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A Base-Catalyzed, Domino Aldol/*hetero*-Diels–Alder Synthesis of Tricyclic Pyrano[3,4-*c*]chromenes in Glycerol

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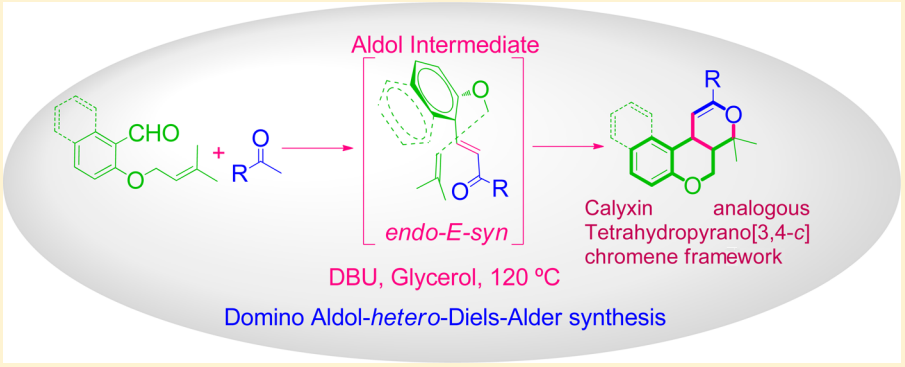
Supporting Information



ABSTRACT: The domino aldol/*hetero*-Diels–Alder synthesis of some new tricyclic pyrano[3,4-*c*]chromene derivatives has been achieved successfully after assembling a variety of acyclic or cyclic monoketones with prenyl ether-tethered aldehydes in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene in glycerol at 120 °C. The hitherto unreported stereochemical outcome of this synthetic sequence was studied and established on the basis of single-crystal X-ray diffraction data and 2D NMR NOESY spectroscopy along with the isolation and characterization of the intermediate Aldol condensation product.

INTRODUCTION

Pyranochromene has gained significant prominence worldwide because of its existence as a principal structural, central skeleton in several bioactive natural and unnatural molecular frameworks as well as in many photosensitive molecular assemblies.[1] Because of the wide spectrum of biological features of these frameworks, such as antihyperglycemic and antioxidant properties, and antidyslipidemic, antifungal, antimalarial, anticancer, anti-inflammatory, antituberculosis, anti-HIV, anti-allergic, antiviral, cytotoxic, and antibacterial activities,[2] this class of candidates has attracted a wider scope of utilizations and studies in the development of medicinal chemistry as potential therapeutic agents. They are cognitive enhancers effective in the treatment of several neurodegenerative diseases, including Alzheimer's disease, AIDS-associated dementia, schizophrenia, amyotrophic lateral sclerosis, Huntington's disease, and Parkinson's disease.[3] Furthermore, the pyranopyranyl core structure is known for conferring a variety of properties on pyranochromene-ring systems through its varied patterns of the fusion existing in this tricyclic system in the molecules.[4] Pyrano[3,2-*c*]chromene, in particular, has seen increasing applications in the development of photonic materials, emerging as a promising photochrometic molecular motif with great technological importance.[5]

The occurrence of a pyrano-chromene nucleus could be possibly recognized in a number of ways, as shown in Figure 1, which ultimately results in several structural arrays or scaffolds that exist between pyran and chromene units, and each can be disguised by the relative position of two oxygen atoms in the pyranopyranyl skeleton.[6] Among these skeletons, the pyrano-[3,4-*c*]chromene unit exists in a number of potentially antiproliferative, polyphenolic compounds available naturally from the plant *Alpinia blepharocalyx*.[7] Recently, a great deal of interest in the chemistry of privileged biomolecules of this family, e.g., calyxin I and its related compounds, has been seen in the literature, in both the partial and total syntheses of analogous systems and compounds[8] that contain a pyrano-fused pyran framework. To date, very few reports have appeared on calyxin and calyxin-analogous scaffolds relative to other pyrano-chromene systems that belong to a class of compounds with a pyrano[3,4-*c*]chromene fusion. Li and co-workers have reported stereoselective synthesis of racemic pyranochromenes **A** (R = Ph, R′ = H) using the Prins–Friedel–Crafts reaction. On the other hand, a stepwise synthetic protocol for analogous systems (R = R′ = *p*-Me-phenyl) was given by Mead and co-workers. Willis and co-

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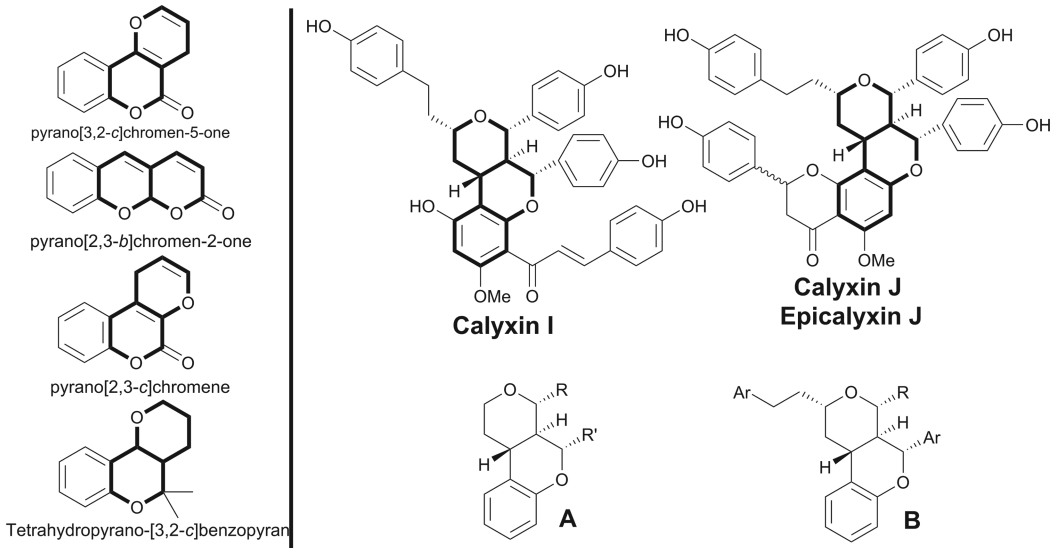

Figure 1. Tetrahydropyranochromene framework from *Alpinia blepharocalyx* and reported synthetic fragments.

workers reported a single-pot synthesis of pyranochromenes **B** (R = aryl, ethyl) using trimethylsilyl trifluoromethanesulfonate.[9] Construction of this system by developing an efficient synthetic methodology is therefore desirable and is an interesting area of synthetic organic chemistry in support of the drug discovery program for the development of many new bioactive scaffolds.

A highly atom economic, efficient, and environmentally friendly method has been the prime synthetic target to be achieved by chemists for synthesizing complex heterocycles over the last few decades.[10] Domino strategies[11] in this context seem to have been widely explored by coupling Knoevenagel transformation with *hetero*-Diels–Alder,[12] ene,[13] allylsilane cyclization,[14] and 1,3-dipolar cycloaddition[15] reactions in the development of cascade synthetic routes for the synthesis of a diverse range of bioactive fused-ring systems. In the same way, imine[16] generation coupled with *hetero*-Diels–Alder transformation happens to be an interesting example of a growing research area in synthetic organic chemistry. Hydroxylation-oxidation Diels–Alder,[17] Sakurai Carbonyl-ene,[18] Pictet–Spengler-ene,[19] alkyl radical addition-aldol,[20] Michael-aldol,[21] and Claisen–Schmidt–Michael[22] reactions are other domino routes that appear in the literature. To the best of our knowledge, aldol condensation coupled to the *hetero*-Diels–Alder reaction remains a very rarely employed synthetic sequence involving the use of a mono ketone unit relative to the domino Knoevenagel-*hetero*-Diels–Alder sequence, which utilizes diketone units.[23] Furthermore, this protocol in general remains applicable to cyclic ketones, which reveal methylene hydrogen activation through C–O carbon-linked methylene carbon. As poorly enolizable CH-activated compounds (pK_a = 19),[24] monoketones, i.e., acetophenone, are prone to show less reactivity toward aldehyde relative to that of 1,3-diketone units, which may have kept this area of research unattended. Notably, assemblies of cyclic and heterocyclic diketones with aldehyde substrates, including our recently studied typical combination diketone with olefin-tethered ketone,[25] have been widely reported in the literature employing domino Knoevenagel-*hetero*-Diels–Alder reactions. In the present work, we demonstrate a domino Aldol-*hetero*-Diels–Alder reaction in the presence of catalyst DBU in glycerol, which is used efficiently for the synthesis of new pyrano[3,4-*c*]chromenes that are analogous to the core tricyclic frameworks of calyxins.

The use of glycerol in the development of new and innovative processes[26] has seen great success in the past few years, as it is associated with many advantages over conventional volatile organic solvents, which are associated with the generation of hazardous wastes. Produced at the end of hydrolysis and trans-esterification of fats, glycerol is an alternative feed source with never-ending resources. As a nonflammable and biodegradable material, it fulfills almost all of the green chemistry principles of being used as a solvent.[27] Preferable over water, especially when hydrophobic substrates are employed, this medium with polar and nonpolar nature allows dissolution of a number of inorganic salts, acids, bases, enzymes, transition metal complexes, and even water-immiscible organic compounds. Not only this, it also helps reaction products to be singled out by simple liquid–liquid phase extraction due to its immiscible nature with hydrophobic ethers and hydrocarbons. Moreover, pharmaceutically active ingredients could be synthesized in glycerol, where little care is required to handle and store them due to the nontoxic nature of this medium in addition to its high boiling point (290 °C). In the present work, we are therefore interested in developing the DAHDA synthetic sequence using glycerol as an effective reaction medium, taking into account the advantages described above. Transformations such as Pd-catalyzed Heck reactions,[28] Suzuki[28a] cross-coupling transformations by Perin[29] and others,[28,30] base-[28b] and acid-[29a] promoted condensations, asymmetric reduction,[28c] catalytic hydrogenation,[28c,30a] multicomponent reactions,[31] and DKHDA,[25g] as reported by us, have successfully been optimized in this medium.

RESULTS AND DISCUSSION

Prenylation of salicylaldehyde **2** and 2-hydroxy-naphthaldehyde **3** gave *O*-prenylated salicylaldehydes **4a** and naphthaldehydes **4b** as requisite aldehyde substrates in higher yields of 95 and 96% (isolated), respectively, with prenyl bromide **1** stirred in the suspension of anhydrous K_2CO_3 in dimethylformamide (DMF) solution at room temperature (Scheme 1).

A combination of 2-prenyloxy-naphthaldehyde **4b** and acetophenone **5a** was taken as a model reaction to study and

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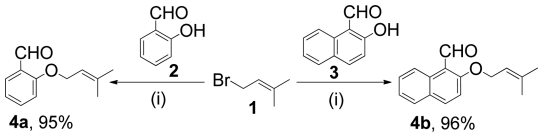
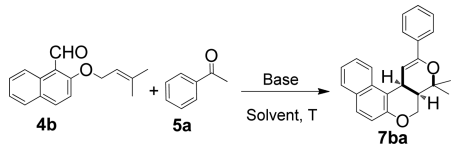
Scheme 1. Reaction Mechanism for 4a and 4b[a]



[a]Reagents and Conditions: (i) DMF, K_2CO_3, RT, 8−10 h.

optimize the reaction conditions (Table 1). The reaction was first examined in the presence of 50% KOH in water at reflux. It

Table 1. Reaction Condition Optimization[a]



entry	catalyst (25 mol %)	solvent	T (°C)	time (h)[b]	yield (%)[c]
1	50% KOH	water	reflux	72	70
2	piperidine	water	reflux	18	70
3	piperidine	ethanol	reflux	15	*d*
4	DBU	water	reflux	12	75
5	DBU	toluene	reflux	24	
6	K_2CO_3	*N*,*N*-dimethylformamide	120	48	15
7	DBU	ethylene glycol	120	7	65
8	piperidine	glycerol	120	7	78
9	TEA	glycerol	120	20	*d*
10	L-proline	glycerol	120	20	*d*
11	DBU	glycerol	120	4	89
12	DBU	glycerol	100	7	80
13	DBU (10)	glycerol	120	7	65
14	DBU (15)	glycerol	120	6	76

[a]Reaction conditions: **4b** (0.2 mmol), **5a** (0.2 mmol), and base in solvent (15 mL) stirred at the specified temperature. [b]Determined by TLC. [c]Isolated yields. [d]Aldol intermediate. DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene. TEA = triethylamine.

yielded 70% of the desired products but after prolonged (72 h) stirring (entry 1). We then examined 25 mol % of piperidine in water at reflux.The reaction time was improved, but it failed to improve the yield (entry 2). Using ethanol in place of water as another protic solvent at reflux favored only aldol intermediate generation (entry 3). The aldol intermediate is stable and can be isolated. Thus, all of these results led to the assumption that hydrogen bonds might be playing a role in influencing the reaction more favorably in water than in ethanol, and so water was continued as a solvent in the next optimization testing (entry 4). Both the yield and reaction time were improved in the presence of basic catalyst DBU in refluxing water (entry 4). The performance of catalyst DBU was very poor in toluene, which may be attributed to its aprotic nature (entry 5). Anhydrous K_2CO_3 in DMF was then tried at 120 °C to bring further improvement to the reaction (entry 6). Unfortunately, a very poor yield of desired product (15%) was seen after a long (48 h) reaction time. The reaction time can be shortened in the presence of DBU in ethylene glycol, where it gave 65% yield (entry 7), but the association with undesirable impurities with the products did not encourage its further testing. These issues no longer held in the presence of piperidine in glycerol (entry 8). Other bases such as TEA (entry 9) and L-proline (entry 10) failed to promote this protocol, though they favored the efficient formation of the aldol intermediate. Finally, the combination of catalyst DBU and solvent glycerol worked effectively at 120 °C, giving excellent yield of DAHDA product **7ba** after 4 h.The product yield was affected however by decreasing the temperature and the DBU amount in glycerol (entries 12−14). This observation was therefore considered better in favor of effective electrophilic activation of the aldehyde relative to that in the water.[32] Effective 25 mol % load of DBU in glycerol at 120 °C (entry 11) was used to synthesize other heterocycles **7aa**−**7af** and **7ba**−**7bf** (Scheme 2). The reaction was monitored periodically for its progress by TLC. The reaction mass was poured into water after completion of the reaction. Viscid matter that subsequently came out of the aqueous mixture was extracted thrice with 20 mL portions of ethyl acetate. Combined extracts were then dried over anhydrous Na_2SO_4 and evaporated to dryness. The solid residue obtained was finally purified by column chromatography on silica gel using a hexane/ethyl acetate (9:1, v/v) mixture as an eluent. The proposed structure of the product tetrahydropyrano[3,4-*c*]chromene, **7ba**, was unambiguously confirmed by single-crystal X-ray diffraction data that was also well-supported by IR, ^{1}H NMR, and ^{13}C NMR spectral data. Intermediates **6aa**−**6af** and **6ba**−**6bf** for the corresponding cyclized products **7aa**−**7af** and **7ba**−**7bf** were also isolated (Table 2) and characterized as aldol condensation products. The structure of aldol intermediate **6af** was further confirmed by the single crystal X-ray diffraction data.

A mechanistic pathway of the reaction is shown in Scheme 3. The reaction proceeds with the aldol condensation reaction initially, which is followed by the *hetero*-Diels−Alder reaction, leading to the formation of cyclized products. The stereochemistry of the product is governed by the orientation of prenyl−dienophile toward aldol, oxa-butadiene, and alkene, which are favorable in the reaction. Theoretically, four possible transition states namely *exo-E-anti*, *endo-E-syn*, *endo-Z-anti*, and *exo-Z-syn*[33] are anticipated to materialize from the exo and endo orientations of dienophile toward aldol *E*-ene and *Z*-ene intermediates. Out of these, *endo-Z-anti* and *exo-Z-syn* did not have the chance to appear in the present case, as all of the isolated aldol intermediates are identified with *E* geometry, as confirmed by ^{1}H NMR data. Here, the *J* value of both of the aldol alkene protons is found in the 15.6−18 Hz range for their characteristic signals, with one at δ 7.76−8.32 ppm and the second at δ 8.11−8.65 ppm, confirming the *E* geometry of the intermediate. The single-crystal X-ray diffraction data of representative **6af** (Scheme 3) confirmed the same unambiguously. Severe angle strain and unfavorable steric interactions are other strong reasons to exclude the possibility of the *endo-Z-anti* state.[34] Thus, *exo-E-anti* and *endo-E-syn* are the only states that might take part in governing the stereochemistry of the products. ^{1}H NMR and nuclear Overhauser effect spectroscopy (NOESY) data in combination with the single-crystal X-ray diffraction study of representative product **7ba**, however, confirmed the *cis* relationship between pyranopyranyl bridgehead protons Ha and Hb, ruling out the *exo-E-anti* transition, a state that leads to *trans*-fused cyclized product formation. 1,3-Allylic strain[35] due to an sp^2 geminal effect further rules out the possibility of the *exo-E-anti* state. The reaction was therefore concluded to occur through the most favored *endo-E-syn* transition state[36] out of the four possible transition states, leading to the formation of *cis* products in all cases. Here, aldol

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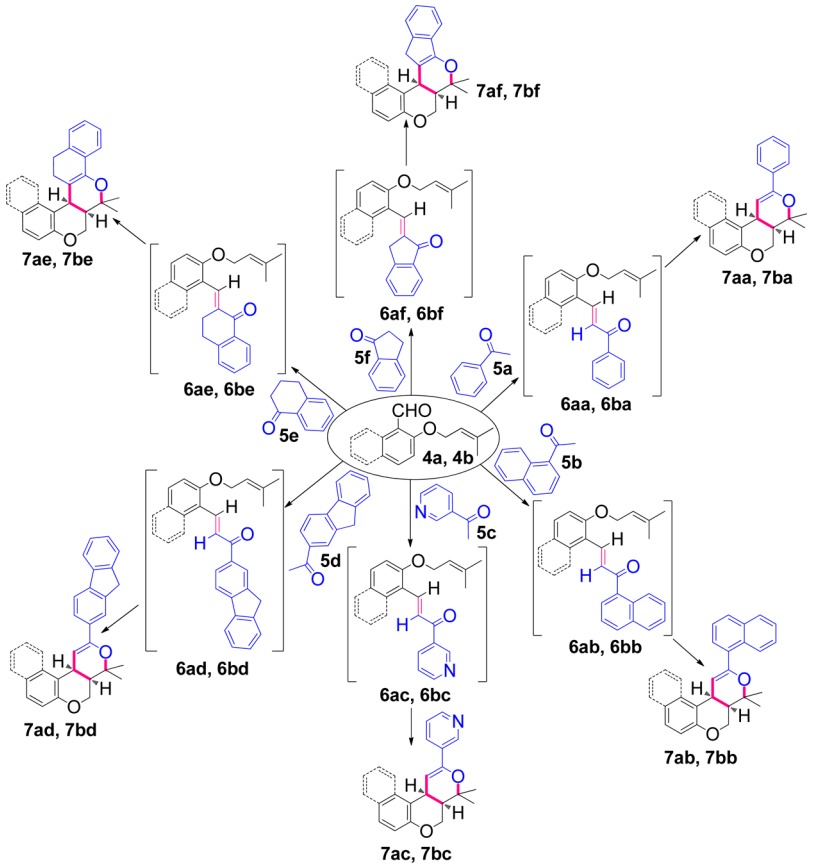
Scheme 2. Synthesis of Aldol Intermediates 6aa−6af and 6ba−6bf and their corresponding pyrano[3,4-*c*]chromene derivatives 7aa−7af and 7ba−7bf[a]



[a]Reagents and conditions: DBU in glycerol at 120 °C.

Table 2. Synthesized Aldol Intermediates 6aa−6af and 6ba−6bf and their corresponding DAHDA products 7aa−7af and 7ba−7bf

entry	aldol intermediate	time (h)	yield (%)[a]	entry	product	time (h)	yield (%)[a]
1	**6aa**	2.0	87	13	**7aa**	4.5	80
2	**6ab**	2.0	89	14	**7ab**	5.0	78
3	**6ac**	2.5	84	15	**7ac**	5.5	75
4	**6ad**	3.0	90	16	**7ad**	6.5	76
5	**6ae**	1.5	89	17	**7ae**	4.5	79
6	**6af**	2.5	88	18	**7af**	5.0	80
7	**6ba**	1.5	91	19	**7ba**	4.0	89
8	**6bb**	2.0	86	20	**7bb**	4.5	85
9	**6bc**	2.5	85	21	**7bc**	5.0	82
10	**6bd**	2.0	82	22	**7bd**	5.5	80
11	**6be**	1.5	91	23	**7be**	3.5	84
12	**6bf**	2.0	90	24	**7bf**	4.0	83

[a]Isolated yield.

oxabutadiene and tethered olefin could be seen interacting well with each other (Scheme 3).

A doublet appearing at δ 3.58−4.58 ppm with a J value in the 3.2−5.6 Hz range can be assigned to a pyranopyranyl bridge-head proton Ha, oriented *cis* to another bridge-head proton Hb, which appeared as multiplet at δ 1.90−2.31 ppm. Pyran alkene CH proton showed a singlet in the δ 5.37−5.74 ppm range in all heterocycles except **7ae**−**7af** and **7be**−**7bf**. There is no alkene CH proton in **7ae**−**7af** or **7be**−**7bf** due to participation of this proton in the fusion. Although protons of methyl attached to the pyran ring showed a singlet at δ 1.28−1.84 ppm, pyranyl-OCH_2 protons appeared at multiplets in the δ 3.61−4.62 ppm range in all compounds. Increased coupling constant J values of the methylene protons to an exceptionally larger magnitude (~22) can be attributed to a rigid disposition of these protons with respect to an adjacent π system in compounds **7af** and **7bf** derived from the monoketone indanone.[37]

Compound **7ba** crystallizes in the monoclinic space group $P21/c$ with the following unit-cell parameters: a = 11.7252(2), b = 12.2681(2), c = 12.3225(3) Å, β = 97.388(2)°, and Z = 4. An ORTEP view with atomic labeling is shown in Figure 2.

The recyclability of glycerol was tested at least three times for the reaction after it was recovered from the reaction mass. Glycerol was recovered using the following treatments. The reaction mass was first poured into water, allowing crude product to appear insoluble and hence be extractable with ethyl acetate. The glycerol−water mixture thus left was heated at 100 °C under reduced pressure to remove water. This recovered glycerol was then reused for the reaction.

CONCLUSIONS

In summary, we demonstrated the synthesis of many new tricyclic pyrano[3,4-*c*]chromene derivatives via a domino aldol/*hetero*-Diels−Alder reaction in the presence of catalyst DBU in glycerol, which has rarely been studied. The use of enolizable CH-activated acyclic monoketone in the present work is

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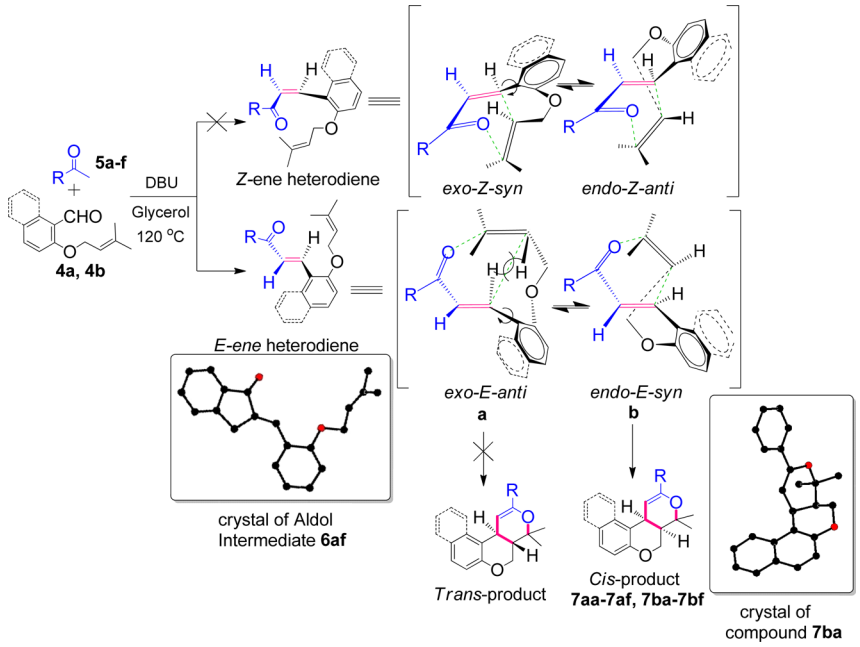
Scheme 3. Proposed Reaction Mechanism



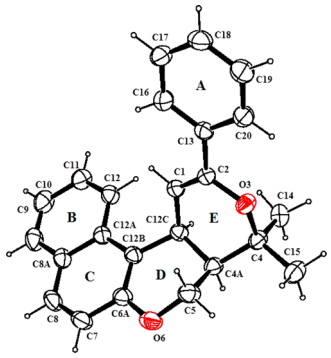


Figure 2. ORTEP view of compound **7ba** with displacement ellipsoids drawn at the 40% probability level.

advantageous over the DKHDA protocol to construct the core structure, which is analogous to the tricyclic pyrano[3,4-*c*]chromene framework present in calyxins known to exhibit strong antiproliferative activity. The DKHDA approach has been explored largely with cyclic or heterocyclic diketone units, generating mostly a tetracyclic pyran framework with the aldehyde substrate, as compared to the present protocol. Glycerol employed in the present study worked not only as an efficient reaction medium but also as a recyclable medium, which can simply be reused at least three times in the same synthetic sequence without losing its activity.

EXPERIMENTAL SECTION

General Considerations. All commercially available reagents, including solvents, were used without purification. All recorded melting points are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded at 400 MHz for ^{1}H NMR and 100 MHz for ^{13}C NMR as solutions in $CDCl_3$ unless otherwise indicated. Chemical shift values are expressed in parts per million (ppm, δ) and referenced to the residual protic solvent. Coupling constants are expressed in Hertz (Hz). Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; and m, multiplet. The degree of substitution (C, CH, CH_2, and CH_3) was determined by the APT method. Elemental analysis was carried out with an elemental analyzer. The ESI mass spectra were measured on a mass spectrometer. TLC was performed on precoated silica plates, and spots were detected either by means of UV (254 nm, 366 nm), permanganate solution [$KMnO_4$ (3 g), K_2CO_3 (20 g), NaOH (5 mL, 5% in H_2O), H_2O (300 mL)], or 2,4-dinitro phenyl hydrazine solution [2,4-DNP (12 g), concd H_2SO_4 (6 mL), water (8 mL), EtOH (20 mL)].

General Procedure for Synthesis of *O*-Prenylated Aldehydes 4a and 4b. To a stirred solution of **2** or **3** (10 mmol; 1.22 g of **2**, 1.72 g of **3**) suspended in anhydrous potassium carbonate (15 mmol, 2.07 g) in DMF (25 mL) was added dropwise a solution of prenyl bromide **1** (13 mmol, 1.94 g) prepared in DMF (5 mL). The mixture was stirred further at room temperature until the reaction was complete, as confirmed by TLC (10−12 h). The reaction mass gave products **4a** and **4b** when poured into 100 g of ice with constant stirring. Oily product **4a** was extracted with three 25 mL diethyl ether portions. The combined ether extracts were dried using anhydrous sodium sulfate and evaporated to remove ether to obtain aldehyde **4a**. The yield of **4a** was 95%, and the bp was 203−206 °C. Solid product **4b** was filtered, washed with three 10 mL portions of cold water, and dried at room temperature. The yield of **4b** was 96%, and the mp was 58−60 °C.

General Experimental Procedure for the Synthesis of Aldol Intermediates (6aa−6af and 6ba−6bf) and Cyclized Products Pyrano[3,4-*c*]chromenes (7aa−7af and 7ba−7bf). A mixture of acetophenone (0.240 g of **5a**), 1-aceto-naphthone (0.340 g of **5b**), 3-acetylpyridine (0.242 g of **5c**), 2-acetyl fluorene (0.416 g of **5d**), 1-tetralone (0.292 g of **5e**), or 1-indanone (0.264 g of **5f**) and *O*-prenylated salicylaldehyde (0.380 g of **4a**) or *O*-prenylated naphthaldehyde (0.480 g of **4b**) in equimolar amounts (2 mmol) was put in glycerol (15 mL) in a round-bottom flask, and a catalytic amount of DBU (25 mol %) was added. The resulting reaction mass was then heated at 120 °C and continuously monitored

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for the formation of the aldol intermediate by TLC. Heating was stopped after confirming the formation of aldol intermediate by TLC (**6aa**−**6af** and **6ba**−**6bf**). The reaction mass was poured into water, and the crude product was extracted thrice with ethyl acetate. The content of combined ethyl acetate extracts was dried over anhydrous Na_2SO_4 and evaporated. The desired product left in the residue was purified further by column chromatography on silica gel using an ethyl acetate/*n*-hexane mixture of appropriate polarity as an eluent giving pure intermediate product (**6aa**−**6af** and **6ba**−**6bf**). The glycerol−water mixture that was left after the extraction of the crude product with ethyl acetate was heated at 100 °C under reduced pessure to remove water. This recovered glycerol was reused again for the reaction.

For cyclized products **7aa**−**7af** and **7ba**−**7bf** to be accessed, the reaction was continued further to convert the corresponding Aldol intermediates into *hetero*-Diels−Alder products, as monitered by TLC. The workup and purification described here are similar to those applied to the isolation of aldol intermediates. All of the aldol intermediates and their corresponding products were characterized on the basis of their mass, IR, ^{1}H NMR, and ^{13}C NMR spectral data.

*2-((3-Methylbut-2-en-1-yl)oxy)benzaldehyde (**4a**).* Yellow oil, yield 95% (1807.2 mg), bp 203−206 °C; δ_H (400 MHz, $CDCl_3$) 1.75 (s, 3H), 1.80 (s, 3H), 4.63 (d, J = 6.8 Hz, 2H), 5.49 (m, 1H), 7.00 (m, 2H), 7.52 (m, 1H), 7.82 (m, 1H), 10.49 (s, 1H); δ_C (100 MHz, $CDCl_3$) 18.3, 25.7, 65.5, 113.0, 119.0, 120.5, 125.2, 128.2, 135.8, 138.6, 161.4, 189.9; anal. calcd for $C_{12}H_{14}O_2$ C 75.76, H 7.42; found C 75.53, H 7.71; m/z (ESI) 191.2 $[M + H]^+$.

*2-((3-Methylbut-2-en-1-yl)oxy)-1-naphthaldehyde (**4b**).* Creamy white solid, yield 96% (2306.9 mg), mp 58−60 °C; δ_H (400 MHz, $CDCl_3$) 1.80 (s, 3H), 1.83 (s, 3H), 4.79 (d, J = 6.4 Hz, 2H), 5.55 (t, J = 6.8 Hz, 1H), 7.28−8.06 (m, 5H), 9.30 (d, J = 8.8 Hz, 1H), 10.92 (m, 1H); δ_C (100 MHz, $CDCl_3$) 18.3, 25.8, 65.6, 114.2, 117.3, 118.9, 124.7, 125.0, 128.1, 128.6, 129.8, 131.7, 137.3, 139.3, 163.7, 192.5; anal. calcd for $C_{16}H_{16}O_2$ C 79.97, H 6.71; found C 79.63, H 6.95; m/z (ESI) 241.3 $[M + H]^+$.

*(E)-3-(2-((3-Methylbut-2-en-1-yl)oxy)phenyl)-1-phenylprop-2-en-1-one (**6aa**).* Yellow solid, yield 87% (508.8 mg), mp 60−62 °C; ν_{max} (cm^{-1}) 2927, 2828, 1679, 1600, 1488, 1455, 1360, 1290, 1268, 1230, 1199, 1161, 1120, 1092, 1051, 999, 976, 955, 909, 853, 753, 741, 687; δ_H (400 MHz, $CDCl_3$) 1.79 (s, 3H), 1.86 (s, 3H), 4.63 (d, J = 6.8 Hz, 2H), 5.60 (tt, J = 6.4, J = 1.2 Hz, 1H), 6.97−7.65 (m, 7H), 7.80 (d, J = 16 Hz, 1H), 8.04−8.06 (m, 2H), 8.12 (d, J = 15.6 Hz, 1H); δ_C (100 MHz, $CDCl_3$) 18.3, 25.8, 65.3, 112.5, 119.5, 120.7, 123.0, 124.2, 128.5, 130.2, 131.6, 132.5, 138.5, 138.6, 140.9, 158.4, 191.0; anal. calcd for $C_{20}H_{20}O_2$ C 82.16, H 6.89; found C 82.45, H 6.60; m/z (ESI) 293.1 $[M + H]^+$.

*(E)-3-(2-((3-Methylbut-2-en-1-yl)oxy)phenyl)-1-(naphthalen-1-yl)prop-2-en-1-one (**6ab**).* Yellow liquid, yield 89% (609.6 mg); ν_{max} (cm^{-1}) 2928, 2828, 1680, 1602, 1481, 1457, 1358, 1293, 1271, 1236, 1197, 1160, 1125, 1090, 1058, 994, 972, 950, 901, 850, 758, 746, 688; δ_H (400 MHz, $CDCl_3$) 1.70 (s, 3H), 1.78 (s, 3H), 4.55 (d, J = 6.8 Hz, 2H), 5.47 (t, J = 6.4 Hz, 1H), 6.91−7.99 (m, 11H), 8.11 (d, J = 16.4 Hz, 1H), 8.52 (d, 1H); δ_C (100 MHz, $CDCl_3$) 18.6, 26.1, 65.4, 112.7, 119.5, 120.8, 124.0, 124.6, 126.0, 126.4, 127.3, 127.4, 127.5, 128.5, 129.5, 130.7, 131.6, 132.0, 134.1, 137.6, 138.2, 141.7, 158.0, 195.9; anal. calcd for $C_{24}H_{22}O_2$ C 84.18, H 6.48; found C 84.42, H 6.25; m/z (ESI) 343.2 $[M + H]^+$.

*(E)-3-(2-((3-Methylbut-2-en-1-yl)oxy)phenyl)-1-(pyridin-3-yl)prop-2-en-1-one (**6ac**).* Yellow solid, yield 84% (492.9 mg), mp 57−59 °C; ν_{max} (cm^{-1}) 2924, 2854, 1720, 1659, 1598, 1568, 1488, 1451, 1414, 1381, 1332, 1281, 1245, 1199, 1164, 1123, 1085, 1051, 996, 978, 860, 813, 750, 703; δ_H (400 MHz, $CDCl_3$) 1.79 (s, 3H), 1.87 (s, 3H), 4.65 (d, J = 6.8 Hz, 2H), 5.59 (m, 1H), 6.98−7.65 (m, 5H), 7.76 (d, J = 15.6 Hz, 1H), 8.13 (d, J = 15.6 Hz, 1H), 8.30 (m, 1H), 8.81 (m, 1H), 9.24 (d, 1H); δ_C (100 MHz, $CDCl_3$) 18.8, 25.9, 65.3, 112.5, 119.3, 120.8, 122.4, 123.5, 123.8, 130.6, 132.0, 133.9, 135.9, 138.8, 142.2, 149.9, 153.0, 158.5, 189.8; anal. calcd for $C_{19}H_{19}NO_2$ C 77.79, H 6.53, N 4.77; found C 77.54, H 6.81, N 4.49; m/z (ESI) 294.1 $[M + H]^+$.

*(E)-1-(9H-Fluoren-2-yl)-3-(2-((3-methylbut-2-en-1-yl)oxy)-phenyl)prop-2-en-1-one (**6ad**).* Yellow solid, yield 90% (684.9 mg), mp 107−109 °C; ν_{max} (cm^{-1}) 2927, 2828, 1678, 1568, 1488, 1454, 1360, 1290, 1230, 1161, 1093, 1051, 999, 853, 754; δ_H (400 MHz, $CDCl_3$) 1.81 (s, 3H), 1.88 (s, 3H), 4.01 (s, 2H), 4.65 (d, J = 6.4 H_Z, 2H), 5.63 (s, 1H), 6.98−7.68 (m, 7H), 7.86 (d, J = 14.8 H_Z, 1H), 7.88−8.14 (m, 3H), 8.16 (d, J = 16 H_Z, 1H), 8.26 (s, 1H); δ_C (100 MHz, $CDCl_3$) 18.3, 25.9, 36.9, 65.3, 112.5, 119.5, 119.7, 120.7, 120.8, 123.2, 124.4, 125.3, 127.1, 127.9, 130.1, 131.5, 137.1, 138.4, 140.5, 140.7, 143.4, 144.5, 146.0, 158.4, 190.7; anal. calcd for $C_{27}H_{24}O_2$ C 85.23, H 6.36; found C 85.46, H 6.59; m/z (ESI) 381.2 $[M + H]^+$.

*(E)-2-(2-((3-Methylbut-2-en-1-yl)oxy)benzylidene)-3,4-dihydronaphthalen-1(2H)-one (**6ae**).* Yellow liquid, yield 89% (566.8 mg); ν_{max} (cm^{-1}) 2926, 2827, 1675, 1603, 1481, 1451, 1367, 1295, 1272, 1235, 1194, 1160, 1122, 1091, 1056, 990, 971, 957, 906, 857, 750, 747, 682; δ_H (400 MHz, $CDCl_3$) 1.76 (s, 3H), 1.80 (s, 3H), 2.95 (t, 2H), 3.08 (t, 2H), 4.60 (d, J = 6.4 Hz, 2H), 5.52 (t, 1H), 6.97−7.02 (m, 2H), 7.25−7.51 (m, 5H), 8.08 (s, 1H), 8.19 (m, 1H); δ_C (100 MHz, $CDCl_3$) 18.3, 25.8, 27.7, 29.1, 65.5, 112.2, 119.9, 120.0, 125.3, 126.9, 128.1, 128.2, 130.1, 130.3, 133.1, 133.6, 135.3, 137.5, 143.5, 157.7, 188.0; anal. calcd for $C_{22}H_{22}O_2$ C 82.99, H 6.96; found C 82.76, H 7.29; m/z (ESI) 319.2 $[M + H]^+$.

*(E)-2-(2-((3-Methylbut-2-en-1-yl)oxy)benzylidene)-2,3-dihydro-1H-inden-1-one (**6af**).* Yellow solid, yield 88% (535.7 mg), mp 89−91 °C; ν_{max} (cm^{-1}) 2925, 2828, 1670, 1609, 1487, 1455, 1366, 1299, 1270, 1233, 1192, 1168, 1120, 1094, 1058, 995, 974, 959, 902, 851, 757, 740, 687; δ_H (400 MHz, $CDCl_3$) 1.78 (s, 3H), 1.82 (s, 3H), 4.01 (s, 2H), 4.63 (d, J = 6.4 Hz, 2H), 5.54 (tt, J = 6.4 Hz, 1.2 Hz, 1H), 6.96−7.06 (m, 2H), 7.34−7.71 (m, 5H), 7.92 (d, 1H), 8.19 (t, 1H); δ_C (100 MHz, $CDCl_3$) 18.3, 25.8, 32.4, 65.5, 112.5, 119.7, 120.4, 124.3, 124.8, 126.1, 127.5, 129.0, 129.8, 131.0, 134.4, 134.6, 137.8, 138.3, 149.8, 158.5, 194.4; anal. calcd for $C_{21}H_{20}O_2$ C 82.86, H 6.62; found C 82.59, H 6.86; m/z (ESI) 305.1 $[M + H]^+$.

*(E)-3-(2-((3-Methylbut-2-en-1-yl)oxy)naphthalen-1-yl)-1-phenylprop-2-en-1-one (**6ba**).* Yellow solid, yield 91% (623.2 mg), mp 113−115 °C; ν_{max} (cm^{-1}) 2960, 2908, 2857, 1653, 1623, 1598, 1586, 1559, 1501, 1455, 1438, 1377, 1353, 1283, 1267, 1180, 1153, 1110, 1091, 1017, 979, 911, 852, 811, 799, 777, 753, 712, 658; δ_H (400 MHz, $CDCl_3$) 1.81 (s, 3H), 1.87 (s, 3H), 4.79 (d, J = 6.8 Hz, 2H), 5.68 (t, J = 6.4 Hz, 1H), 7.34−8.34 (m, 12H), 8.60 (d, J = 16 Hz, 1H); δ_C (100 MHz, $CDCl_3$) 18.3, 25.9, 66.1, 114.3, 117.5, 119.5, 123.3, 124.0, 126.8, 127.1, 127.5, 127.7, 128.5, 128.6, 128.7, 129.1, 131.8, 132.5, 133.4, 137.5, 138.8, 139.0, 156.9, 191.2; anal. calcd for $C_{24}H_{22}O_2$ C 84.18, H 6.48; found C 84.34, H 6.25; m/z (ESI) 343.2 $[M + H]^+$.

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*(E)-3-(2-((3-Methylbut-2-en-1-yl)oxy)naphthalen-1-yl)-1-(naphthalen-1-yl)prop-2-en-1-one (**6bb**).* Yellow solid, yield 86% (675.1 mg), mp 98−100 °C; ν_{max} (cm^{-1}) 2962, 2901, 2854, 1649, 1619, 1593, 1580, 1555, 1508, 1450, 1431, 1374, 1348, 1276, 1262, 1178, 1149, 1108, 1097, 1022, 977, 917, 856, 814, 795, 776, 745, 710, 655; δ_H (400 MHz, $CDCl_3$) 1.75 (s, 3H), 1.78 (s, 3H), 4.76 (d, J = 6.4 Hz, 2H), 5.54 (tt, J = 6.8, J = 1.2 Hz, 1H), 7.31−7.64 (m, 6H), 7.79 (d, J = 16 Hz, 1H), 7.83−8.20 (m, 6H), 8.41 (d, J = 16 Hz, 1H), 8.52 (d, 1H); δ_C (100 MHz, $CDCl_3$) 18.3, 25.8, 66.2, 114.3, 117.3, 119.4, 123.3, 124.0, 124.6, 126.1, 126.4, 127.4, 127.5, 127.5, 128.4, 128.7, 129.0, 130.7, 131.6, 131.7, 132.0, 133.1, 133.9, 137.6, 138.6, 139.0, 156.7, 196.4; anal. calcd for $C_{28}H_{24}O_2$ C 85.68, H 6.16; found C 85.43, H 6.42; m/z (ESI) 392.1 $[M]^+$.

*(E)-3-(2-((3-Methylbut-2-en-1-yl)oxy)naphthalen-1-yl)-1-(pyridin-3-yl)prop-2-en-1-one (**6bc**).* Yellow solid, yield 85% (583.8 mg), mp 106−108 °C; ν_{max} (cm^{-1}) 3033, 2933, 1658, 1599, 1558, 1512, 1462, 1414, 1381, 1353, 1294, 1274, 1246, 1190, 1150, 1099, 1056, 1022, 1004, 972, 914, 851, 813, 790, 737, 710, 680; δ_H (400 MHz, $CDCl_3$) 1.82 (s, 3H), 1.89 (s, 3H), 4.81 (d, J = 6.8 Hz, 2H), 5.67 (tt, J = 6.8, J = 1.2 Hz, 1H), 7.35−7.93 (m, 6H), 8.10 (d, J = 15.6 Hz, 1H), 8.30−8.38 (m, 2H), 8.65 (d, J = 15.6 Hz, 1H), 8.83 (s, 1H), 9.30 (s, 1H); δ_C (100 MHz, $CDCl_3$) 18.3, 25.8, 66.0, 114.1, 116.8, 119.3, 123.1, 123.6, 124.1, 125.7, 127.7, 128.7, 129.0, 132.4, 133.5, 134.0, 135.9, 138.5, 139.5, 150.0, 152.9, 157.4, 189.8; anal. calcd for $C_{23}H_{21}NO_2$ C 80.44, H 6.16, N 4.08; found C 80.72, H 5.86, N 4.28; m/z (ESI) 342.2 $[M - H]^+$.

*(E)-1-(9H-Fluoren-2-yl)-3-(2-((3-methylbut-2-en-1-yl)oxy)-naphthalen-1-yl)prop-2-en-1-one (**6bd**).* Yellow solid, yield 82% (706.1 mg), mp 101−103 °C; ν_{max} (cm^{-1}) 2965, 2907, 2850, 1656, 1623, 1598, 1576, 1551, 1502, 1446, 1435, 1370, 1350, 1279, 1264, 1180, 1153, 1113, 1099, 1028, 971, 910, 850, 811, 790, 769, 748, 715, 651; δ_H (400 MHz, $CDCl_3$) 1.83 (s, 3H), 1.89 (s, 3H), 4.02 (s, 2H), 4.81 (d, J = 6.8 Hz, 2H), 5.70 (tt, J = 6.8, J = 1.6 Hz, 1H), 7.36−8.18 (m, 13H), 8.32 (d, J = 18 Hz, 1H), 8.61 (d, J = 15.6 Hz, 1H); δ_C (100 MHz, $CDCl_3$) 18.4, 26.1, 37.1, 66.4, 114.4, 119.6, 119.7, 120.9, 123.5, 124.0, 125.3, 125.4, 127.1, 127.2, 127.4, 127.9, 128.0, 128.6, 129.1, 131.7, 133.4, 137.2, 138.9, 140.7, 143.4, 144.5, 146.0, 156.8, 166.3, 190.9; anal. calcd for $C_{31}H_{26}O_2$ C 86.48, H 6.09; found C 86.69, H 6.33; m/z (ESI) 431.1 $[M + H]^+$.

*(E)-2-((2-((3-Methylbut-2-en-1-yl)oxy)naphthalen-1-yl)-methylene)-3,4-dihydronaphthalene-1(2H)-one (**6be**).* Yellow solid, yield 91% (670.6 mg), mp 117−119 °C; ν_{max} (cm^{-1}) 2925, 2828, 1670, 1609, 1480, 1456, 1366, 1291, 1278, 1242, 1199, 1167, 1116, 1093, 1049, 991, 978, 951, 912, 848, 757, 754, 688; δ_H (400 MHz, $CDCl_3$) 1.73 (s, 3H), 1.76 (s, 3H), 2.69 (t, 2H), 2.92 (t, 2H), 4.68 (d, J = 6.4 Hz, 2H), 5.47 (t, J = 6.8 Hz, 1H), 7.25−7.54 (m, 6H), 7.80−7.89 (m, 3H), 8.13 (s, 1H), 8.25 (d, 1H); δ_C (100 MHz, $CDCl_3$) 18.3, 25.7, 28.5, 29.1, 66.6, 115.3, 119.6, 120.1, 123.9, 124.7, 126.7, 126.9, 128.2, 128.3, 128.9, 130.0, 131.5, 132.7, 133.1, 133.7, 137.7, 138.6, 144.2, 154.0, 187.5; anal. calcd for $C_{26}H_{24}O_2$ C 84.75, H 6.57; found C 84.95, H 6.79; m/z (ESI) 369.2 $[M + H]^+$.

*(E)-2-((2-((3-Methylbut-2-en-1-yl)oxy)naphthalen-1-yl)-methylene)-2,3-dihydro-1H-inden-1-one (**6bf**).* Yellow solid, yield 90% (638.0 mg), mp 78−80 °C; ν_{max} (cm^{-1}) 2927, 2826, 1667, 1611, 1485, 1451, 1360, 1297, 1283, 1244, 1200, 1161, 1111, 1097, 1053, 994, 970, 957, 915, 850, 751, 747, 680; δ_H (400 MHz, $CDCl_3$) 1.73 (s, 3H), 1.75 (s, 3H), 3.64 (s, 2H), 4.70 (d, J = 6.8 Hz, 2H), 5.46 (m, 1H), 7.34−7.61 (m, 6H), 7.84−7.97 (m, 4H), 8.15 (m, 1H); δ_C (100 MHz, $CDCl_3$) 18.1, 25.8, 32.1, 66.8, 115.3, 116.3, 119.4, 119.9, 124.0, 124.4, 124.6, 126.1, 127.0, 127.4, 128.4, 129.0, 129.5, 130.5, 132.3, 134.5, 138.6, 139.9, 150.16, 153.4; anal. calcd for $C_{25}H_{22}O_2$ C 84.72, H 6.26; found C 84.51, H 6.14; m/z (ESI) 355.2 $[M + H]^+$.

*4,4-Dimethyl-2-phenyl-4,4a,5,10b-tetrahydropyrano[3,4-c]chromene (**7aa**).* White solid, yield 80% (467.8 mg), mp 142−144 °C; ν_{max} (cm^{-1}) 3062, 2960, 2926, 2873, 1800, 1714, 1680, 1602, 1583, 1533, 1490, 1452, 1380, 1230, 1177, 1117, 1024, 972, 755, 698; δ_H (400 MHz, $CDCl_3$) 1.39 (s, 3H), 1.46 (s, 3H), 2.18 (m, 1H), 3.62 (t, J = 10.4 Hz, 1H), 3.71 (d, J = 5.6 Hz, 1H), 4.41 (d, J = 10.4 Hz, 1H), 5.43 (s, 1H), 6.79−7.54 (m, 9H); δ_C (100 MHz, $CDCl_3$) 25.3, 26.1, 30.9, 37.0, 63.6, 75.2, 100.2, 116.6, 121.2, 124.8, 125.1, 127.3, 127.8, 128.5, 128.6, 130.5, 135.8, 146.9, 154.2; anal. calcd for $C_{20}H_{20}O_2$ C 82.16, H 6.89; found C 81.84, H 7.12; m/z (ESI) 293.1 $[M + H^+]$.

*4,4-Dimethyl-2-(naphthalen-1-yl)-4,4a,5,10b-tetrahydropyrano[3,4-c]chromene (**7ab**).* White solid, yield 78% (534.2 mg), mp 158−160 °C; ν_{max} (cm^{-1}) 3059, 2963, 2928, 2875, 1803, 1711, 1678, 1600, 1586, 1530, 1494, 1450, 1382, 1237, 1174, 1111, 1026, 968, 756, 695; δ_H (400 MHz, $CDCl_3$) 1.59 (s, 3H), 1.74 (s, 3H), 2.25 (m, 1H), 3.87(d, J = 5.6 Hz, 1H), 4.19 (m, 1H), 4.59 (m, 1H), 5.20 (s, 1H), 7.00−7.04 (m, 2H), 7.23−7.33 (m, 2H), 7.44−7.58 (m, 4H), 7.85−7.90 (m, 2H), 8.28 (d, 1H); δ_C (100 MHz, $CDCl_3$) 25.7, 26.2, 29.8, 31.5, 38.4, 63.7, 104.1, 116.7, 121.0, 125.2, 125.6, 125.8, 126.2, 127.1, 127.7, 128.4, 129.0, 129.8, 131.5, 133.8, 134.7, 149.3, 154.3; anal. calcd for $C_{24}H_{22}O_2$ C 84.18, H 6.48; found C 84.44, H 6.23; anal. calcd for $C_{24}H_{22}O_2$ C 84.18, H 6.48; found C 84.44, H 6.23; m/z (ESI) 343.2 $[M + H^+]$.

*3-(4,4-Dimethyl-4,4a,5,10b-tetrahydropyrano[3,4-c]-chromen-2-yl)pyridine (**7ac**).* White solid, yield 75% (440.1 mg), mp 134−136 °C; ν_{max} (cm^{-1}) 3060, 2957, 2925, 2874, 1804, 1712, 1683, 1601, 1586, 1537, 1488, 1455, 1383, 1235, 1179, 1120, 1029, 977, 750, 692; δ_H (400 MHz, $CDCl_3$) 1.39 (s, 3H), 1.46 (s, 3H), 2.06−2.12 (m, 1H), 3.66 (d, J = 6 Hz, 1H), 3.74 (t, J = 11.2 Hz, 1H), 4.33 (m, 1H), 5.33 (m, 1H), 6.77−8.71 (m, 8H); δ_C (100 MHz, $CDCl_3$) 25.3, 26.0, 31.3, 37.5, 63.6, 75.2, 101.1, 114.1, 116.7, 120.9, 122.9, 124.1, 127.8, 129.6, 132.0, 145.3, 146.3, 148.9, 154.2; anal. calcd for $C_{19}H_{19}NO_2$ C 77.79, H 6.53, N 4.77; found C 78.13, H 6.90, N 4.89; m/z (ESI) 294.1 $[M + H^+]$.

*2-(9H-Fluoren-2-yl)-4,4-dimethyl-4,4a,5,10b-tetrahydropyrano[3,4-c]chromene (**7ad**).* White solid, yield 76% (578.4 mg), mp 160−162 °C; ν_{max} (cm^{-1}) 3063, 2950, 2928, 2878, 1810, 1708, 1688, 1600, 1589, 1540, 1482, 1457, 1381, 1239, 1182, 1122, 1033, 971, 756, 697; δ_H (400 MHz, $CDCl_3$) 1.41 (s, 3H), 1.48 (s, 3H), 2.08 (m, 1H),3.67 (d, J = 4.8 Hz, 1H), 3.80 (m, 3H), 4.34 (m, 1H), 5.31 (s, 1H), 6.77−7.70 (m, 11H); δ_C (100 MHz, $CDCl_3$) 25.3, 26.2, 31.5, 36.9, 37.6, 63.8, 74.8, 99.4, 114.1, 116.7, 119.5, 119.9, 120.9, 121.4, 123.7, 124.7, 125.0, 126.7, 126.8, 127.6, 129.7, 141.4, 141.7, 143.2, 143.6, 147.8, 154.2; anal. calcd for $C_{27}H_{24}O_2$ C 85.23, H 6.36; found C 85.61, H 6.73; m/z (ESI) 381.2 $[M + H^+]$.

*14,14-Dimethyl-1,6b,7,8,14,14a-hexahydronaphtho-[3′,4′:5,6]pyrano[3,4-c]chromene (**7ae**).* White solid, yield 79% (503.2 mg), mp 100−102 °C; ν_{max} (cm^{-1}) 3063, 3030, 1947, 1897, 1804, 1634, 1606, 1582, 1491, 1452, 1428, 1381, 1367, 1299, 1277, 1257, 1238, 1144, 1113, 1083, 1056, 1041, 862, 828, 767, 750, 737, 710; δ_H (400 MHz, $CDCl_3$) 1.44 (s, 3H), 1.54 (s, 3H), 2.15 (m, 1H), 2.26 (m, 1H), 2.47 (m, 1H), 2.75 (m, 2H), 3.66 (d, J = 3.2 Hz, 1H), 4.05 (t, J = 11.2 Hz, 1H), 4.46 (dd, J = 10.8, J = 2 Hz, 1H), 6.86−7.55 (m, 8H); δ_C

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(100 MHz, $CDCl_3$) 24.1, 25.7, 26.2, 28.1, 34.8, 37.8, 64.1, 73.8, 106.9, 116.6, 119.3, 121.4, 121.8, 126.2, 126.8, 127.2, 128.2, 132.0, 132.6, 136.0, 141.4, 154.4; anal. calcd for $C_{22}H_{22}O_2$ C 82.99, H 6.96; found C 82.75, H 7.19; *m*/*z* (ESI) 318.2 $[M]^+$.

*7,7-Dimethyl-6a,7,13,13b-tetrahydro-6H-indeno-[2′,1′:5,6]pyrano[3,4-c]chromene (**7af**).* White solid, yield 80% (487.0 mg), mp 166−168 °C; ν_{max} (cm^{-1}) 3060, 3034, 1950, 1899, 1800, 1637, 1608, 1580, 1495, 1450, 1427, 1380, 1368, 1292, 1275, 1255, 1231, 1148, 1112, 1086, 1055, 1040, 863, 829, 760, 756, 731, 711; δ_H (400 MHz, $CDCl_3$) 1.47 (s, 3H), 1.61 (s, 3H), 2.23 (m, 1H), 3.09 (d, *J* = 21.6 Hz, 1H), 3.42 (d, *J* = 22 Hz, 1H), 3.89 (t, *J* = 11.2 Hz, 1H), 3.97 (d, *J* = 4.8 Hz, 1H), 4.45 (d, *J* = 10.4 Hz, 1H), 6.85−7.35 (m, 8H); δ_C (100 MHz, $CDCl_3$) 25.6, 26.0, 32.8, 35.5, 38.6, 63.7, 76.5, 112.6, 116.7, 117.4, 120.3, 123.3, 123.7, 124.9, 126.2, 127.9, 130.8, 139.5, 141.8, 148.0, 154.2; anal. calcd for $C_{21}H_{20}O_2$ C 82.86, H 6.62; found C 82.98, H 6.76; *m*/*z* (ESI) 305.2 $[M + H^+]$.

*4,4-Dimethyl-2-phenyl-4,4a,5,12c-tetrahydrobenzo[f]-pyrano[3,4-c]chromene (**7ba**).* White solid, yield 89% (609.6 mg), mp 194−196 °C; ν_{max} (cm^{-1}) 3061, 1720, 1656, 1619, 1599, 1517, 1464, 1438, 1380, 1368, 1297, 1240, 1131, 1101, 1089, 1072, 1020, 998, 881, 865, 842, 811, 799, 782, 753; δ_H (400 MHz, $CDCl_3$) 1.61 (s, 6H, 2× 4-CH_3), 2.22 (m, 1H, 4a-H), 4.05 (t, *J* = 10.8 Hz, 1H, 5-H), 4.28 (d, *J* = 5.6 Hz, 1H, 12c-H), 4.51 (dd, *J* = 10.8, *J* = 3.6 Hz, 1H, 5-H), 5.59 (d, *J* = 1.2 Hz, 1H, 1-H), 7.09−8.07 (m, 11H, Ar−H); δ_C (100 MHz, $CDCl_3$) 25.6, 26.3, 28.1, 36.8, 63.6, 75.0, 97.6, 115.3, 118.8, 121.9, 123.3, 124.9, 126.7, 128.1, 128.1, 128.4, 129.0, 129.5, 132.6, 135.9, 148.0, 151.6; anal. calcd for $C_{24}H_{22}O_2$ C 84.18, H 6.48; found C 84.39, H 6.11; *m*/*z* (ESI) 342.2 $[M]^+$.

*4,4-Dimethyl-2-(naphthalen-1-yl)-4,4a,5,12c-tetrahydrobenzo[f]pyrano[3,4-c]chromene (**7bb**).* White solid, yield 85% (667.3 mg), mp 214−216 °C; ν_{max} (cm^{-1}) 3057, 1722, 1653, 1623, 1597, 1511, 1462, 1435, 1382, 1367, 1292, 1236, 1128, 1108, 1087, 1068, 1021, 994, 884, 861, 839, 810, 796, 778, 749; δ_H (400 MHz, $CDCl_3$) 1.60 (s, 3H), 1.84 (s, 3H), 2.29 (m, 1H), 4.31 (t, *J* = 11.2 Hz, 1H), 4.37 (d, *J* = 5.6 Hz, 1H), 4.62 (dd, *J* = 10.8, *J* = 3.2 Hz, 1H), 5.37 (s, 1H), 7.13−8.25 (m, 13H); δ_C (100 MHz, $CDCl_3$) 25.9, 26.4, 28.3, 37.1, 63.6, 75.6, 102.0, 115.5, 118.8, 121.9, 123.3, 125.1, 125.5, 125.7, 126.2, 126.7, 127.3, 128.3, 128.4, 128.9, 129.0, 129.5, 131.4, 132.6, 133.8, 134.6, 149.7, 151.7; anal. calcd for $C_{28}H_{24}O_2$ C 85.68, H 6.16; found C 85.40, H 5.86; *m*/*z* (ESI) 392.00 $[M]^+$.

*3-(4,4-Dimethyl-4,4a,5,12c-tetrahydrobenzo[f]pyrano-[3,4-c]chromen-2-yl)pyridine (**7bc**).* White solid, yield 82% (563.2 mg), mp 178−180 °C; ν_{max} (cm^{-1}) 3060, 3041, 1940, 1906, 1640, 1623, 1600, 1568, 1515, 1474, 1432, 1408, 1382, 1370, 1346, 1306, 1294, 1254, 1234, 1190, 1175, 1146, 1131, 1089, 1074, 1027, 1004, 991, 952, 885, 851, 810, 796, 771, 745, 718, 707, 697; δ_H (400 MHz, $CDCl_3$) 1.61 (s, 6H), 2.24 (m, 1H), 4.02 (t, *J* = 10.8 Hz, 1H), 4.29 (d, *J* = 5.6 Hz, 1H), 4.53 (ddd, *J* = 10.8, 3.6, 1.2 Hz, 1H), 5.64 (t, *J* = 1.6 Hz, 1H), 7.09−8.79 (m, 10H); δ_C (100 MHz, $CDCl_3$) 25.6, 26.2, 28.0, 36.7, 63.4, 75.4, 99.1, 114.8, 118.8, 121.7, 122.9, 123.4, 126.9, 128.6, 129.1, 129.5, 131.4, 132.1, 132.5, 145.8, 146.5, 149.1, 151.7; anal. calcd for $C_{23}H_{21}NO_2$ C 80.44, H 6.16, N 4.08; found C 80.19, H 6.39, N 4.31; *m*/*z* (ESI) 344.1 $[M + H]^+$.

*2-(9H-Fluoren-2-yl)-4,4-dimethyl-4,4a,5,12c-tetrahydrobenzo[f]pyrano[3,4-c]chromene (**7bd**).* White solid, yield 80% (688.9 mg), mp 212−214 °C; ν_{max} (cm^{-1}) 3075, 3017, 1908, 1640, 1622, 1599, 1513, 1469, 1455, 1427, 1402, 1382, 1365, 1320, 1256, 1234, 1180, 1141, 1089, 1067, 1055, 1025, 990, 944, 906, 887, 860, 835, 818, 762, 747, 731, 699; δ_H (400 MHz, $CDCl_3$) 1.47 (s, 3H), 1.65 (s, 3H), 2.24 (m, 1H), 3.88 (s, 2H), 4.10 (t, *J* = 11.2 Hz, 1H), 4.32 (d, *J* = 5.2 Hz, 1H), 4.54 (dd, *J* = 10.8, 2.8 Hz, 1H), 5.65 (s, 1H), 7.11−8.12 (m, 13H); δ_C (100 MHz, $CDCl_3$) 25.6, 26.4, 28.2, 36.9, 36.9, 63.6, 75.1, 97.5, 115.4, 118.8, 119.5, 120.0, 121.5, 122.0, 123.3, 123.8, 125.1, 126.8, 126.8, 128.4, 129.1, 129.6, 132.7, 134.6, 141.4, 141.8, 143.2, 143.6, 148.3, 151.7; anal. calcd for $C_{31}H_{26}O_2$ C 86.48, H 6.09; found C 86.19, H 6.34; *m*/*z* (ESI) 430.2 $[M]^+$.

*16,16-Dimethyl-1,8c,9,10,16,16a-hexahydrobenzo[f]-naphtho[3′,4′:5,6]pyrano[3,4-c]chromene (**7be**).* White solid, yield 84% (619.0 mg), mp 170−172 °C; ν_{max} (cm^{-1}) 3061, 3034, 1949, 1894, 1801, 1637, 1609, 1580, 1494, 1458, 1430, 1382, 1366, 1300, 1272, 1251, 1242, 1147, 1116, 1088, 1050, 1037, 868, 821, 762, 754, 744, 711; δ_H (400 MHz, $CDCl_3$) 1.59 (s, 6H), 1.93 (m, 1H), 2.17 (m, 1H), 2.51 (m, 3H), 4.29 (t, *J* = 11.2 Hz, 1H), 4.45 (d, *J* = 3.2 Hz, 1H), 4.55 (ddd, *J* = 10.8, 4, 1.2 Hz, 1H), 7.06−8.03 (m, 10H); δ_C (100 MHz, $CDCl_3$) 24.8, 26.4, 26.6, 28.5, 30.0, 37.2, 63.8, 74.0, 107.7, 114.1, 118.9, 121.6, 122.8, 122.9, 126.2, 126.3, 126.8, 127.2, 128.8, 128.9, 129.0, 132.0, 134.4, 136.4, 141.8, 152.1; anal. calcd for $C_{26}H_{24}O_2$ C 84.75, H 6.57; found C 84.54, H 6.54; *m*/*z* (ESI) 369.2 $[M + H]^+$.

*9,9-Dimethyl-8a,9,15,15b-tetrahydro-8H-benzo[f]indeno-[2′,1′:5,6]pyrano[3,4-c]chromene (**7bf**).* White solid, yield 83% (588.4 mg), mp 231−233 °C; ν_{max} (cm^{-1}) 3065, 3031, 1955, 1899, 1800, 1632, 1612, 1586, 1498, 1460, 1437, 1388, 1360, 1307, 1278, 1250, 1244, 1153, 1114, 1081, 1053, 1044, 861, 820, 768, 753, 748, 717; δ_H (400 MHz, $CDCl_3$) 1.62 (s, 3H), 1.66 (s, 3H), 2.27 (m, 1H), 2.74 (d, *J* = 22 Hz, 1H), 3.50 (dd, *J* = 22.4, 2 Hz, 1H), 4.06 (t, *J* = 11.2 Hz, 1H), 4.52 (ddd, *J* = 10.8, 3.6, 1.2 Hz, 1H), 4.58 (d, *J* = 4 Hz, 1H), 7.07−8.19 (m, 10H); δ_C (100 MHz, $CDCl_3$) 25.9, 26.1, 28.9, 36.3, 37.8, 63.3, 76.5, 112.7, 114.9, 117.3, 118.8, 122.5, 123.2, 123.6, 125.0, 126.1, 126.3, 128.6, 128.8, 129.3, 133.4, 139.1, 141.9, 148.3, 151.7; anal. calcd for $C_{25}H_{22}O_2$ C 84.72, H 6.26; found C 84.91, H 6.48; *m*/*z* (ESI) 355.4 $[M + H]^+$.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00107.

Copies of ^1H and ^{13}C NMR spectra of all of the compounds and NOESY spectra of **7ba** (PDF)

X-ray structure and crystal data of **6af** (CIF)

X-ray structure and crystal data of **7ba** (CIF)

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Notes

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Figure 1 labels **1** and **2** were corrected to **A** and **B** on May 31, 2016.

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