 170 (24), 108 (7); HRMS (ESI$^+$) calcd for [M + Na]$^+$ $C_{15}H_{15}NO_3Na$ 280.0944; found 280.0932.

(3-Methylphenoxy)(pyridin-2-yl)methyl acetate ***10c***. Flash chromatography (25% ethyl acetate/hexanes) gave **10c** as a colorless oil (0.319 g, 62% yield). R_f = 0.23 (30% ethyl acetate/hexanes); IR (neat) ν_{max} 3030, 2924, 1740, 1589, 1506, 1439, 1368, 1236, 1205, 1179, 1105, 1009, 995, 954, 817, 773 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (1H, ddd, J = 1.0, 1.5, 5.0 Hz), 7.78 (1H, ddd, J = 1.5, 7.5, 7.5 Hz), 7.69 (1H, ddd, J = 1.0, 1.0, 7.5 Hz), 7.37 (1H, s), 7.32 (1H, ddd, J = 1.0, 5.0, 7.5 Hz), 7.18 (1H, dd, J = 8.0, 8.0 Hz), 6.84−6.94 (3H, m), 2.37 (3H, s), 2.16 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8, 156.1, 155.7, 149.6, 139.9, 137.1, 129.5, 124.3, 124.0, 121.3, 117.9, 113.8, 94.9, 21.5, 21.2; MS (EI) m/z 257 (2, M$^+$), 214 (2), 198 (8), 183 (2), 170 (2), 150 (22), 108 (100), 91 (2), 78 (8), 65 (2), 51 (2); HRMS (EI) calcd for [M]$^+$ $C_{15}H_{15}NO_3$ 257.1052; found 257.1051.

(4-Methylphenoxy)(pyridin-2-yl)methyl acetate ***10d***. Flash chromatography (25% ethyl acetate/hexanes) gave **10d** as a colorless oil (0.339 g, 66% yield). R_f = 0.23 (30% ethyl acetate/hexanes); IR (neat) ν_{max} 3061, 3030, 2924, 1748, 1593, 1510, 1439, 1371, 1240, 1204, 1179, 1105, 1011, 995, 955, 773 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (1H, ddd, J = 1.0, 2.0, 5.0 Hz), 7.77 (1H, ddd, J = 2.0, 8.0, 8.0 Hz), 7.68 (1H, ddd, J = 1.0, 1.0, 8.0 Hz), 7.34 (1H, s) 7.31 (1H, ddd, J = 1.0, 5.0, 7.5 Hz), 7.10 (2H, d, J = 9.0 Hz), 6.98 (2H, d, J = 9.0 Hz), 2.14 (3H, s), 2.05 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 155.7, 154.0, 149.7, 137.2, 132.7, 130.3, 124.3, 121.4, 117.2, 95.3, 21.2, 20.8; MS (EI) m/z 257 (2, M$^+$), 214 (4), 198 (20), 170 (3), 150 (15), 108 (100), 91 (5), 78 (10), 65 (3), 51 (7); HRMS (EI) calcd for [M]$^+$ $C_{15}H_{15}NO_3$ 257.1052; found 257.1049.

3-Chlorophenoxy)(pyridin-2-yl)methyl acetate ***10f***. Flash chromatography (20% ethyl acetate/hexanes) gave **10f** as a colorless oil (0.072 g, 13% yield). R_f = 0.19 (30% ethyl acetate/hexanes); IR (neat) ν_{max} 3068, 3024, 2930, 1751, 1593, 1474, 1439, 1370, 1236, 1206, 1103, 1076, 1012, 995, 943, 889, 771 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (1H, ddd, J = 1.0, 1.5, 5.0 Hz), 7.79 (1H, ddd, J = 2.0, 4.5, 4.5 Hz), 7.66 (1H, ddd, J = 1.0, 1.0, 8.0 Hz), 7.32−7.35 (2H, m), 7.22 (1H, dd, J = 8.0, 8.0 Hz), 7.11 (1H, dd, J = 2.0, 2.0 Hz), 7.04 (1H, ddd, J = 1.0, 2.0, 8.0 Hz), 6.99 (1H, ddd, J = 1.0, 2.5, 8.0 Hz), 2.16 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.7, 156.8, 155.2, 149.8, 137.3, 135.2, 130.6, 124.6, 123.5, 121.3, 118.1, 115.2, 94.9, 21.2; MS (ESI$^+$) m/z 277.1 (5, [M]$^+$), 218 (6), 190 (1), 183 (31), 170 (7) 154 (2), 150 (7), 128 (39) 108 (100), 78 (6); HRMS (ESI$^+$) calcd for [M]$^+$ $C_{14}H_{12}NO_3Cl$ 277.0506; found 277.0502.

4-Chlorophenoxy)(pyridin-2-yl)methyl acetate ***10g***. Flash chromatography (30% ethyl acetate/hexanes) gave **10g** as a colorless oil (0.244 g, 44% yield). R_f = 0.28 (40% ethyl acetate/hexanes); IR (thin film) ν_{max} 3094, 3063, 3021, 2994, 1748, 1593, 1489, 1439, 1370, 1242, 1204, 1173, 1072, 991, 964, 899 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (1H, ddd, J = 1.0, 2.0, 5.0 Hz), 7.78 (1H, ddd, J = 2.0, 8.0, 8.0 Hz), 7.66 (1H, ddd, J = 1.0, 1.0, 8.0 Hz), 7.30−7.34 (2H, m), 7.25 (2H, ddd, J = 2.5, 2.5, 9.0 Hz), 7.04 (2H, ddd, J = 2.5, 2.5, 9.0 Hz), 2.14 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.5, 155.1, 154.6, 149.5, 137.1, 129.6, 128.1, 124.4, 121.1, 118.4, 94.9, 21.0; MS (ESI$^+$) m/z 300 (15, [M + Na]$^+$), 218 (100), 190 (22), 183 (31), 154 (5), 108 (4); HRMS (ESI$^+$) calcd for [M + Na]$^+$ $C_{14}H_{12}NO_3ClNa$ 300.0404; found 300.0397.

(2-Methoxyphenoxy)(pyridin-2-yl)methyl acetate ***10h***. Flash chromatography (40% ethyl acetate/hexanes) gave **10h** as a colorless oil (0.300 g, 55% yield). R_f = 0.16 (40% ethyl acetate/hexanes); IR (thin film) ν_{max} 3067, 3013, 2943, 2839, 1748, 1593, 1574, 1439, 1370, 1261, 1231, 1204, 1177, 1126, 957, 887, 748 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (1H, ddd, J = 1.5, 1.5, 4.5 Hz), 7.72−7.79 (2H, m,), 7.34 (1H, s), 7.29 (1H, ddd, J = 2.5, 5.0, 8.0 Hz), 7.14 (1H, dd, J =1.5, 8.0 Hz), 7.06 (1H, ddd, 1.5, 7.5, 7.5 Hz), 6.92 (1H, dd, J = 1.0, 8.0 Hz), 6.88 (1H, ddd, J = 1.5, 7.5, 7.5 Hz), 3.84 (3H, s), 2.10 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8, 155.8, 151.1, 149.5, 145.2, 137.0, 124.8, 124.2, 121.6, 120.9, 120.1, 112.6, 96.0, 56.0, 21.2; MS (ESI$^+$) m/z 296 (13, [M + Na]$^+$), 214 (100), 199 (7), 182 (11), 170 (4), 156 (5), 121 (5), 110 (12), 108 (9), 92 (15); HRMS(ESI) calcd for [M + Na]$^+$ $C_{15}H_{15}NO_4Na$ 296.0893; found 296.0902.

(3-Methoxyphenoxy)(pyridin-2-yl)methyl acetate ***10i***. Flash chromatography (40% ethyl acetate/hexanes) gave **10i** as a colorless oil (0.257 g, 47% yield). R_f = 0.19 (40% ethyl acetate/hexanes); IR (thin film) ν_{max} 3067, 3009, 2940, 2835, 1748, 1589, 1454, 1439, 1370, 1285, 1265, 1219, 1011, 857, 841 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (1H, ddd, J = 1.0, 2.0, 5.0 Hz), 7.79 (1H, ddd, J = 2.0, 8.0, 8.0 Hz), 7.68 (1H, ddd, J = 1.0, 1.0, 8.0 Hz), 7.37 (1H, s), 7.32 (1H, ddd, J = 1.0, 5.0, 8.0 Hz), 7.20 (1H, dddd, J = 2.0, 2.0, 8.5, 8.5 Hz), 6.66−6.70 (2H, m), 6.62 (1H, ddd, J = 1.0, 2.5, 8.5 Hz), 3.80 (3H, s), 2.18 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.7, 161.1, 157.2, 155.5, 149.7, 137.2, 130.3, 124.4, 121.4, 109.1, 108.8, 103.3, 94.8, 55.5, 21.2; MS (EI) m/z 273 (2, M$^+$), 214 (4), 183 (1), 166 (19), 124 (100), 108 (16), 94 (6), 78 (3), 52 (2); HRMS (EI) calcd for [M]$^+$ $C_{15}H_{15}NO_4$ 273.1001; found 273.1025.

(4-Methoxyphenoxy)(pyridin-2-yl)methyl acetate ***10j***. Flash chromatography (40% ethyl acetate/hexanes) gave **10j** as a white solid (0.389 g, 71% yield). R_f = 0.19 (40% ethyl acetate/hexanes); mp 45−46 °C (hexanes, ethyl acetate); IR (thin film, CH_2Cl_2) ν_{max} 3063, 3050, 2994, 2963, 2835, 1740, 1593, 1508, 1424, 1366, 1289, 1238, 1188, 1076, 995, 950, 883, 822, 787, 741 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (1H, ddd, J = 1.0, 1.5, 5.0 Hz), 7.78 (1H, ddd, J = 2.0, 8.0, 8.0 Hz), 7.68 (1H, ddd, J = 1.0, 1.0, 8.0 Hz), 7.32 (1H, ddd, J = 1.0, 5.0, 7.5 Hz), 7.26 (1H, s), 7.05 (2H, d, J = 9.0 Hz), 6.83 (2H, d, J = 9.0 Hz), 3.77 (3H, s), 2.13 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 155.83, 155.80, 150.1, 149.7, 137.2, 124.4, 121.4, 119.0, 114.9, 96.1, 55.8, 21.2; MS (EI) m/z 273 (0.3, M$^+$), 214 (3), 199 (0.7), 186 (3), 166 (8), 124 (100), 108 (27), 95 (1), 78 (4), 65 (0.7), 51 (1); HRMS (EI) calcd for [M]$^+$ $C_{15}H_{15}NO_4$ 273.1001; found 273.0995.

(3,5-Dimethylphenoxy)(pyridin-2-yl)methyl acetate ***10l***. Flash chromatography (25% ethyl acetate/hexanes) gave **10l** as a colorless oil (0.257 g, 63% yield). R_f = 0.31 (40% ethyl acetate/hexanes); IR (thin film) ν_{max} 3055, 3017, 2947, 2862, 1740, 1613, 1593, 1474, 1439, 1370, 1296, 1219, 1150, 1107, 1080, 1011, 995, 957, 837, 775, 748, 683 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (1H, ddd, J = 1.0, 2.0, 5.0 Hz), 7.77 (1H, ddd, J = 1.0, 7.5, 7.5 Hz), 7.68 (1H, ddd, J = 1.0, 1.0, 8.0 Hz), 7.35 (1H, s), 7.30 (1H, ddd, J = 1.0, 4.5, 7.5 Hz), 6.76 (3H, m), 2.28 (6H, s), 2.14 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 156.2, 155.8, 149.7, 139.6, 137.2, 125.0, 124.3, 121.3, 114.7, 95.0, 21.6, 21.3; MS (ESI$^+$) m/z 272 (60, ([M + H]$^+$), 230(20), 212 (100), 190 (22), 183 (31), 154 (5), 108 (4); HRMS (ESI$^+$) calcd for [M + H]$^+$ $C_{16}H_{18}NO_3$ 272.1287; found 272.1292.

General Procedure for Oxa-Povarov Reaction. A solution of **10** (1.0 mmol) and dienophile (1.1 to 4.0 mmol) in CH_2Cl_2 (6.6 mL) was cooled to −78 °C. $SnCl_4$ (2.0 mmol, 1 M in CH_2Cl_2) was added slowly, and the reaction was warmed to −15 °C and then stirred for 24 h under an argon atmosphere. The reaction was then quenched with saturated $NaHCO_3$ (2 mL) and warmed to room temperature. The reaction was extracted with CH_2Cl_2, and the combined extracts were washed with water and brine. After drying over Na_2SO_4 and evaporation of the solvent at reduced pressure, the products were purified by silica gel column chromatography.

Chroman ***11a***. Flash chromatography (20% ethyl acetate/hexanes) gave **11a** as a white solid (0.213 g, 77% yield). R_f = 0.19 (10% ethyl acetate/hexanes); mp 83−85 °C (hexanes, ethyl acetate); IR (thin film, CH_2Cl_2) ν_{max} 3063, 2955, 2870, 1589, 1489, 1435, 1366, 1335, 1250, 1235, 1111, 1080, 995, 748 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58

(1H, ddd, J = 1.0, 1.5, 5.0 Hz), 7.75 (1H, ddd, J = 1.5, 7.5, 7.5 Hz), 7.69 (1H, d, J = 7.0 Hz), 7.16−7.22 (2H, m), 7.10 (1H, ddd, J = 2.0, 8.0, 8.0 Hz), 6.91−6.99 (2H, m), 4.92 (1H, d, J = 4.0 Hz), 3.09 (1H, d, J = 9.0 Hz), 2.58 (1H, dd, J = 3.0, 8.5 Hz), 2.19 (1H, d, J = 4.5 Hz), 1.79 (1H, d, J = 3.0), 1.59 (1H, tt, J = 4.0, 12.0 Hz), 1.28−1.49 (3H, m), 1.19 (1H, tt, J = 3.0, 8.5 Hz), 0.84 (1H, d, J = 10.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7, 156.7, 149.2, 136.6, 130.0, 129.7, 126.8, 122.2, 122.1, 120.9, 117.6, 80.6, 48.3, 47.9, 45.4, 37.1, 34.6, 31.3, 28.4; MS (ESI$^+$) m/z 278 (100, [M + H]$^+$); HRMS (ESI$^+$) calcd for [M + H]$^+$ $C_{19}H_{20}NO$ 278.1539; found 278.1547.

11b. Flash chromatography (15% ethyl acetate/hexanes) gave **11b** as a white solid (0.184 g, 64% yield). Additional flash chromatography (10% to 25% ethyl acetate/hexanes gradient) afforded pure samples of **11b**-*endo* and **11b**-*exo*.

2-((2S,4R*)-4-Phenylchroman-2-yl)pyridine* ***11b****-endo.* R_f = 0.10 (10% ethyl acetate/hexanes); mp 140−141 °C (ether); IR (thin film, CH_2Cl_2) ν_{max} 3024, 2916, 2870, 1574, 1481, 1450, 1435, 1234, 1111, 1072, 995, 918, 756, 702 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (1H, ddd, J = 1.0, 2.0, 5.0 Hz), 7.76 (1H, ddd, J = 2.0, 7.5, 7.5 Hz), 7.67 (1H, d, J = 8.0 Hz), 7.30 (2H, tt, J = 1.0, 6.5 Hz), 7.28−7.35 (4H, m), 7.15 (1H, ddd, J = 1.0, 2.5, 6.0 Hz), 7.01 (1H, d, J = 8.0 Hz), 6.80−6.82 (2H, m), 5.33 (1H, dd, J = 2.0, 11.5 Hz), 4.40 (1H, dd, J = 5.5, 12.0 Hz), 2.70 (1H, ddd, J = 2.0, 5.5, 13.5 Hz), 2.16 (1H, ddd, J = 11.5, 12.0, 13.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.6, 155.2, 149.2, 144.7, 137.1, 130.1, 128.8, 128.0, 126.9, 126.1, 122.9, 121.0, 120.3, 117.2, 78.8, 43.4, 39.6; MS (ESI$^+$) m/z 288 (100, [M + H]$^+$), 183 (7), 106 (5); HRMS (ESI$^+$) calcd for [M + H]$^+$ $C_{20}H_{18}NO$ 288.1382; found 288.1380.

2-((2R,4R*)-4-Phenylchroman-2-yl)pyridine* ***11b****-exo.* R_f = 0.16 (10% ethyl acetate/hexanes); mp 116−117 °C (ether); IR (thin film, CH_2Cl_2) ν_{max} 3059, 3024, 2920, 1589, 1497, 1435, 1343, 1238, 1126, 1073, 995, 918, 756, 702 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (1H, d, J = 5.0 Hz), 7.69 (1H, ddd, J = 2.0, 8.0, 8.0 Hz), 7.54 (1H, d, J = 8.0 Hz), 7.30 (2H, t, J = 7.5 Hz), 7.12−7.24 (5H, m), 7.05 (1H, dd, J = 1.0, 9.0 Hz), 6.95 (1H, dd, J = 1.5, 7.5 Hz), 6.87 (1H, ddd, J = 1.0, 7.0, 7.0 Hz), 5.20 (1H, dd, J = 3.5, 9.0 Hz), 4.15 (1H, t, J = 5.0 Hz), 2.44−2.56 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.9, 154.9, 149.3, 145.8, 136.9, 130.9, 128.9, 128.7, 128.3, 126.7, 123.9, 122.7, 120.9, 120.8, 117.2, 74.5, 39.9, 36.5; MS (ESI$^+$) m/z 288 (100, [M + H]$^+$); HRMS (ESI$^+$) calcd for [M + H]$^+$ $C_{20}H_{18}NO$ 288.1388; found 288.1384.

2-((2S,4R*)-4-(p-Tolyl)chroman-2-yl)pyridine* ***11c****-endo.* Flash chromatography (15% ethyl acetate/hexanes) gave **11c** as a white solid (0.060 g, 20% yield). Further purification by flash chromatography (10% ethyl acetate/hexanes) afforded pure **11c**-*endo*. R_f = 0.12 (10% ethyl acetate/hexanes); mp 98−99 °C (ethyl acetate/hexanes); IR (thin film, CH_2Cl_2) ν_{max} 3059, 3024, 2920, 2862, 1589, 1474, 1339, 1273, 1242, 1219, 1123, 1072, 1049, 995, 883, 814, 760, 702 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (1H, ddd, J = 1.0, 2.0, 5.0 Hz), 7.76 (1H, ddd, J = 2.0, 7.5, 7.5 Hz), 7.67 (1H, d, J = 8.0 Hz), 7.22 (1H, ddd, J = 1.0, 4.5, 7.5 Hz), 7.08−7.16 (4H, m), 6.98−7.04 (2H, m), 6.80 (1H, d, J = 4.5 Hz.), 5.33 (1H, dd, J = 2.0, 11.5 Hz), 4.36 (1H, dd, J = 6.0, 12.5 Hz), 2.66 (1H, ddd, J = 2.0, 6.0, 13.5 Hz), 2.33 (3H, s), 2.15 (1H, ddd, J = 11.5, 12.5, 13.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7, 155.2, 149.2, 144.7, 137.1, 130.1, 128.8, 128.0, 126.9, 126.1, 122.9, 121.0, 120.3, 117.2, 78.8, 43.4, 39.6; MS (EI) m/z 301 (8, M$^+$), 282 (4), 197 (100), 165 (3), 152 (2), 93 (4); HRMS (EI) calcd for [M]$^+$ $C_{21}H_{19}NO$ 301.1467; found 301.1470.

11d. Flash chromatography (15% ethyl acetate/hexanes) gave **11d** as a white solid (0.173 g, 54% yield). Further purification by flash chromatography (10% ethyl acetate/hexanes) afforded pure **11d**-*endo* and **11d**-*exo*.

2-((2S,4R*)-4-(4-Chlorophenyl)chroman-2-yl)pyridine* ***11d****-endo.* R_f = 0.11 (10% ethyl acetate/hexanes); mp 124−125 °C (ether); IR (thin film, CH_2Cl_2) ν_{max} 3061, 3026, 1593, 1582, 1485, 1452, 1435, 1292, 1236, 1113, 993, 914, 829, 754 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (1H, ddd, J = 1.0, 1.5, 5.0 Hz), 7.77 (1H, ddd, J = 1.5, 8.0, 8.0 Hz), 7.67 (1H, d, J = 8.0 Hz), 7.17−7.28 (3H, m), 7.12−7.19 (3H, m), 7.00 (1H, dd, J = 1.0, 8.0 Hz), 6.83 (1H, ddd, J = 1.5, 8.0, 8.0 Hz), 6.76 (1H, ddd, J = 1.5, 1.5, 7.5 Hz), 5.31 (1H, dd, J = 1.5, 11.5 Hz), 4.39 (1H, dd, J = 5.5, 12.0 Hz), 2.68 (1H, ddd, J = 2.0, 6.0, 13.5 Hz), 2.12 (1H, ddd, J = 11.5, 12.0, 13.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.4, 155.2, 149.3, 143.2, 137.2, 132.6, 130.1, 129.9, 129.0, 128.2, 125.5, 123.0, 121.1, 120.3, 117.3, 78.6, 42.8, 39.5; MS (ESI$^+$) m/z 322 (100, [M + H]$^+$), 183 (4); HRMS (ESI$^+$) calcd for [M + H]$^+$ $C_{20}H_{17}ClNO$ 322.0999; found 322.0999.

2-((2R,4R*)-4-(4-Chlorophenyl)chroman-2-yl)pyridine* ***11d****-exo.* R_f = 0.21 (10% ethyl acetate/hexanes); mp 94−95 °C (ether); IR (thin film) ν_{max} 3063, 3021, 2955, 2870, 1582, 1485, 1454, 1358, 1227, 1107, 984, 752 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (1H, ddd, J = 1.0, 2.0, 5.0 Hz), 7.70 (1H, ddd, J = 1.5, 7.5, 7.5 Hz), 7.67 (1H, d, J = 7.5 Hz), 7.27 (2H, d, J = 8.5 Hz) 7.18−7.24 (2H, m), 7.04−7.08 (3H, m), 6.86−6.92 (2H, m), 5.16 (1H, dd, J = 3.0, 9.0 Hz), 4.13 (1H, t, J = 5.0 Hz), 2.40−2.55 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7, 154.9, 149.3, 144.3, 137.0, 132.6, 130.8, 130.3, 128.9, 128.6, 123.4, 122.8, 121.0, 120.8, 117.4, 74.4, 39.4, 36.5; MS (ESI$^+$) m/z 322 (100, [M + H]$^+$); HRMS (ESI$^+$) calcd for [M + H]$^+$ $C_{20}H_{17}ClNO$ 322.0999; found 322.0994.

Chroman ***11e.*** Flash chromatography (10% ethyl acetate/hexanes) gave **11e** as a white solid (0.105 g, 42% yield). R_f = 0.15 (10% ethyl acetate/hexanes); IR (thin film) ν_{max} 3063, 3021, 2955, 2870, 1582, 1485, 1454, 1358, 1227, 1107, 984, 752 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (1H, ddd, J = 1.0, 1.5, 3.5 Hz), 7.76 (1H, ddd, J = 1.0, 8.0, 8.0 Hz), 7.69 (1H, d, J = 7.5 Hz), 7.18−7.22 (2H, m), 7.12 (1H, ddd, J = 1.5, 7.5, 7.5 Hz), 6.92−6.98 (2H, m), 5.25 (1H, d, J = 2.5 Hz), 3.58 (1H, t, J = 7.5 Hz), 2.85−3.00 (1H, m), 2.10−2.20 (1H, m), 1.80−1.88 (1H, m), 1.42−1.58 (3H, m), 1.20−1.30 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7, 155.0, 149.0, 136.7, 129.4, 127.9, 127.0, 122.3, 121.8, 120.4, 117.4, 78.4, 43.6, 39.6, 35.0, 23.8, 23.5; MS (ESI$^+$) m/z 252 (100, [M + H]$^+$); HRMS (ESI$^+$) calcd for [M + H]$^+$ $C_{17}H_{18}NO$ 252.1382; found 252.1383.

Chroman ***11f.*** Flash chromatography (10% ethyl acetate/hexanes) gave **11f** as a white solid (0.067 g, 25% yield). R_f = 0.16 (10% ethyl acetate/hexanes); IR (thin film) ν_{max} 3060, 3021, 2955, 2870, 1589, 1485, 1459, 1358, 1227, 1105, 984, 752 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (1H, ddd, J = 1.0, 1.5, 3.5 Hz), 7.74 (1H, ddd, J = 1.0, 8.0, 8.0 Hz), 7.66 (1H, d, J = 7.5 Hz), 7.14−7.22 (2H, m), 7.02 (1H, d, J = 7.5 Hz), 6.93−6.98 (2H, m), 5.24 (1H, d, J = 2.0 Hz), 3.46 (1H, d, J = 3.0 Hz), 2.48−2.50 (2H, m), 1.76 (1H, tt, J = 4.0, 13.0 Hz), 1.55 (1H, d, J = 2.5 Hz), 1.42 (1H, dd, J = 3.5, 11.0 Hz), 1.08−1.21 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7, 156.4, 148.5, 137.1, 129.7, 127.3, 122.7, 121.3, 121.2, 120.4, 115.7, 80.9, 38.1, 35.5, 28.5, 25.5, 20.6, 20.1; MS (ESI$^+$) m/z 266 (100, [M + H]$^+$); HRMS (ESI$^+$) calcd for [M + H]$^+$ $C_{18}H_{20}NO$ 266.1522; found 266.1519.

Chroman ***11g.*** Flash chromatography (10% ethyl acetate/hexanes) gave **11g** as a white solid (0.070 g, 27% yield). R_f = 0.14 (10% ethyl acetate/hexanes); mp 94−95 °C (ether); IR (thin film, CH_2Cl_2) ν_{max} 3140, 3063, 3028, 2932, 2909, 2862, 2839, 1651, 1593, 1578, 1489, 1454, 1435, 1354, 1304, 1265, 1111, 1076, 1049, 995, 752, 733 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (1H, ddd, J = 1.0, 2.0, 5.0 Hz), 7.75 (1H, ddd, J = 2.0, 7.5, 7.5 Hz), 7.69 (1H, d, J = 7.5 Hz), 7.30 (1H, d, J = 7.5 Hz), 7.20 (1H, ddd, J = 1.5, 5.0, 7.5 Hz.), 7.13 (1H, dddd, J = 1.0, 1.5, 7.5, 7.5 Hz), 6.95 (2H, d, J = 7.5 Hz), 6.22 (1H, dddd, J = 2.0, 5.5, 10.0, 12.0 Hz), 5.76−5.82 (1H, m), 5.27 (1H, d, J = 2.0 Hz), 3.83 (1H, t, J = 5.5 Hz), 2.60−2.64 (1H, m), 1.90−1.98 (2H, m), 1.34−1.46 (1H, m), 1.20 (1H, dd, J = 3.0, 13.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 153.1, 149.2, 136.4, 128.9, 128.4, 128.0, 127.1, 125.9, 122.3, 121.4, 121.0, 117.2, 80.6, 36.1, 25.6, 25.2, 17.1; MS (EI) m/z 263 (10, M$^+$), 262 (12), 244 (1), 234 (3), 183 (100), 155 (18), 130 (3), 117 (4), 93 (8), 78(2); HRMS (EI) calcd for [M]$^+$ $C_{18}H_{17}NO$ 263.1310; found 263.1311.

Chroman ***11h.*** Flash chromatography (10% ethyl acetate/hexanes) gave **11h** as a white solid (0.044 g, 15% yield). R_f = 0.15 (10% ethyl acetate/hexanes); isolated as a colorless oil in 15% yield; IR (thin film, CH_2Cl_2) ν_{max} 3059, 3009, 2936, 2889, 1589, 1578, 1485, 1474, 1434, 1358, 1308, 1227, 1208, 1184, 1115, 1084, 961, 903, 764, 748 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (1H, ddd, J = 1.0, 1.5, 5.0 Hz), 7.75−7.83 (2H, m), 7.55 (1H, d, J = 7.5 Hz), 7.45 (1H, d, J = 7.5 Hz), 7.25 (1H, ddd, J = 1.5, 5.0, 9.0 Hz), 7.17 (1H, dd, J = 7.5, 7.5 Hz), 7.08−7.13 (2H, m), 7.04 (1H, d, J = 7.5 Hz), 6.91−6.98 (2H, m), 5.40 (1H, d, J = 2.5 Hz), 4.64 (1H, d, J = 8.5 Hz), 3.59−3.67 (1H, m), 3.05 (1H, dd, J = 11.0, 16.0 Hz), 2.44 (1H, dd, J = 8.0, 15.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.9, 154.4, 149.2, 145.8, 142.5, 136.9, 129.6, 127.5, 127.4,

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126.8, 125.2, 125.1, 122.6, 122.0, 120.5, 117.9, 78.2, 44.8, 44.7, 30.5; MS (ESI$^+$) m/z 300 (100, $[M + H]^+$), 124 (6); HRMS (ESI$^+$) calcd for $[M + H]^+$ $C_{21}H_{18}NO$ 300.1388; found 300.1391.

12b. Flash chromatography (15% ethyl acetate/hexanes) gave **12b** as a white solid (0.198 g, 66% yield). Further purification by flash chromatography (10% to 20% ethyl acetate/hexanes) afforded pure **12b**-*endo* and **12b**-*exo*.

2-((2S,4R*)-8-Methoxy-4-phenylchroman-2-yl)pyridine* ***12b***-*endo*. mp 136−137 °C (hexanes/ethyl acetate); IR (thin film, CH_2Cl_2) ν_{max} 3063, 3013, 2963, 2924, 1589, 1466, 1435, 1335, 1300, 1261, 1211, 1180, 1084, 1045, 995, 914, 787, 768, 702, cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (1H, ddd, J = 1.0, 1.5, 5.0 Hz), 7.71−7.78 (2H, m), 7.28 (2H, dddd, J = 1.5, 1.5, 7.5, 7.5 Hz), 7.18−7.23 (4H, m), 7.03 (1H, ddd, J = 1.0, 1.0, 7.0 Hz), 6.71 (1H, dd, J = 8.0, 8.0 Hz), 6.64 (1H, d, J = 8.0 Hz), 5.33 (1H, dd, J = 1.5, 11.5 Hz), 4.40 (1H, dd, J = 6.0, 12.0 Hz), 2.75 (1H, ddd, J = 2.0, 6.0, 13.5 Hz), 2.28 (3H, s), 2.10 (1H, ddd, J = 11.5, 12.0, 13.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.1, 153.2, 149.1, 144.9, 137.1, 129.1, 128.8, 128.7, 127.7, 126.8, 126.2, 125.6, 122.7, 120.2, 120.0, 78.5, 43.6, 39.7, 16.5; MS (EI) m/z 301 (4, $[M]^+$), 197 (100), 169 (26), 165 (4), 152 (3), 115 (1), 106 (3), 93 (4); HRMS (EI) calcd for $[M]^+$ $C_{21}H_{19}NO$ 301.1467; found 301.1470.

2-((2R,4R*)-8-Methoxy-4-phenylchroman-2-yl)pyridine* ***12b***-*exo*. mp 115−117 °C (hexanes/ethyl acetate); IR (thin film, CH_2Cl_2) ν_{max} 3059, 3024, 2934, 1589, 1483, 1435, 1343, 1238, 1126, 1073, 1030, 995, 922, 813, 759, 702 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (1H, ddd, J = 1.0, 2.0, 5.0 Hz), 7.71 (1H, ddd, J = 2.0, 7.5, 7.5 Hz), 7.58 (1H, d, J = 8.0 Hz), 7.29 (2H, dd, J = 7.5, 7.5 Hz), 7.17−7.22 (2H, m), 7.14 (2H, d, J = 7.5 Hz), 7.08 (1H, dd, J =2.5, 6.5 Hz), 6.78−6.83 (2H, m), 5.21 (1H, dd, J = 3.0, 9.5 Hz), 4.16 (1H, t, J = 5.0 Hz), 2.41−2.57 (2H, m), 2.36 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4, 153.0, 149.1, 146.0, 136.9, 129.4, 129.0, 128.6, 128.5, 126.6, 126.2, 123.3, 122.5, 120.5, 120.2, 74.4, 40.1, 36.6, 16.5; MS (ESI$^+$) m/z 302 (100, $[M + H]^+$); HRMS (ESI$^+$) calcd for $[M + H]^+$ $C_{21}H_{20}NO$ 302.1545; found 302.1555.

12d. Flash chromatography (15% ethyl acetate/hexanes) gave **12d** as a white solid (0.179 g, 59% yield). Further purification by flash chromatography (10% to 30% ethyl acetate/hexanes) afforded pure **12d**-*endo* and **12d**-*exo*.

2-((2S,4R*)-6-Methyl-4-phenylchroman-2-yl)pyridine* ***12d***-*endo*. mp 146−148 °C (hexanes/ethyl acetate); IR (thin film, CH_2Cl_2) ν_{max} 3059, 3024, 2920, 2862, 1589, 1474, 1339, 1273, 1242, 1219, 1123, 1072, 1049, 995, 883, 814, 760, 702 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (1H, ddd, J = 1.0, 1.5, 5.0 Hz), 7.75 (1H, ddd, J = 2.0, 8.0, 8.0 Hz), 7.66 (1H, ddd, J = 1.5, 1.5, 8.0 Hz), 7.30 (2H, dddd, J = 1.5, 1.5, 7.5, 7.5 Hz), 7.18−7.26 (4H, m), 6.96 (1H, ddd, J = 1.0, 1.5, 7.5 Hz), 6.90 (1H, d, J = 8.5 Hz), 6.61 (1H, d, J = 0.5 Hz), 5.28 (1H, dd, J = 1.0, 11.5 Hz), 4.36 (1H, dd, J = 5.5, 12.0), 2.67 (1H, ddd, J = 2.0, 6.0, 13.5 Hz), 2.09−2.19 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7, 153.1, 149.2, 144.8, 137.1, 130.3, 130.1, 128.8, 128.7, 128.6, 126.8, 125.7, 122.8, 120.3, 117.0, 78.8, 43.5, 39.9, 20.8; MS (EI) m/z 301 (6, M$^+$), 282 (2), 197 (100), 169 (23), 165 (3), 152 (2), 93 (4); HRMS (EI) calcd for $[M]^+$ $C_{21}H_{19}NO$ 301.1467; found 301.1472.

2-((2R,4R*)-6-Methyl-4-phenylchroman-2-yl)pyridine* ***12d***-*exo*. mp 93−96 °C (hexanes/ethyl acetate); IR (thin film, CH_2Cl_2) ν_{max} 3059, 3024, 2920, 1589, 1497, 1435, 1343, 1238, 1126, 1073, 1030, 995, 922, 813, 759, 702 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (1H, ddd, J = 1.0, 2.0, 5.0 Hz), 7.69 (1H, ddd, J = 2.0, 8.0, 8.0 Hz), 7.54 (1H, ddd, J = 1.0, 1.0, 8.0 Hz), 7.30 (2H, dddd, J = 1.0, 1.0, 7.5, 7.5 Hz), 7.14−7.23 (4H, m), 7.02 (1H, dd, J = 2.0, 8.5 Hz), 6.95 (1H, d, J = 8.0 Hz), 6.76 (1H, d, J = 1.0 Hz), 5.17 (1H, dd, J = 3.5, 5.5 Hz), 4.12 (1H, t, J = 5.0 Hz), 2.42−2.54 (2H, m), 2.21 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0, 152.8, 149.2, 145.9, 136.9, 131.0, 130.0, 129.0, 128.9, 128.6, 126.6, 123.4, 122.6, 120.9, 116.9, 74.4, 40.0, 36.6, 20.7; MS (EI) m/z 301 (100, M$^+$), 282 (27), 195 (14), 178 (2), 165 (6), 152 (5), 115 (2), 93 (65); HRMS (EI) calcd for $[M]^+$ $C_{21}H_{19}NO$ 301.1467; found 301.1466.

12g. Flash chromatography (15% ethyl acetate/hexanes) gave **12g** as a white solid (0.089 g, 28% yield). Further purification by flash chromatography (10% to 20% ethyl acetate/hexanes) afforded pure **12g**-*endo* and **12g**-*exo*.

2-((2S,4R*)-6-Chloro-4-phenylchroman-2-yl)pyridine* ***12g***-*endo*. mp 116−117 °C (hexanes/ethyl acetate); IR (thin film, CH_2Cl_2) ν_{max} 3059, 3024, 2920, 1589, 1497, 1435, 1343, 1304, 1238, 1126, 1072, 1030, 995, 922, 814, 760, 702 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (1H, ddd, J = 1.0, 2.0, 5.0 Hz), 7.76 (1H, ddd, J = 1.5, 7.5, 7.5 Hz), 7.64 (1H, ddd, J = 1.5, 1.5, 6.5 Hz), 7.32 (2H, dddd, J = 1.5, 1.5, 7.0, 7.0 Hz), 7.17−7.26 (4H, m), 7.10 (1H, ddd, J = 1.0, 2.5, 8.5 Hz), 6.93 (1H, d, J = 9.0 Hz), 6.77 (1H, dd, J = 1.0, 2.5 Hz), 5.29 (1H, dd, J = 2.0 Hz, 11.5 Hz), 4.34 (1H, dd, J = 6.0, 12.0 Hz), 2.68 (1H, ddd, J = 2.0, 6.0, 13.5 Hz), 2.15 (1H, ddd, J = 13.5, 11.5, 12.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.1, 153.9, 149.3, 143.7, 137.2, 129.6, 129.0, 128.7, 128.1, 127.8, 127.3, 125.8, 123.0, 120.3, 118.6, 79.0, 43.4, 39.1; MS (ESI$^+$) m/z 301 (100, $[M + H]^+$); HRMS (ESI$^+$) calcd for $[M + H]^+$ $C_{20}H_{17}ClNO$ 322.0999; found 322.0999.

2-((2R,4R*)-6-Chloro-4-phenylchroman-2-yl)pyridine* ***12g***-*exo*. mp 102−104 °C (hexanes/ethyl acetate); IR (thin film, CH_2Cl_2) ν_{max} 3059, 3024, 2924, 1593, 1477, 1435, 1223, 1123, 1072, 1030, 995, 818, 748, 698 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (1H, ddd, J = 1.0, 2.0, 5.0 Hz), 7.68 (1H, ddd, J = 2.0, 8.0, 8.0 Hz), 7.48 (1H, d, J = 8.0 Hz), 7.30 (2H, dd, J = 7.5, 7.5 Hz), 7.05−7.22 (5H, m), 6.98 (1H, d, J = 8.5 Hz), 6.91 (1H, dd, J = 0.5, 2.5 Hz), 5.18 (1H, dd, J = 3.5, 9.0 Hz), 4.09 (1H, t, J = 5.5 Hz), 2.40−2.55 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.4, 153.6, 149.4, 145.0, 137.0, 130.3, 128.9, 128.8, 128.4, 127.0, 125.7, 125.6, 122.8, 120.9, 118.6, 74.8, 39.8, 36.0; MS (ESI$^+$) m/z 301 (100, $[M + H]^+$); HRMS (ESI$^+$) calcd for $[M + H]^+$ $C_{20}H_{17}ClNO$ 322.0999; found 322.0996.

12h. Flash chromatography (25% ethyl acetate/hexanes) gave **12h** as a white solid (0.142 g, 45% yield). Further purification by flash chromatography (10% to 40% ethyl acetate/hexanes) afforded pure **12h**-*endo* and **12h**-*exo*.

2-((2S,4R*)-8-Methoxy-4-phenylchroman-2-yl)pyridine* ***12h***-*endo*. mp 137−139 °C (hexanes, ethyl acetate); IR (thin film, CH_2Cl_2) ν_{max} 3061, 3025, 2931, 2835, 1593, 1474, 1454, 1263, 1217, 1092, 1020, 993, 916, 781, 761, 735, 700 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (1H, ddd, J = 1.5, 4.5, 4.5 Hz), 7.72−7.74 (2H, m), 7.16−7.30 (6H, m), 6.72−6.79 (2H, m), 6.40 (1H, ddd, J = 1.0, 2.5, 7.0 Hz), 5.35 (1H, dd, J = 2.0, 11.5 Hz), 4.16 (1H, dd, J = 6.0, 12.0 Hz), 3.89 (3H, s), 2.71 (1H, ddd, J = 2.0, 6.0, 13.5), 2.16 (1H, ddd, J = 11.5, 12.0, 13.5); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.6, 149.1, 148.8, 144.9, 144.7, 137.2, 128.7, 126.9, 122.8, 126.8, 122.8, 121.9, 120.4, 120.2, 110.0, 78.9, 56.3, 43.4, 39.6; MS (ESI$^+$) m/z 318 (100, $[M + H]^+$); HRMS (ESI$^+$) calcd for $[M + H]^+$ $C_{21}H_{20}NO_2$ 318.1494; found 318.1502.

2-((2R,4R*)-8-Methoxy-4-phenylchroman-2-yl)pyridine* ***12h***-*exo*. Colorless oil; IR (thin film, CH_2Cl_2) ν_{max} 3061, 3025, 2931, 2835, 1589, 1493, 1473, 1263, 1251, 1092, 1026, 995, 926, 781, 761, 735, 702 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (1H, ddd, J = 1.0, 2.0, 4.5 Hz), 7.68 (1H, ddd, J = 2.0, 8.0, 8.0 Hz), 7.57 (1H, d, J = 8.0 Hz), 7.29 (2H, dd, J = 7.5, 7.5 Hz), 7.13−7.23 (4H, m), 6.78−6.84 (2H, m), 6.51 (1H, ddd, J = 1.0, 2.5, 7.0 Hz), 5.21 (1H, dd, J = 3.5, 8.5 Hz), 4.08 (1H, t, J = 5.5 Hz), 3.95 (3H, s), 2.47−2.61 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.8, 149.2, 148.8, 145.5, 144.3, 137.0, 128.9, 128.7, 126.7, 125.0, 122.6, 122.5, 120.9, 120.2, 109.9, 75.0, 56.2, 39.7, 36.2; MS (ESI$^+$) m/z 318 (100, $[M + H]^+$); HRMS (ESI$^+$) calcd for $[M + H]^+$ $C_{21}H_{20}NO_2$ 318.1494; found 318.1506.

12j. Flash chromatography (25% ethyl acetate/hexanes) gave **12j** as a white solid (0.183 g, 58% yield). Further purification by flash chromatography (10% to 40% ethyl acetate/hexanes) afforded pure **12j**-*endo* and **12j**-*exo*.

2-((2S,4R*)-6-Methoxy-4-phenylchroman-2-yl)pyridine* ***12j***-*endo*. mp 104−106 °C (hexanes/ethyl acetate); IR (thin film, CH_2Cl_2) ν_{max} 3063, 3028, 2947, 2832, 1589, 1474, 1435, 1338, 1265, 1211, 1150, 1099, 1072, 1057, 1038, 926, 872, 818, 733, 702 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (1H, ddd, J = 1.0, 2.0, 5.0 Hz), 7.75 (1H, ddd, J = 1.5, 7.5, 7.5 Hz), 7.66 (1H, d, J = 8.0 Hz), 7.29 (2H, dddd, J = 1.0, 1.0, 7.5, 7.5 Hz), 7.18−7.24 (4H, m), 6.94 (1H, d, J = 9.0 Hz), 6.74 (1H, ddd, J = 1.0, 3.0, 9.0 Hz), 6.34 (1H, dd, J = 1.0, 3.0 Hz), 5.26 (1H, dd, J = 1.5 Hz, 11.5 Hz), 4.37 (1H, dd, J = 6.0, 12.0 Hz), 3.81 (3H, s), 2.67 (1H, ddd, J = 2.0, 6.0, 13.5 Hz), 2.14 (1H, ddd, J = 13.5, 11.5, 12.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7, 153.8, 149.5, 149.2, 144.6, 137.1, 128.9, 128.8, 127.0, 126.7, 122.9, 120.3, 117.8, 114.8, 114.0, 78.8, 55.9, 43.7, 39.8; MS (ESI$^+$) m/z 318 (100, $[M + H]^+$); HRMS (ESI$^+$) calcd for $[M + H]^+$ $C_{21}H_{20}NO_2$ 318.1494; found 318.1508.

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2-((2R,4R*)-6-Methoxy-4-phenylchroman-2-yl)pyridine* ***12j-exo.*** mp 99−101 °C (hexanes/ethyl acetate); IR (thin film, CH_2Cl_2) ν_{max} 3059, 2916, 1591, 1493, 1271, 1217, 1202, 1152, 1072, 1044, 851, 766, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.53 (1H, ddd, J = 1.0, 2.0, 5.0 Hz), 7.67 (1H, ddd, J = 2.0, 8.0, 8.0 Hz), 7.53 (1H, d, J = 8.0 Hz), 7.29 (2H, dddd, J = 1.0, 1.0, 7.5, 7.5 Hz), 7.13−7.23 (4H, m), 6.99 (1H, d, J = 9.0 Hz), 6.80 (1H, ddd, J = 2.5, 7.0, 7.0 Hz), 6.47 (1H, d, J = 3.0 Hz), 5.16 (1H, dd, J = 3.0, 9.5 Hz), 4.13 (1H, t, J = 5.0 Hz), 3.65 (3H, s), 2.42−2.55 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0, 153.7, 149.3, 149.1, 145.7, 136.9, 128.9, 128.7, 126.7, 124.3, 122.6, 120.9, 117.8, 114.9, 114.8, 74.4, 55.9, 40.3, 36.6; MS (ESI^+) m/z 318 (100, $[M + H]^+$), 132 (63); HRMS (ESI^+) calcd for $C_{21}H_{20}NO_2$ $[M + H]^+$ 318.1494; found 318.1510.

Chroman ***13b.*** Flash chromatography (10% ethyl acetate/hexanes) gave **13b** as a white solid (0.238 g, 82% yield); mp 136−138 °C (hexanes/ethyl acetate); IR (thin film, CH_2Cl_2) ν_{max} 3063, 3052, 2953, 2924, 2870, 1589, 1572, 1472, 1433, 1362, 1335, 1258, 1215, 1109, 991, 774, 748; ^1H NMR (400 MHz, $CDCl_3$) δ 8.60 (1H, ddd, J = 1.5, 1.5, 5.0 Hz), 7.76−7.82 (2H, m), 7.21 (1H, ddd, J = 0.5, 3.5, 8.5 Hz), 7.07 (1H, d, J = 7.5 Hz), 6.99 (1H, d, J = 7.5 Hz), 6.88 (1H, dd, J = 7.5, 7.5 Hz), 4.90 (1H, d, J = 4.0 Hz), 3.11 (1H, d, J = 9.0 Hz), 2.65 (1H, dd, J = 3.0, 8.0 Hz), 2.28 (3H, s), 2.19 (1H, d, J = 4.5 Hz), 1.77 (1H, d, J = 3.0 Hz), 1.59 (1H, tt, J = 4.0, 12.0 Hz), 1.30−1.49 (3H, m), 1.23 (1H, tt, J = 3.0, 8.5 Hz), 0.84 (1H, d, J = 10.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.1, 154.8, 149.1, 136.6, 129.2, 127.9, 127.5, 126.6, 122.1, 121.5, 120.7, 80.4, 48.3, 47.8, 45.5, 37.2, 34.6, 31.3, 28.5, 16.0; MS (ESI^+) m/z 292 (100, $[M^+H]^+$); HRMS (ESI^+) calcd for $[M + H]^+$ $C_{20}H_{22}NO$ 292.1701 found 292.1707.

Chroman ***13c.*** Flash chromatography (10% ethyl acetate/hexanes) gave **13c** as a white solid (0.236 g, 81% yield). Pure samples of **13c-A** and **13c-B** were obtained by semipreparative reverse phase HPLC (Eclipse XDB-C18 (5 μm) 9.4 × 250 mm, 20 to 95% acetonitrile/water).

13c-A. mp 129−130 °C; IR (thin film, CH_2Cl_2) ν_{max} 3063, 2955, 2924, 2870, 1591, 1573, 1472, 1435, 1359, 1261, 1130, 1105, 991, 804, 765; ^1H NMR (400 MHz, $CDCl_3$) δ 8.60 (1H, ddd, J = 1.0, 2.0, 5.0 Hz), 7.77 (1H, ddd, J = 2.0, 8.0, 8.0 Hz), 7.59 (1H, d, J = 7.5 Hz), 7.20 (1H, ddd, J = 1.0, 3.5, 6.0 Hz), 7.10 (1H, d, J = 8.0 Hz), 6.81 (1H, d, J = 9.0 Hz), 6.78 (1H, s), 4.91 (1H, d, J = 4.0 Hz), 3.07 (1H, d, J = 9.0 Hz), 2.57 (1H, dd, J = 4.0, 9.0 Hz), 2.30 (3H, s), 2.19 (1H, d, J = 4.5 Hz), 1.79 (1H, d, J = 3.0 Hz), 1.59 (1H, tt, J = 4.0, 12.0 Hz), 1.29−1.50 (3H, m), 1.23 (1H, tt, J = 3.0, 8.5 Hz), 0.85 (1H, d, J = 10.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.8, 156.5, 149.1, 136.7, 136.6, 129.7, 126.5, 123.1, 122.1, 120.9, 118.0, 80.6, 48.2, 47.8, 45.5, 37.1, 34.6, 31.3, 28.4, 21.3; MS (ESI^+) m/z 292 (100, $[M + H]^+$). HRMS (ESI^+) calcd for $[M + H]^+$ $C_{20}H_{22}NO$ 292.1701 found 292.1702.

13c-B. mp 76−78 °C; IR (thin film, CH_2Cl_2) ν_{max} 3067, 3005, 2959, 2870, 1589, 1574, 1497, 1474, 1439, 1366, 1335, 1242, 1227, 1134, 1107, 1080, 991, 818, 787, 768, 694, 656; ^1H NMR (400 MHz, $CDCl_3$) δ 8.60 (1H, ddd, J = 1.0, 2.0, 5.0 Hz), 7.78 (1H, ddd, J = 1.5, 8.0, 8.0 Hz), 7.72 (1H, d, J = 1.0 Hz), 7.21 (1H, ddd, J = 1.0, 5.0, 8.0 Hz), 7.03 (1H, dd, J = 8.0, 8.0 Hz), 6.85 (1H, d, J = 7.5 Hz), 6.81 (1H, d, J = 8.0 Hz), 4.88 (1H, d, J = 4.0 Hz), 3.12 (1H, d, J = 9.0 Hz), 2.63 (1H, dd, J = 3.0, 8.0 Hz), 2.37 (3H, s), 2.20 (1H, d, J = 4.5 Hz), 1.80 (1H, d, J = 3.0 Hz), 1.60 (1H, tt, J = 4.0, 12.0 Hz), 1.32−1.49 (3H, m), 1.24 (1H, tt, J = 3.0, 8.5 Hz), 0.88 (1H, d, J = 10.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.5, 156.7, 148.9, 137.6, 136.4, 128.0, 126.2, 123.8, 121.9, 120.7, 115.4, 80.3, 48.3, 45.3, 42.7, 37.2, 35.0, 30.9, 28.5, 19.1; MS (ESI^+) m/z 292 (100, $[M + H]^+$); HRMS (ESI^+) calcd for $[M + H]^+$ $C_{20}H_{22}NO$ 292.1701 found 292.1707.

Chroman ***13d.*** Flash chromatography (10% ethyl acetate/hexanes) gave **13d** as a white solid (0.229 g, 79% yield). mp 129−131 °C (hexanes/ethyl acetate); IR (thin film, CH_2Cl_2) ν_{max} 3067, 3005, 2959, 2870, 1589, 1574, 1497, 1474, 1439, 1366, 1335, 1242, 1227, 1134, 1107, 1080, 991, 818, 787, 768, 694, 656; ^1H NMR (400 MHz, $CDCl_3$) δ 8.60 (1H, ddd, J = 1.0, 1.5, 4.5 Hz), 7.76 (1H, ddd, J = 2.0, 7.5, 7.5 Hz), 7.70 (1H, d, J = 8.0), 7.20 (1H, ddd, J = 1.0, 5.0, 7.5 Hz), 7.03 (1H, d, J = 1.5 Hz), 6.92 (1H, dd, J = 2.0, 8.5 Hz), 6.83 (1H, d, J = 8.0 Hz), 4.88 (1H, d, J = 3.5 Hz), 3.06 (1H, d, J = 9.0 Hz), 2.57 (1H, dd, J = 3.5, 9.0 Hz), 2.31 (3H, s), 2.22 (1H, d, J = 4.0 Hz), 1.79 (1H, d, J = 3.0 Hz), 1.60 (1H, tt, J = 4.0, 12.0 Hz), 1.49 (1H, td, J = 2.0, 10.0 Hz), 1.30−1.46 (2H, m), 1.19 (1H, tt, J = 3.0, 8.5 Hz), 0.86 (1H, d, J = 10.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.8, 154.5, 149.1, 136.6, 131.3, 130.3, 129.3, 127.5, 122.1, 120.9, 117.3, 80.7, 48.2, 47.9, 45.4, 37.2, 34.7, 31.3, 28.5, 21.0; MS (EI) m/z 291 (100, M^+), 262 (16), 250 (7), 224(15), 197 (85), 169 (6), 146 (23), 130 (8), 117 (4), 93 (13); HRMS (EI) calcd for $[M]^+$ $C_{20}H_{21}NO$ 291.1623 found 291.1624.

Chroman ***13f.*** Flash chromatography (15% ethyl acetate/hexanes) gave **13f** as a colorless oil (0.170 g, 55% yield). Further purification by flash chromatography (5% to 20% ethyl acetate/hexanes) afforded pure **13f-A** and **13f-B**.

13f-A. colorless oil; IR (thin film, CH_2Cl_2) ν_{max} 3063, 2955, 1589, 1474, 1359, 1247, 1191, 1123, 1076, 957, 899, 764, 687 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.59 (1H, ddd, J = 1.0, 1.5, 4.5 Hz), 7.77 (1H, ddd, J = 2.0, 7.5, 7.5 Hz), 7.66 (1H, ddd, J = 1.0, 2.0, 8.0 Hz), 7.22 (1H, dddd, J = 0.5, 1.0, 4.5, 7.5 Hz), 7.14 (1H, d, J = 9.0 Hz), 6.94−6.97 (2H, m), 4.90 (1H, d, J = 4.0 Hz), 3.07 (1H, d, J = 9.0 Hz), 2.60 (1H, ddd, J = 1.0, 3.5, 8.5 Hz), 2.18 (1H, d, J = 4.5 Hz), 1.80 (1H, d, J = 4.0 Hz), 1.60 (1H, tt, J = 4.5, 12.5 Hz), 1.30−1.46 (3H, m), 1.20 (1H, tt, J = 3.0, 8.5 Hz), 0.87 (1H, d, J = 10.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.2, 157.2, 149.2, 136.8, 131.8, 130.9, 128.2, 122.5, 122.3, 120.8, 117.8, 80.8, 48.2, 47.6, 44.9, 37.1, 34.6, 31.2, 28.3; MS (ESI^+) m/z 312 (100, $[M + H]^+$); HRMS (ESI^+) calcd for $[M + H]^+$ $C_{19}H_{19}ClNO$ 312.1155; found 312.1153.

13f-B. colorless oil; IR (thin film, CH_2Cl_2) ν_{max} 3059, 2953, 2909, 2970, 2834, 1591, 1483, 1453, 1333, 1264, 1221, 1188, 1109, 1094, 1084, 991, 837, 774, 741; ^1H NMR (400 MHz, $CDCl_3$) δ 8.58 (1H, ddd, J = 1.0, 1.5, 5.0 Hz), 7.74 (1H, ddd, J = 2.0, 8.0, 8.0 Hz), 7.65 (1H, d, J = 8.0 Hz), 7.20 (1H, ddd, J = 1.5, 5.0, 8.5 Hz), 7.03 (2H, d, J = 4.5 Hz), 6.86 (1H, dd, J = 4.5, 4.5 Hz), 4.86 (1H, d, J = 4.0 Hz), 3.28 (1H, d, J = 9.0 Hz), 2.61 (1H, dd, J = 3.5, 9.0 Hz), 2.40 (1H, d, J = 4.0 Hz), 1.81 (1H, d, J = 2.5 Hz), 1.60 (1H, tt, J = 4.0, 12.5 Hz), 1.40−1.50 (2H, m), 1.36 (1H, tt, J = 2.0, 10.0 Hz), 1.20 (1H, tt, J = 3.0, 9.5 Hz), 0.87 (1H, d, J = 10.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.1, 157.8, 149.2, 136.7, 134.7, 128.0, 127.2, 123.3, 122.3, 120.8, 116.5, 80.9, 48.0, 45.4, 43.6, 37.6, 35.0, 31.1, 28.6; MS (ESI^+) m/z 312 (100, $[M + H]^+$); HRMS (ESI^+) calcd for $[M + H]^+$ $C_{19}H_{19}ClNO$ 312.1155; found 312.1150.

Chroman ***13g.*** Flash chromatography (15% ethyl acetate/hexanes) gave **13g** as a white solid (0.180 g, 58% yield). mp 95−96 °C (hexanes/ethyl acetate); IR (thin film, CH_2Cl_2) ν_{max} 3063, 2955, 1589, 1474, 1362, 1254, 1184, 1123, 1076, 957, 899, 817, 764, 687 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.60 (1H, ddd, J = 3.5, 4.5, 6.0 Hz), 7.76 (1H, ddd, J = 2.0, 7.5, 7.5 Hz), 7.66 (1H, ddd, J = 1.0, 2.0, 8.0 Hz), 7.19−7.23 (2H, m), 7.06 (1H, ddd, J = 0.5, 2.5, 4.5 Hz), 6.87 (1H, d, J = 8.5 Hz), 4.89 (1H, d, J = 4.0 Hz), 3.60 (1H, d, J = 9.0 Hz), 2.58 (1H, ddd, J = 1.0, 3.5, 8.5 Hz), 2.21 (1H, d, J = 4.5 Hz), 1.80 (1H, d, J = 4.0 Hz), 1.60 (1H, tt, J = 4.5, 12.5 Hz), 1.30−1.46 (3H, m), 1.23 (1H, tt, J = 3.0, 8.5 Hz), 0.87 (1H, d, J = 10.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.2, 155.2, 149.2, 136.7, 131.3, 129.6, 126.9, 126.8, 122.3, 120.8, 118.9, 80.8, 48.2, 47.6, 45.3, 37.1, 34.6, 31.2, 28.3; MS (ESI^+) m/z 312 (100, $[M + H]^+$); HRMS (ESI^+) calcd for $[M + H]^+$ $C_{19}H_{19}ClNO$ 312.1155; found 312.1169.

Chroman ***13h.*** Flash chromatography (20% ethyl acetate/hexanes) gave **13h** as a white solid (0.208 g, 68% yield). mp 120−122 °C (hexanes/ethyl acetate); IR (thin film, CH_2Cl_2) ν_{max} 3059, 2953, 2909, 2970, 2834, 1591, 1483, 1453, 1333, 1264, 1221, 1188, 1109, 1094, 1084, 991, 837, 774, 741; ^1H NMR (400 MHz, $CDCl_3$) δ 8.58 (1H, ddd, J = 0.5, 1.0, 4.5 Hz), 7.74−7.81 (2H, m), 7.19 (1H, ddd, J = 1.5, 5.0, 8.5 Hz), 6.92 (1H, dd, J = 8.0, 7.5 Hz), 6.84 (1H, dd, J = 1.5, 7.5 Hz), 6.73 (1H, dd, J = 1.5, 8.0 Hz), 4.93 (1H, d, J = 4.0 Hz), 3.85 (3H, s), 3.11 (1H, d, J = 9.0 Hz), 2.61 (1H, dd, J = 3.5, 9.0 Hz), 2.21 (1H, d, J = 4.5 Hz), 1.81 (1H, d, J = 2.5 Hz), 1.60 (1H, tt, J = 4.0, 12.5 Hz), 1.30−1.52 (3H, m), 1.22 (1H, tt, J = 3.0, 9.5 Hz), 0.86 (1H, d, J = 10.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7, 149.1, 149.0, 146.2, 136.8, 130.6, 122.1, 121.9, 121.6, 121.0, 109.4, 80.9, 56.3, 48.1, 47.8, 45.4, 37.1, 34.7, 31.2, 28.4; MS (ESI^+) m/z 308 (100, $[M + H]^+$); HRMS (ESI^+) calcd for $[M + H]^+$ $C_{20}H_{22}NO_2$ 308.1651 found 308.1656.

Chroman ***13i.*** Flash chromatography (15% ethyl acetate/hexanes) gave **13i** as a white solid (0.174 g, 57% yield). Further purification by flash chromatography (5% to 30% ethyl acetate/hexanes) afforded pure **13i-A** and **13i-B**.

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13i-A. mp 102−122 °C (hexanes/ethyl acetate); IR (thin film, CH_2Cl_2) ν_{max} 3063, 2953, 1618, 1582, 1502, 1453, 1360, 1267, 1161, 1113, 1038, 993, 835, 766; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (1H, ddd, J = 1.0, 1.5, 4.5 Hz), 7.77 (1H, ddd, J = 2.0, 8.0, 8.0 Hz), 7.69 (1H, d, J = 8.0 Hz), 7.22 (1H, ddd, J = 1.0, 5.0, 9.0 Hz), 7.10 (1H, d, J = 8.0 Hz), 6.59 (1H, dd, J = 2.5, 8.5 Hz), 6.51 (1H, d, J = 2.5 Hz), 4.94 (1H, d, J = 3.5 Hz), 3.77 (3H, s), 3.06 (1H, d, J = 9.0 Hz), 2.55 (1H, dd, J = 3.0, 8.5 Hz), 2.16 (1H, d, J = 4.5 Hz), 1.79 (1H, d, J = 3.0 Hz), 1.58 (1H, tt, J = 4.0, 12.0 Hz), 1.28−1.47 (3H, m), 1.14−1.21 (1H, m), 0.85 (1H, d, J = 10 . 0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7, 158.9, 157.4, 149.2, 136.6, 130.4, 122.2, 121.7, 120.9, 109.2, 102.4, 80.8, 55.5, 48.1, 47.7, 44.7, 37.1, 34.5, 31.3, 28.2; MS (ESI$^+$) m/z 308 (100, $[M + H]^+$). HRMS (ESI$^+$) calcd for $[M + H]^+$ $C_{20}H_{22}NO_2$ 308.1651 found 308.1649.

Chroman ***13i-B.*** mp 95−96 °C (hexanes/ethyl acetate); IR (thin film, CH_2Cl_2) ν_{max} 3059, 2953, 2909, 2970, 2834, 1591, 1483, 1453, 1333, 1264, 1221, 1188, 1109, 1094, 1084, 991, 837, 774, 741; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (1H, ddd, J = 1.0, 2.0, 5.0 Hz), 7.76 (1H, ddd, J = 2.0, 8.0, 8.0 Hz), 7.69 (1H, d, J = 8.0 Hz), 7.22 (1H, ddd, J = 1.0, 5.0, 7.0 Hz), 7.08 (1H, dd, J = 8.0, 8.0 Hz), 6.60 (1H, d, J = 8.0 Hz), 6.53 (1H, d, J = 8.0 Hz), 4.90 (1H, d, J = 4.0 Hz), 3.86 (3H, s), 3.24 (1H, d, J = 9.0 Hz), 2.56 (1H, dd, J = 4.0, 9.0 Hz), 2.28 (1H, d, J = 4.5 Hz), 1.78 (1H, d, J = 3.0 Hz), 1.57 (1H, tt, J = 4.0, 12.0 Hz), 1.40−1.44 (2H, m), 1.33 (1H, tt, J = 4.5, 12.0 Hz), 1.20 (1H, tt, J = 3.5, 8.0 Hz), 0.85 (1H, d, J = 10.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.8, 158.2, 157.7, 149.1, 136.6, 126.7, 122.2, 120.9, 118.4, 110.5, 103.8, 80.6, 55.7, 47.6, 45.2, 40.2, 37.3, 35.2, 31.3, 28.5; MS (ESI$^+$) m/z 308 (100, $[M + H]^+$); HRMS (ESI$^+$) calcd for $[M + H]^+$ $C_{20}H_{22}NO_2$ 308.1651 found 308.1656.

Chroman ***13j.*** Flash chromatography (20% ethyl acetate/hexanes) gave **13j** as a white solid (0.199 g, 65% yield). mp 113−115 °C (hexanes/ethyl acetate); IR (thin film, CH_2Cl_2) ν_{max} 3053, 2953, 2924, 2870, 1593, 1572, 1472, 1435, 1362, 1338, 1288, 1252, 1213, 1155, 1103, 991, 812, 764, 747; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (1H, ddd, J = 1.0, 2.0, 5.0 Hz), 7.76 (1 H, ddd, J = 2.0, 8.0, 8.0 Hz), 7.69 (1H, d, J = 8.0), 7.20 (1H, ddd, J = 1.0, 5.0, 7.5 Hz), 6.87 (1H, d, J = 9.0 Hz), 6.76 (1H, d, J = 3.0 Hz), 6.68 (1H, dd, J = 3.0, 9.0 Hz), 4.88 (1H, d, J = 4.0 Hz), 3.19 (3H, s), 3.07 (1H, d, J = 9.0 Hz), 2.56 (1H, dd, J = 3.5, 9.0 Hz), 2.23 (1H, d, J = 4.5 Hz), 1.79 (1H, d, J = 3.0 Hz), 1.60 (1H, tt, J = 4.0, 12.5 Hz), 1.51 (1H, dt, J = 2.0, 10.0 Hz), 1.30−1.46 (2H, m), 1.20 (1H, tt, J = 3.0, 9.0 Hz), 0.87 (1 H, d, J = 10.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.8, 154.7, 150.7, 149.1, 136.6, 130.3, 122.1, 120.9, 118.2, 114.3, 112.8, 80.8, 55.8, 48.2, 47.8, 45.9, 37.1, 34.7, 31.2, 28.5; MS (ESI$^+$) m/z 308 (100, $[M + H]^+$). HRMS (ESI$^+$) calcd for $[M + H]^+$ $C_{20}H_{22}NO_2$ 308.1651 found 308.1651.

Chroman ***13l.*** Flash chromatography (15% ethyl acetate/hexanes) gave **13l** as a white solid (0.200 g, 66% yield). IR (thin film, CH_2Cl_2) ν_{max} 3055, 3005, 2959, 2924, 2870, 1590, 1573, 1489, 1474, 1439, 1366, 1335, 1242, 1227, 1126, 1012, 995, 889, 814, 746, 721, 698, 650, 621; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (1H, ddd, J = 1.0, 2.0, 5.0 Hz), 7.75 (1H, ddd, J = 2.0, 2.0, 7.5 Hz), 7.69 (1H, ddd, J = 0.5, 1.5, 3.0 Hz), 7.19 (1H, dddd, J = 0.5, 1.3, 5.0, 6.5 Hz), 6.66 (2H, d, J = 12.0 Hz), 4.84 (1H, d, J = 4.0 Hz), 3.07 (1H, d, J = 9.0 Hz), 2.59 (1H, ddd, J = 1.0, 4.0, 8.0 Hz), 2.32 (3H, s), 2.25 (3H, s), 2.18 (1H, d, J = 4.5 Hz), 1.78 (1H, d, J = 1.5 Hz), 1.51−1.59 (2H, m), 1.31−1.45 (2H, m), 1.20 (1H, tt, J = 3.0, 8.5 Hz), 0.86 (1H, d, J = 10.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.8, 156.8, 149.1, 137.2, 136.6, 136.2, 125.1, 125.0, 122.1, 120.9, 116.1, 80.6, 48.4, 45.6, 42.7, 37.4, 35.2, 31.1, 28.7, 21.1, 16.0; MS (ESI$^+$) m/z 306 (100, $[M + H]^+$); HRMS (ESI$^+$) calcd for $[M + H]^+$ $C_{21}H_{24}NO$ 306.1858; found 306.1866.

18a. Flash chromatography (15% ethyl acetate/hexanes) gave **18a** as a white solid (0.087 g, 29% yield). Further purification by flash chromatography (5% to 20% ethyl acetate/hexanes) afforded pure **18a**-*endo-trans* and **18a**-*exo-trans*.

2-((2S,3S*,4R*)-3-Methyl-4-phenylchroman-2-yl)pyridine* ***18a****-endo-trans.* isolated as a white solid, mp 140−141 °C (ether); IR (thin film, CH_2Cl_2) ν_{max} 3063, 3013, 2963, 2924, 1589, 1466, 1435, 1335, 1300, 1261, 1211, 1180, 1084, 1045, 995, 914, 787, 768 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 (1H, ddd, J = 0.5, 1.5, 5.0 Hz), 7.76 (1H, ddd, J = 2.0, 7.5, 7.5 Hz), 7.52 (1H, ddd, J = 1.0, 1.0, 8.0 Hz), 7.32 (2H, dddd, J = 1.0, 1.0, 7.0, 7.0 Hz), 7.24−7.28 (2H, m), 7.20 (2H, dd, J = 1.5, 8.5 Hz), 7.11 (1H, dddd, J = 1.0, 1.5, 7.0, 7.0 Hz), 6.92 (1H, dd, J = 1.0, 8.5 Hz), 6.78 (1H, ddd, J = 1.0, 7.5, 7.5 Hz), 6.67 (1H, ddd, J = 1.0, 1.0, 8.0 Hz), 4.94 (1H, d, J = 10.0 Hz), 3.85 (1H, d, J = 11.0 Hz), 2.40−2.51 (1H, m), 0.64 (3H, d, J = 6.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 155.2, 149.4, 143.8, 137.1, 130.4, 129.7, 128.7, 127.7, 126.9, 126.5, 123.5, 122.5, 120.9, 116.9, 84.9, 51.0, 40.4, 15.4; MS (ESI$^+$) m/z 302 (100, $[M + H]^+$), 183 (5), 120 (5); HRMS (ESI$^+$) calcd for $[M + H]^+$ $C_{21}H_{20}NO$ 302.1539; found 302.1552.

2-((2S,3R*,4S*)-3-Methyl-4-phenylchroman-2-yl)pyridine* ***18a****-exo-trans.* isolated as a white solid, mp 96−98 °C (ether); IR (thin film, CH_2Cl_2) ν_{max} 3059, 3024, 2920, 1589, 1497, 1435, 1343, 1238, 1126, 1073, 1030, 995, 922, 813, 759, 702 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (1H, ddd, J = 1.0, 2.0, 5.0 Hz), 7.76 (1H, ddd, J = 2.0, 7.5, 7.5 Hz), 7.52 (1H, d, J = 7.5 Hz), 7.32 (2H, dd, J = 7.5, 7.5 Hz), 7.12−7.27 (5H, m), 7.09 (1H, dd, J = 1.0, 8.2 Hz), 7.04 (1H, dd, J = 1.5, 7.5 Hz), 6.93 (1H, ddd, J = 1.0, 7.5, 7.5 Hz), 5.15 (1H, d, J = 2.5 Hz), 4.04 (1H, d, J = 2.0 Hz), 2.71 (1H, tq, J = 2.5, 7.0 Hz), 0.84 (3H, d, J = 7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.1, 154.6, 149.0, 146.5, 136.5, 132.0, 129.1, 128.7, 128.2, 126.6, 122.3, 122.2, 121.3, 121.2, 116.9, 75.5, 48.6, 38.8, 13. 9; MS (ESI$^+$) m/z 302 (100, $[M + H]^+$), 183 (5), 120 (5); HRMS (ESI$^+$) calcd for $[M + H]^+$ $C_{21}H_{20}NO$ 302.1539; found 302.1552.

18d. Flash chromatography (10% ethyl acetate/hexanes) gave **18d** as a white solid (0.144 g, 46% yield). Further purification by flash chromatography (5% to 20% ethyl acetate/hexanes) afforded pure **18d**-*endo-trans* and **18d**-*exo-trans*.

2-((2S,3S*,4R*)-3,6-Dimethyl-4-phenylchroman-2-yl)pyridine* ***18d****-endo-trans.* isolated as a white solid, mp 149−150 °C (hexanes/ethyl acetate); IR (thin film, CH_2Cl_2) ν_{max} 3063, 3024, 2920, 2962, 1589, 1474, 1339, 1273, 1242, 1219, 1123, 1072, 1049, 883, 814, 759 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (1H, ddd, J = 1.0, 1.5, 4.5 Hz), 7.75 (1H, ddd, J = 1.5, 7.5, 7.5 Hz), 7.51 (1H, d, J = 8.0 Hz), 7.32 (2H, dddd, J = 1.0, 1.0, 7.0, 7.0 Hz), 7.24−7.28 (2H, m), 7.20 (2H, ddd, J = 1.5, 6.5, 6.5 Hz), 6.91 (1H, dd, J = 2.0, 8.0 Hz), 6.82 (1H, d, J = 9.0 Hz), 6.47 (1H, s), 4.89 (1H, d, J = 10.0 Hz), 3.81 (1H, d, J = 10.5 Hz), 2.48−2.50 (1H, m), 2.12 (3H, s), 0.63 (3H, d, J = 6.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 153.1, 149.4, 144.0, 137.1, 130.5, 130.1, 129.7, 128.7, 128.4, 126.9, 126.1, 123.4, 122.5.2, 116.7, 84.9, 51.1, 40.7, 20.8, 15.5; MS (ESI$^+$) m/z 316 (100, $[M + H]^+$); HRMS (ESI$^+$) calcd for $[M + H]^+$ $C_{22}H_{22}NO$ 316.1707; found 316.1705.

2-((2S,3R*,4S*)-3,6-Dimethyl-4-phenylchroman-2-yl)pyridine* ***18d****-exo-trans.* isolated as a white solid, mp 93−94 °C (hexanes/ethyl acetate); IR (thin film, CH_2Cl_2) ν_{max} 3059, 3024, 2956, 1591, 1493, 1426, 1343, 1238, 1126, 1055, 1030, 926, 816, 702, 687 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (1H, ddd, J = 1.0, 1.5, 4.5 Hz), 7.70 (1H, ddd, J = 2.0, 8.0, 8.0 Hz), 7.65 (1H, ddd, J = 1.0, 1.5, 3.0 Hz), 7.28 (2H, dddd, J = 0.5, 0.5, 7.5, 7.5 Hz), 7.19 (1H, tt, J = 1.0, 7.5 Hz), 7.10−7.15 (3H, m), 7.02 (1H, dd, J = 2.0, 8.0 Hz), 6.96 (1H, d, J = 8.0 Hz), 6.82 (1 H, d, J = 1.5 Hz), 5.10 (1H, d, J = 2.5 Hz), 3.97 (1H, d, J = 1.5 Hz), 2.68 (1H, tq, J = 2.0, 7.0 Hz), 2.23 (3H, s), 0.81 (3H, d, J = 7.0 Hz); ^{13}C δ NMR (100 MHz, $CDCl_3$) 160.3, 152.4, 149.0, 146.7, 136.5, 132.1, 130.3, 129.1, 129.0, 128.6, 126.6, 122.2, 121.8, 121.3, 116.6, 75.4, 48.7, 38.9, 20.8, 13.9; MS (ESI$^+$) m/z 316 (100, $[M + H]^+$); HRMS (ESI$^+$) calcd for $[M + H]^+$ $C_{22}H_{22}NO$ 316.1707; found 316.1701.

18j. Flash chromatography (20% ethyl acetate/hexanes) gave **18j** as a white solid (0.207 g, 63% yield). Further purification by flash chromatography (10% to 25% ethyl acetate/hexanes) afforded pure **18j**-*endo-trans*, **18a**-*exo-trans*, and **18j**-*endo-cis*.

2-((2S,3S*,4R*)-6-Methoxy-3-methyl-4-phenylchroman-2-yl)-pyridine* ***18j****-endo-trans.* isolated as a white solid, mp 124−125 °C (hexanes/ethyl acetate); IR (thin film, CH_2Cl_2) ν_{max} 3063, 2964, 2927, 1591, 1490, 1342, 1270, 1214, 1151, 1028, 819, 700 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (1H, ddd, J = 1.0, 2.0, 5.0 Hz), 7.75 (1H, ddd, J = 2.0, 7.5, 7.5 Hz), 7.50 (1H, d, J = 8.0 Hz), 7.18−7.33 (6H, m), 6.86 (1H, d, J = 9.0 Hz), 6.68 (1H, ddd, J = 1.0, 3.0, 9.0 Hz), 6.21 (1H, dd, J = 1.0, 3.0 Hz), 4.87 (1H, d, J = 10.0 Hz), 3.82 (1H, d, J = 11.0 Hz), 3.59 (3H, s), 2.39−2.49 (1H, m), 0.63 (3H, d, J = 6.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4, 153.8, 149.5, 149.4, 143.7, 137.1, 129.7, 128.7, 127.2, 127.0, 123.4, 125.5, 117.5, 115.2, 113.6, 84.9, 55.8, 51.4, 40.6, 15.5; MS (ESI$^+$) m/z 332 (100, $[M + H]^+$); HRMS (ESI$^+$) calcd for $[M + H]^+$ $C_{22}H_{22}NO_2$ 332.1656; found 332.1655.

2-((2S,3R*,4S*)-6-Methoxy-3-methyl-4-phenylchroman-2-yl)-pyridine* ***18j****-exo-trans.* isolated as a white solid, mp 105−106 °C (hexanes/ethyl acetate); IR (thin film, CH_2Cl_2) ν_{max} 3063, 2962, 1594, 1490, 1356, 1276, 1224, 1153, 1035, 964, 885, 821, 755, 703 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.50 (1H, ddd, J = 0.9, 1.7, 4.8 Hz), 7.70 (1H, ddd, J = 1.8, 7.8, 7.8 Hz), 7.65 (1H, d, J = 8.0 Hz), 7.30 (1H, t, J = 7.5 Hz), 7.20 (2H, dddd, J = 2.0, 2.0, 7.5, 7.5 Hz), 7.12−7.16 (3H, m), 7.01 (1H, d, J = 9.0 Hz), 6.83 (1H, dd, J = 3.1, 9.0 Hz), 6.55 (1H, d, J = 3.0 Hz), 5.10 (1H, d, J = 2.3 Hz), 4.00 (1 H, d, J = 1.6 Hz), 3.71 (3H, s), 2.68 (1H, app. tq, J = 2.3, 6.0 Hz), 0.83 (3H, d, J = 7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7, 154.1, 149.1, 148.7, 146.4, 136.5, 129.1, 128.7, 126.7, 122.7, 122.2, 121.3, 117.6, 115.7, 115.0, 75.5, 55.9, 49.1, 38.9, 14.0; MS (ESI^+) m/z 332 (100, $[M + H]^+$); HRMS (ESI^+) calcd for $[M + H]^+$ $C_{22}H_{22}NO_2$ 332.1656; found 332.1654.

2-((2S,3R*,4R*)-6-Methoxy-3-methyl-4-phenylchroman-2-yl)-pyridine* ***18j****-endo-cis.* isolated as white solid, mp 109−110 °C (hexanes/ethyl acetate); IR (thin film, CH_2Cl_2) ν_{max} 3063, 2963, 1591, 1491, 1270, 1214, 1122, 1031, 924, 815, 743; ^1H NMR (400 MHz, $CDCl_3$) δ 8.60 (1H, ddd, J = 0.9, 1.7, 4.8 Hz), 7.70−7.78 (2H, m), 7.21−7.35 (6H, m), 6.97 (1H, d, J = 9.0 Hz), 6.78 (1H, dd, J = 3.1, 9.0 Hz), 6.57 (1H, d, J = 3.0 Hz), 5.40 (1H, d, J = 1.0 Hz), 4.79 (1H, d, J = 5.5 Hz), 3.66 (3H, s), 2.66−2.74 (1H, m), 0.46 (3H, d, J = 7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.0, 153.8, 149.3, 149.1, 141.8, 136.7, 130.2, 128.3, 127.0, 124.5, 122.4, 120.9, 117.8, 115.2, 114.2, 81.2, 55.9, 48.9, 37.4, 7.8; MS (ESI^+) m/z 332 (100, $[M + H]^+$), 132 (63); HRMS (ESI^+) calcd for $[M + H]^+$ $C_{22}H_{22}NO_2$ 332.1651; found 332.1657.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of ^1H NMR and ^{13}C NMR spectra, ORTEP X-ray crystal structure displays, and CIF files for **11a**-*exo-endo* and **11b**-*endo*. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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(30) The minor isomer was identified from the ^1H NMR spectrum of the crude reaction mixtures. The H2 proton appeared at 4.54 ppm, slightly upfield compared to the endo isomer, with a large coupling

constant of 9.6 Hz. The relatively large coupling constant, as well as the upfield shift of these protons, is consistent with that of the exo-exo stereoisomers observed for the products of aza-Povarov reactions of norbornene (ref 35.).

(31) See Supporting Information for ORTEP X-ray crystal structure displays of **11a**-*exo-endo* and **11b**-*endo*.

(32) Coupling constants for 4-substituted flavans have been previously shown to adhere well to the Karplus equation, see: Whalley, W. B. *The Chemistry of Flavonoid Compounds*; Pergamon Press: London, 1962.

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(37) The corresponding aza-Povarov reactions using norbornene occur with modest selectivity to give the regioisomer having the substituent at the 7-position of the tetrahydroquinoline ring system using 3,4-dimethylaniline (3:2 ratio), and at the 5-position (64:36 ratio) using *m*-chloroaniline (see ref 35). The 7-substituted tetrahydroquinolines were obtained exclusively as the exo-exo diastereomers and the 5-substituted isomers were obtained as the exo-endo diastereomers. A concerted [4 + 2] mechanism was proposed to account for the exo-exo diastereomers and a stepwise mechanism for the exo-endo diastereomers. The change in mechanism from concerted to stepwise for the formation of the exo-endo 5-substituted tetrahydroquinolines was attributed to additional unfavorable steric interactions that occur between norbornene and the R^1 substituents present in the exo-exo transition states. The preference for the formation *exo-endo*-norbornene-derived adducts in the oxa-Povarov reaction may reflect a similar steric effect and either an earlier transition state for the oxa-Povarov reaction or shorter C−O compared to C−N bond lengths in the respective transition states.

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(44) Pure samples of this compound were unobtainable; however, it could be identified in the ^{1}H NMR spectra of the crude reaction mixtures.

(45) While cis/trans scrambling is also conceivable through isomerization of the chroman products (e.g., via a reversible Friedel−Crafts alkylation), isomerization was not detected when **18j**-*endo-trans*, **18j**-*exo-trans*, or **18j**-*endo-cis* were resubjected to the reaction conditions.

(46) One of the closest mechanistic comparisons to rationalize the relative stereoselectivity (C2/C3) obtained in a stepwise oxa-Povarov reaction is to consider stereoselective Prins reactions between 1,2-disubsituted alkenes and aldehydes RCHO. However, most Prins reactions utilize monosubstituted alkenes and formaldehyde as substrates. One rare example is the iodine-promoted reaction of *trans*-*β*-methylstyrene and propanal, which was recently described to give a pure adduct in 88% yield (no dr was reported). The relative stereochemistry of this adduct corresponds to the major diastereomer **18**-*exo-trans* obtained for the oxa-Povarov reaction of *trans*-*β*-methylstyrene. See: Yadav, J. S.; Subba Reddy, B. V.; Hara Gopal, A. V.; Narayana Kumar, G. G. K. S.; Madavi, C.; Kunwar, A. C. *Tetrahedron Lett.* **2008**, *49*, 4420−4423.

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