Article

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

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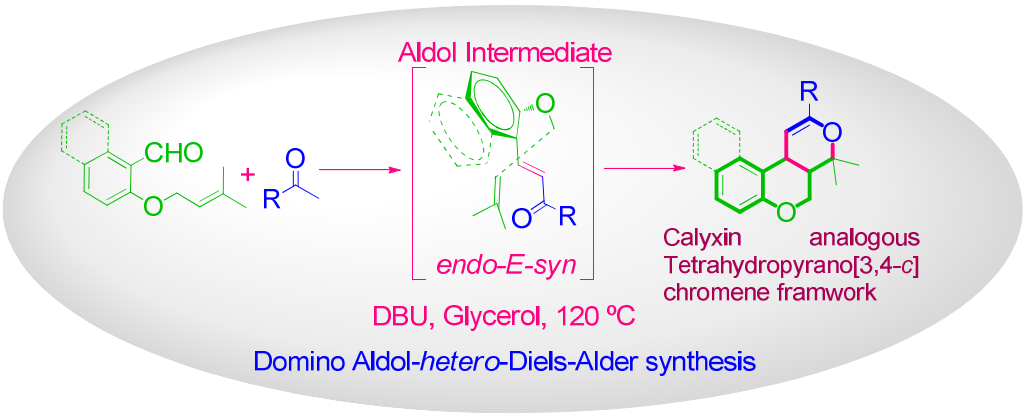


Abstract

The dominoAldol-*hetero*-Diels-Alder (DAHDA) synthesis of some new tricyclic pyrano[3,4-*c*]chromene derivatives has been achieved, successfully after assembling a variety of acyclic or cyclic monoketoneswith prenyl-ether-tethered aldehydes in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU)in glycerol at 120 ºC. Hitherto unreported stereo-chemical outcome of this synthetic sequence was studied and established on the basis of the single-crystal X-ray diffraction data and 2D NMR NOESY spectroscopy,along with the isolation and characterization of the intermediate, Aldolcondensation product.

Introduction

The pyranochromene has gained much prominence worldwide because of its existence as a principal structural, central skeletonin several bioactive natural and unnatural molecular frameworks, as well as in many photosensitive molecular assemblies.[1] Due to a wide spectrum of biological features of these frameworks such as anti-hyperglycemic and anti-oxidant properties, and anti-dyslipidemic, anti-fungal, anti-malarial, anti-cancer, anti-inflammatory, anti-tuberculosis, anti-HIV, antialergic, antiviral, cytotoxic and anti-bacterial activities,[2] class of these candidates has attracted a wider scope of its 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 diseases, AIDS-associated dementia, Schizophrenia, amyotrophic lateral Sclerosis, Huntington's diseases and Parkinson's diseases.[3]Further, the pyranopyranyl core structure is known for conferring a variety of properties on pyranochromene-ring systems through its varied patterns of the fusionexisting in thistricyclic system in the molecules.[4] Pyrano[3,2-*c*]chromene, especially, finds an increasing applicationsin the development of photonic materials, emerging as a promising photochrometic molecular motif with great technological imortance.[5]

Occurrence of pyrano-chromenenucleus could be recognized possibly in number of ways, as shown in **Figure 1**, which ultimately results into several structural arrays or scaffolds which are existing between pyran and chromene units, and each can be disguised by a relative position of two oxygen atoms in pyranopyranyl skeleton.[6]Among these skeletons, pyrano[3,4-*c*]chromeneunit exists in number of potentially anti-proliferative,polyphenolic compoundsavailable naturally from the plants *Alpinia blepherocalyx.*[7] Recently, a great deal of interest in the chemistry of these privileged biomolecules of this family; say Calyxin I and itsrelated compounds, has been seenin the

literature, in both the partial and total syntheses of analogous systems and compounds[8]which contains pyrano-fused pyran framework. To date,a very fewreports have been appeared onCalyxin and Calyxin-analogous scaffolds,relative to other pyrano-chromene systemswhich belongs to a class of compounds with a pyrano[3,4-*c*]chromene fusion. Li and co-workers have reported stereo-selective synthesis ofracemicpyranochromenes**A** (R = Ph, R' = H), using Prins−Friedel−Crafts reaction. On the other hand, a stepwise synthetic protocolfor analogous systems (R = R' =*p*-Me-phenyl) was given by Mead and co-workers. Willis and co-workersreported a single-pot synthesis of pyranochromenes B (R = Aryl, Ethyl) using trimethylsilyl trifluoromethanesulfonate.[9]Construction of this system by developingthe efficient synthetic methodology is therefore desirable and worth interesting area of synthetic organic chemistry, in support of the drug discovery program, with many new bioactive scaffolds.

A highly atom economic, efficientand yet environmentally friendly method has been the prime synthetic target to be achieved by the chemists for synthesizing complex heterocycles,since last few decades.[10] Domino strategies[11]in this context seem to have 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 synthesis of diverse range of bioactive fused-ring systems.In the same way, imine[16] generation coupled with *hetero*-Diels-Alder transformation happened to be interesting example of growing research areas of the 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 appeared in the literature. To the best of our knowledge, Aldolcondensation coupled to the *hetero*-Diels-Alder reactionremained a very rarely employed synthetic sequenceinvolving use of mono ketone unit, relative to domino Knoevenagel-*hetero*-Diels-Alder sequence which utilized diketone units.[23]Further, thisprotocol in general

remained applicable to cyclic ketoneswhich are revealing methylene hydrogen activation through C-O carbon linked methylene carbon.As poor enolizable CH activated compounds (pKa = 19)[24],mono ketones, i.e. acetophenone, are prone to show less reactivity towards aldehyde, relative to 1,3-diketone units, and which might have kept this area unattended. Notably, assemblies of cyclic and heterocyclic diketones with aldehyde substrates including our recently studied typical combination; diketone witholefin tethered ketone,[25]have been widely reported in the literature,employing domino Knoevenagel-*hetero*-Diels-Alder reaction. In present work, we demonstrate domino Aldol-*hetero*-Diels-Alder reaction in the presence of catalyst DBU in glycerol, used efficiently for the synthesis of new pyrano[3,4-*c*]chromenes which are analogous to the core tricyclicframeworks of Calyxins.

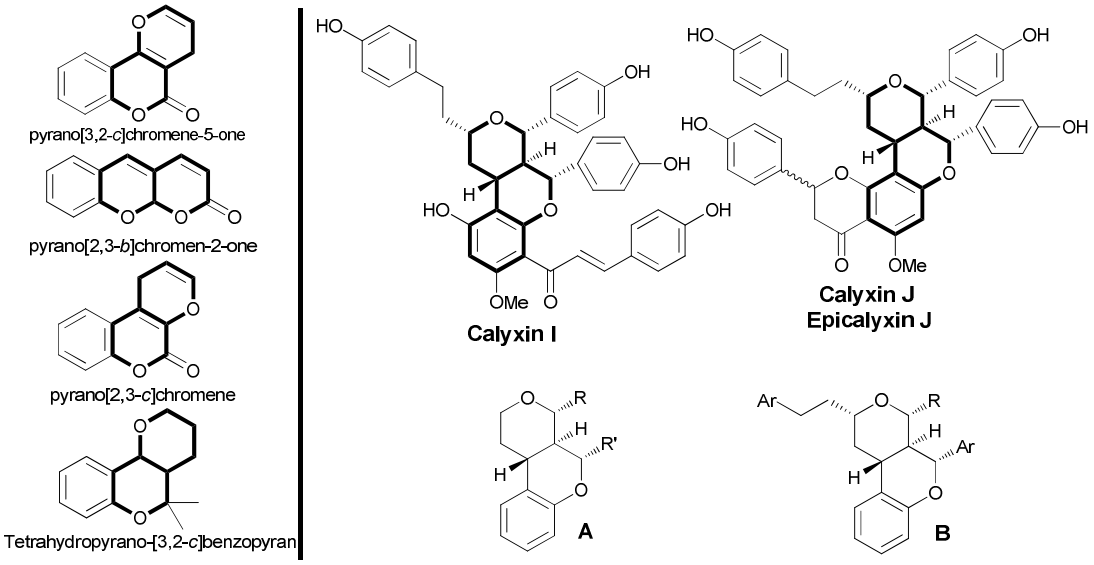


Figure 1.Tetrahydropyranochromene framework from *Alpiniablepherocalyx* and reported synthetic fragments

Use of glycerol in the development of new and innovative processes[26]has been realized greatly in the past few years, as it is associated with many advantages over conventional volatile organic solventswhich 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 non-flammable and biodegradable material, it fulfilsalmost all 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 non-polar nature allowed dissolution of number of inorganic salts, acids, bases, enzymes, transition metal complexes and even water-immiscible organic compounds. Not only this, it also helpedthe reaction products to single out simply by liquid–liquid phase extraction, due to its immiscible nature with hydrophobic ethers and hydrocarbons.Moreover, pharmaceutically active ingredients could be synthesizedin glycerol,where alittle care is required to handle and storagethem due to non-toxicnature of this medium, in addition to its high boiling point (290 ^{o}C). In present work, we therefore interested in developing the DAHDA synthetic sequence using glycerol as an effective reaction medium, taking into account above advantages. 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] reported by us, have successfully been optimized in this medium.

Results and Discussion

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

Scheme 1. Reagents and conditions: (i) DMF, K_2CO_3, RT, 8-10 h

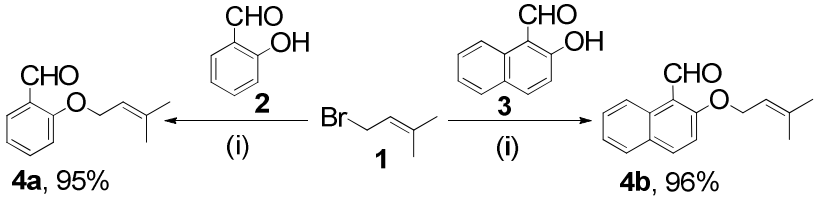
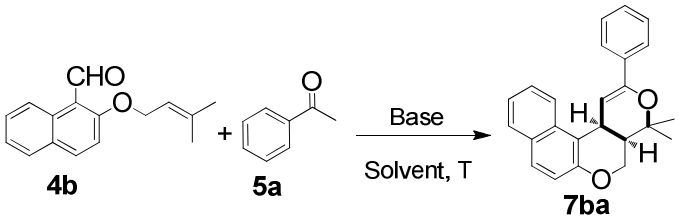


Table 1.Reaction Condition Optimization[a]



Entry	Catalyst (25 mol %)	Solvent	T (ºC)	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-Dimethyl formamide	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) stirredat the specified temperature. [b]Determined by TLC. [c]Isolatedyields. [d]Aldol intermediate.DBU = 1,8-Diazabicyclo[5.4.0]undec-7-ene. TEA = Triethylamine.

A combination between 2-prenyloxy-naphthaldehyde **4b** and acetophenone**5a** was taken as a model reaction to study and optimize the reaction conditions (**Table 1**). The reaction was first

examined in the presence of 50% KOH in water at reflux. It yielded 70% of the desired products but after prolong (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). Trying ethanolreplacing water as another protic solventat refluxfavoured only Aldol intermediate generation (entry 3). Aldolintermediateis stable and can be isolated. Thus, all these results led to the assumption that hydrogen bonds might be playing role to influence the reaction more favourably in the water rather 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 DMFwas then tried at 120 ^oC, to bring further improvement in the reaction (entry 6).Unfortunately, a very poor yield of desired product (15 %) wasseen after long reaction time, i.e. 48 h. Despite the reaction time can be shortened in the presence of DBU in ethylene glycol,where it gave 65% yields (entry 7),association of undesirable impurities with the products didn't encourage its further testing. These issueswere held no longer in the presence of piperidine in glycerol (entry 8). Other bases such as TEA (entry 9) and L-proline (entry 10) were failed to promote this protocol, though favoured the formation of Aldol intermediate efficiently. Finally, the combination of catalyst DBU and solvent glycerol worked effectively at 120 ^oC, giving excellent yields of DAHDA product **7ba**after 4 h.The product yield was however affected by decreasing the temperature and DBU amount in glycerol (entries 12, 13, and 14). This observation was therefore considered better in favour of effective electrophilic activation of the aldehyde, relative to that in the water.[32]Effective25 mol% load of DBU in glycerol at 120 ^oC(entry 11) was used to synthesize other heterocycles;**7aa-7af** and **7ba-7bf** (**Scheme 2**). The reaction was monitored periodically for its progress by the TLC. The reaction mass was poured into water, after completion of the reaction. Viscid matter thus came out of the

aqueous mixture was extracted thrice with 20 mL portion of ethyl acetate. Combined extracts were then dried over anhydrous Na_2SO_4, and evaporated to dry. The solid residue obtained was purified finally by column chromatography on silica gel using a hexaneethyl 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 the single-crystal X-ray diffraction data, supported well by IR, ^{1}H NMR and ^{13}C NMR spectral data, too. Intermediates, **6aa-6af, 6ba-6bf,**for the corresponding cyclised products;**7aa-7af, 7ba-7bf,**were also isolated (**Table 2**), and characterizedas Aldol condensation products.Structure of Aldol intermediate **6af**was further confirmed by the single crystal X-ray diffraction data.

Scheme 2.Synthesis of Aldol intermediates, **6aa-6af** and **6ba-6bf** and their correspondingpyrano[3,4-*c*]chromene derivatives,**7aa-7af** and **7ba-7bf**. Reagent and condition: DBU in Glycerol, 120 ^{o}C

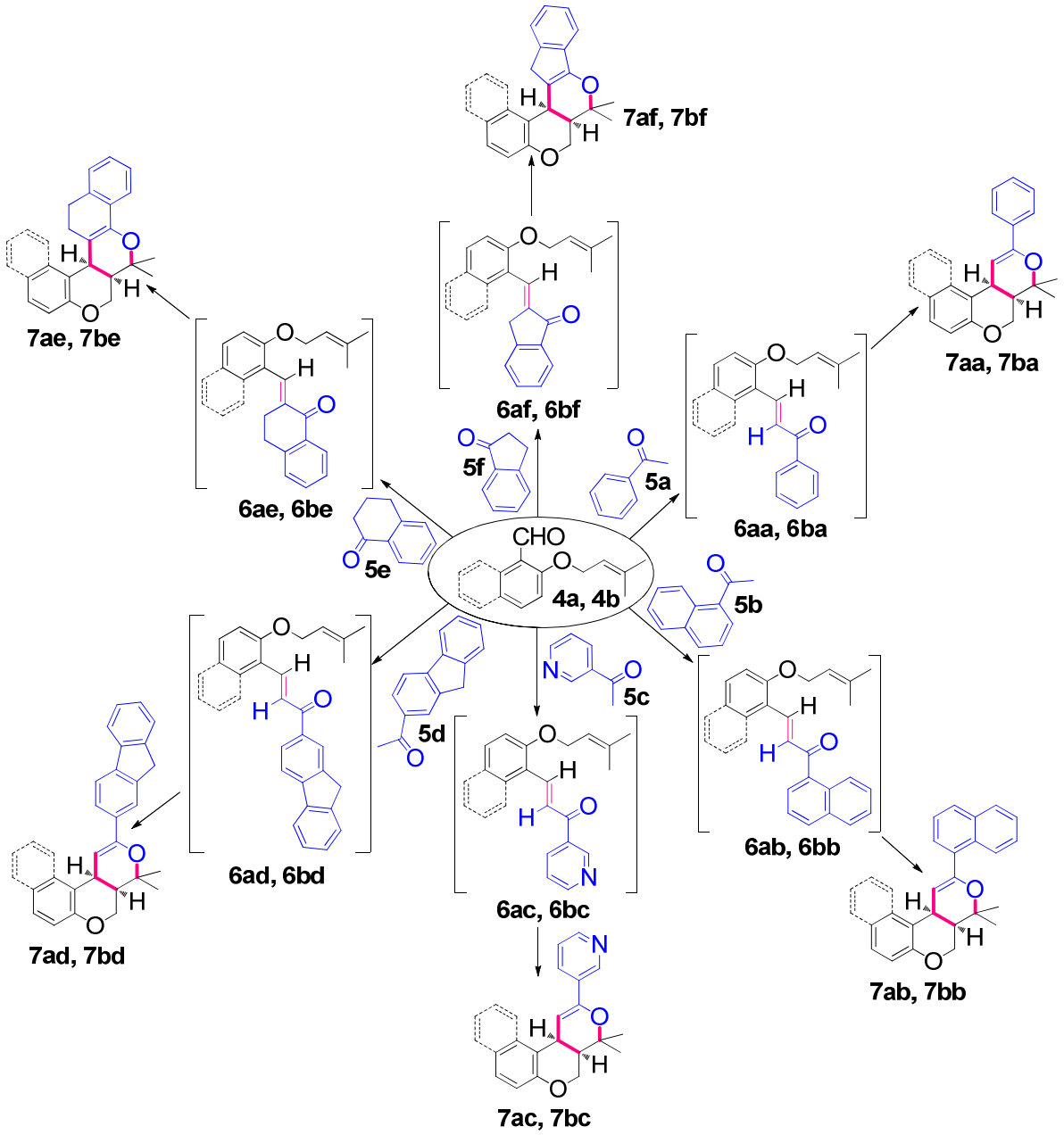


Table 2.**Synthesized Aldol intermediates; 6aa-6af, 6ba-6bf, andtheir corresponding DAHDA products; 7aa–7af,7ba–7bf**

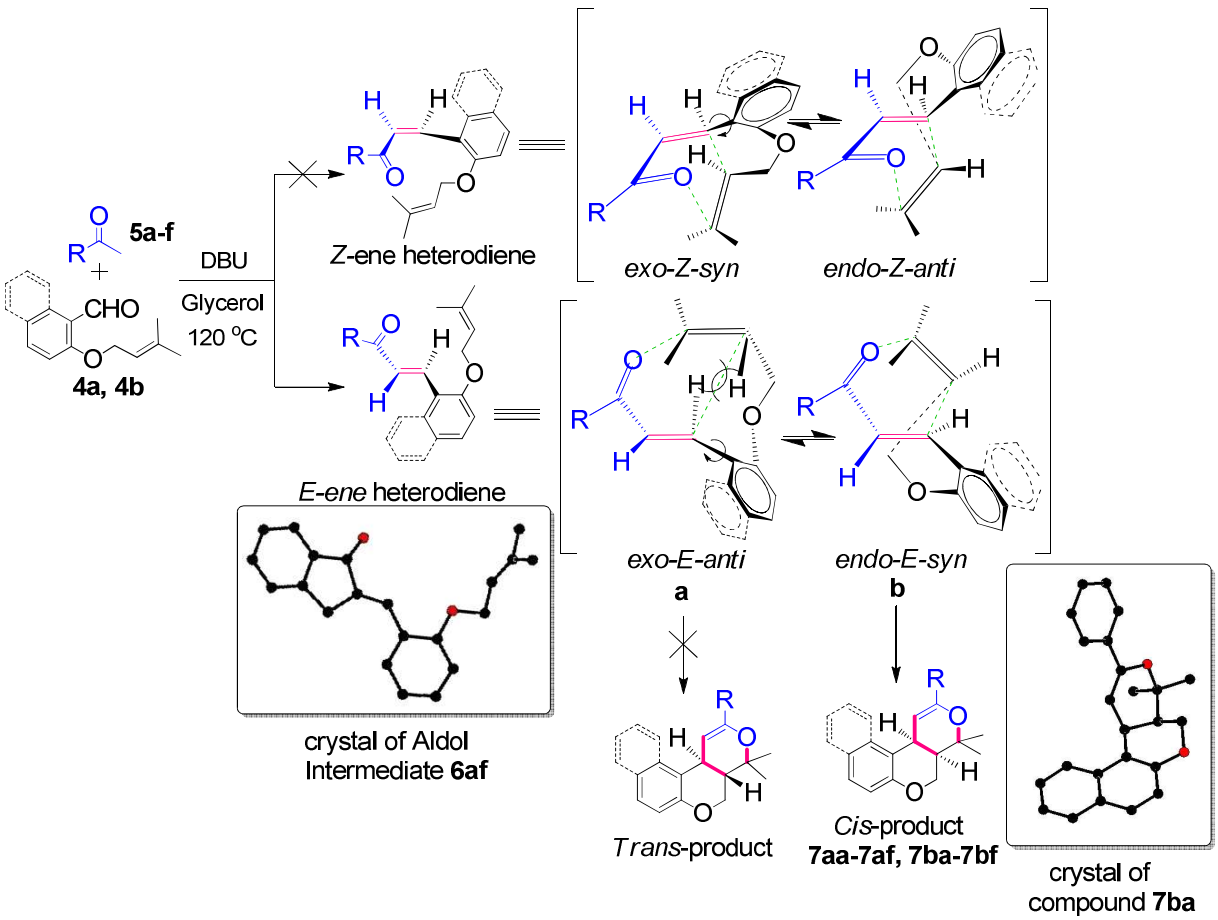
Entry	Aldol Intermediate	Time (h)	Yield (%)[a]	Entry	Product	Time (h)	Yield (%)[a]
1	**6aa**	2.0	87	13	**7aa**	4.5	80
2	**6ab**	2.0	89	14	**7ab**	5.0	78
3	**6ac**	2.5	84	15	**7ac**	5.5	75
4	**6ad**	3.0	90	16	**7ad**	6.5	76
5	**6ae**	1.5	89	17	**7ae**	4.5	79
6	**6af**	2.5	88	18	**7af**	5.0	80
7	**6ba**	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]Isolatedyield.

A mechanistic pathway of the reaction is shown in **Scheme 3**.Reaction proceeds with the Aldolcondensation reaction initially, which is followed by the *hetero*-Diels-Alder reaction, leading to the formation of cyclised products. The stereochemistry of the product is governed by the orientation ofprenyl−dienophiletowards Aldol,oxa-butadiene, alkene, favourable 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 towards Aldol*E*-ene and *Z*-ene intermediates.Out of these, *endo-Z-anti*and *exo-Z-syn* didn't get chance to appear in the present case, as all the isolated Aldol intermediates are identified with *E*-geometry, confirmed by ^{1}H NMR data. Here, *J* value of both of the Aldol alkene protonsis found in the 15.6-18 Hz range, for their characteristic and respective signals; one at δ 7.76-8.32 ppm and second at δ 8.11-8.65 ppm, confirming *E*-geometry of the intermediate. The single-crystal X-ray diffraction data of representative **6af**(**Scheme3**) confirmed the same unambiguously.Severe angle strain and unfavourable steric interactions are other strong reasons to exclude the possibility of *endo-Z-*

*anti*state.[34] Thus, *exo-E-anti*and*endo-E-syn*are the only states that might be taking 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 pyranopyranlybridge-head 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 sp^{2}-geminal effect rules out the possibility of exo-*E*-anti state, further. The reaction was therefore concluded to be occurred through the most favoured *endo-E-syn*transition state[36]out of four possible transition states, leading to the formation of *cis*-products, in all cases.Here, Aldol oxabutadiene and tethered olefin could be seen interacting well with each other (Scheme 3).

Scheme 3.The proposed reaction mechanism



A doublet appeared at δ 3.58-4.58 ppm, with 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 protonHb which appeared as multiplate at δ 1.90-2.31 ppm. Pyran alkene CH proton showed a singlet at 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**, and **7be-7bf,**due to participationof this proton in the fusion. While protons of methyl atteched to the pyran ring showed a singlet at δ 1.28-1.84 ppm, pyranyl -OCH_2 protons were appeared multiplet in the δ 3.61-4.62 ppm range, in all compounds. Increased in coupling constant J values of the methylene protons exceptionally to a larger magnitude (~22), can be attributed to a rigid disposition of these protons with respect to adjucent π system, in compounds **7af** and **7bf** derived from the monoketone indanone.[37]

The compound **7ba** crystallises in the monoclinic space group P21/cwith the following unit-cell parameters: a = 11.7252(2), b = 12.2681(2), c = 12.3225(3) Å, β= 97.388(2)º, Z = 4. An *ORTEP* view with atomic labelling is shown in **Figure 2**.

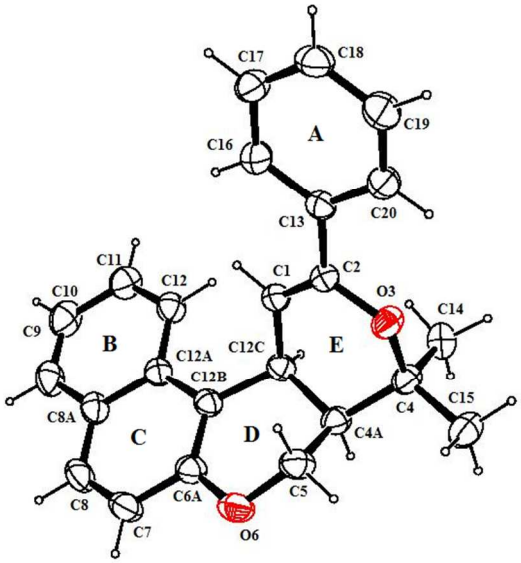


Figure 2.*ORTEP* view of the compound **7ba**, with displacement ellipsoids drawn at the 40% probability level.

The recyclability of glycerol was tested at least three times,for the reaction, after it was recovered from the reaction mass. The glycerol was recovered by using following treatments. The reaction mass was first poured into water, allowing crude product to appear insoluble and hence extractable with the ethyl acetate. The glycerol-water mixture thus left was heated at 100 ^{o} C under reduced 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 reactionin presence of catalyst DBU in glycerol, studied very rarely. Use of enolizable CH activated acyclic monoketone in present work is advantageous over DKHDA protocol, to construct the core structure which is analogues to the tricyclic pyrano[3,4-*c*]chromene framework present in Calyxins, which are known to exhibit strong antiproliferative activity. DKHDA approach has been explored largely with cyclic or heterocyclic diketone units,generating mostly teteracyclicpyran-framework with the aldehyde substrate, compared to the present protocol. Glycerol employed in the present work worked not only as efficient reaction medium, but as recyclable medium too, which can be recycled simply for its re-use, 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.Recorded all melting points are uncorrected.^{1}H NMR 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 and otherwise indicated. Chemical shiftvaluesare 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; 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 analyser.The ESI mass spectra were measured on mass spectrometer.TLC was performed on pre-coated silica plates, and spots were detected either by means of UV (254 nm, 366 nm) or 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), Conc. H_2SO_4 (6 mL), Water (8 mL), EtOH (20 mL)].

General procedure for synthesis of *O*-prenylated aldehydes (4a and4b):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 drop-wise 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, confirmed by the TLC (10−12 h). The reaction mass gave products **4a**/**4b**, when poured into 100 g of ice with constant stirring. The oily product, **4a** was extracted with three 25 ml diethyl ether portions. The combined ether extracts were dried using anhydrous sodium sulphate and evaporated to remove ether to have aldehyde, **4a**.The yield of **4a** was 95% andbp, 203—206℃.The solid product, **4b** was filtered, washed with three 10 ml cold water portions followed by room temperature drying. The yield of **4b** was 96% and mp, 58-60 ℃.

General experimental procedure for the synthesis of Aldol intermediates (6aa-6af and6ba-6bf),and the cyclised products, pyrano[3,4-*c*]chromenes(7aa-7af and 7ba-7bf):A mixture of acetophenone (0.240 g of **5a**) or 1-aceto-naphthone (0.340 g of **5b**) or 3-acetyl pyridine (0.242 g of **5c**) or 2-acetyl fluorene (0.416 g of **5d**) or 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 taken in glycerol (15 ml) in a round-bottom flask,and added

catalytic amount of DBU (25 mol %). The resulted reaction mass was then heated at 120 °C, continuouly monitoring the formation of 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 extracted the crude product thrice with ethyl acetate. The content of combined ethyl acetate extracts was dried over anhydrous Na_2SO_4 and evaporated. The desired product in the residue thus left 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 mixrure that was left after the extraction of the crude product with ethyl acetate was heated at 100 ^{0} C under reduced pessure to remove water.This recovered glycerol was re-used again for the reation.

In order to access all cyclised products, **7aa-7af** and**7ba**-7b**f**, the reaction was continued to carryout further that convertedcorresponding Aldol intermediates into *hetero*-Diels-Alder products, monitered by the TLC. The work-up and purificationinvolved here are similar to what had been applied to the isolation of Aldol intermediates.All the Aldol intermediates andtheir correspnding products were characterized on the basic 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* = 6.8Hz, 2H), 5.47 (t, *J* = 6.4 Hz, 1H), 6.91-7.99 (m, 11H), 8.11 (d, *J* = 16.4Hz, 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-(9*H*-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 (Ar-C); 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(2*H*)-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-1*H*-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), 5.54 (tt, J = 6.4 Hz, 1.2 Hz), 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$[M+H]^+$.

(*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(2*H*)-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-1*H*-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*]chrcomene (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-(9*H*-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(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-6*H*-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, Two 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-(9*H*-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-8*H*-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 $[M+H]^+$.

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Supporting Information Available: Copies of ^{1}H,^{13}C NMR spectraofall the compounds;NOESY spectra of **7ba**;X-ray structure and crystal data of **6af** and **7ba,** in CIF formatare available in Supporting Information.This material is available free of charge via the Internet at http://pubs.acs.org.

References

1. (a) Hepworth, J. *In Comprehensive Heterocyclic Chemistry*; Katrizky, A. R., Rees, C. W., Eds.; Pergamon: Oxford, UK, 1984; *3*, 737. (b) Ellis, G. P. *In Chromenes, Chromanones, and Chromones in the Chemistry of Heterocyclic Compounds*; Wiley: New York, 1977; *31*, 11. (c) Mandal, T. K.; Kuznetsov, V. V.; Soldatenkov, A. T. *Chem. Heterocycl. Compd.***1994**, *30*, 867.(d) Kumar, S.; Hernandez,D.;Hoa,B.; Lee,Y.; Yang, J. S.; McCurdy,A. *Org. Lett.***2008**, *17*, 3761. (e) Shiraishi,Y.;Sumiya,S.; Hirai,T.*Chem. Commun.***2011**,*47*, 4953. (f) Dumitras,M.;Apostolescu,N.; Luca,A.M.;Danac,R.*Acta Chem. Iasi***2009**,*17*, 209. (g) Williams,J.L.R.;Specht,D.P.;Farid,S.*Polym. Eng. Sci.***1983**, *23*, 1022.
2. (a) da Rocha, D. R.; de Souza, A. C. G.; Resende, J. A. L. C.; Santos, W. C.; dos Santos, E. A.; Pessoa, C.; de Moraes, M. O.; Costa-Lotufo, L. V.; Montenegro, R. C.; Ferreira, V. F. *Org. Biomol. Chem.***2011**, *9*, 4315. (b) Wang, S. M.; Milne, G. W. A.; Yan, X. J.; Posey, I. J.; Nicklaus, M. C.; Graham, L.; Rice, W. G. *J. Med. Chem.***1996**, *39*, 2047. (c) Edwards, A. M.; Howell, J. B. L. *Clin. Experim. Allergy***2000**, *30*, 756. (d) Kumar, A.; Maurya, R. A.; Sharma, S. A.; Ahmad, P.; Singh, A. B.; Bhatia, G.; Srivastava, A. K. *Bioorg. Med. Chem. Lett.***2009**, *19*, 6447. (e)Mungra,D.C.; Patel,M.P.;Rajani,D.P.; Patel,R.G.*Eur. J. Med. Chem.***2011**, *46*, 4192. (f) Raj, T.; Bhatia, R. K.; Kapur, A.; Sharma, M.; Saxena, A. K.; Ishar, M. P. S. *Eur. J. Med. Chem.***2010**, *45*, 790. (g) Elisa, P. S.; Ana, E. B.; Ravelo, A. G.; Yapu, D. J.; Turba, A. G. *Chem. Biodiversity***2005**, *2*, 264.

3. Konkoy,C. S.; Fick,D. B.;Cai,S. X.;Lan, N. C.;Keana,J. F. W.WO PCT Int Appl. 0075123,**2000**; *Chem. Abstr*, **2001**, *134*, 29313a.

4. (a) *Comprehensive Medicinal Chemistry*; Hansch, C.; Sammes, P. G.; Taylor, J. B. Eds.; Pergamon: New York, **1990**,*6*. (b) Cardellina, J. H.; Bokesch, H. R.; McKee, T. C.; Boyd, M. R. *Bioorg. Med. Chem. Lett.***1995**, *5*, 1011. (c) McKee, T.; Fuller, R. W.; Covington, C. D.; Cardellina, J. H., II; Gulakowski, R. J.; Krepps, B. L.; McMahon, J. B.; Boyd, M. R. *J. Nat. Prod.***1996**, *59*, 754. (d) Galinis, D. L.; Fuller, R. W.; McKee, T. C.; Cardellina, J. H., II; Gulakowski, R. J.; McMahon, J. B.; Boyd, M. R. *J. Med. Chem.***1996**, *39*, 4507. (e) Kumar, A.; Maurya, R. A.; Sharma, S.; Ahmad, A.; Singh, A. B.; Bhatia, G.; Srivastava, A. K. *Bioorg. Med. Chem. Lett.***2009**, *19*, 6447. (f) Ying, W.; Mo, S. Y.; Wang, S. J.; Li, S.; Yang, Y. C.; Shi, J. G. *Org. Lett.***2005**, *7*, 1675.

5. (a) Ahluwalia, V. K.; Arora, K. K.; Mukherjee, I. *Heterocycles***1984**, *22*, 223. (b) Huang, C. N.; Kuo, P. Y.; Lin, C. H.; Yang, D. Y. *Tetrahedron***2007**, *63*, 10025. (c) Lin,C.-C.; Hsieh,C.-C.; Yu,Y.-C.; Lai,C.-H.; Huang,C.-N.;Kuo,P.-Y.; Lin,C.-H.; Yang, D.-Y.; Chou,P.-T. *J. Phys. Chem. A***2009**, *113*, 9321.

6. (a) Paul, S.;Bhattacharyya,P.; Das,A. R.*Tetrahedron Lett.***2011**, *52*, 4636. (b)Lácová, M.;Gašparová, R.;Koiš, P.;Boháč,A.;El-Shaaer, H. M. *Tetrahedron***2010**, *66*, 1410. (c) Miyazaki,H.; Honda,K.;Asami,M.;Inoue, S.*J. Org. Chem.* **1999,** *64,* 9507. (d) Abdolmohammadia, S.;Balalaie, S.*Tetrahedron Lett.***2007**, *48*, 3299. (e) Emmadi,N. R.;Atmakur,K.;Chityal,G. K.;Pombala,S.;Nanubolu, J. B.*Bioorg. Med. Chem.Lett.***2012**, *22*, 7261.

7. (a) Prasain, J. K.; Tezuka, Y.; Li, J.-X.; Tanaka, K.; Basnet, P.;Dong, H.; Namba, T.; Kadota, S. *J. Nat. Prod.* **1998**, *61*, 212. (b) Tezuka,Y.;Gewali,M. B.; Ali,M. S.;Banskota,A. H.;Kadota,S.*J. Nat. Prod.* **2001,** *64,* 208. (c) Ali,M. S.;Tezuka,Y.;Banskota,A. H.;

Kadota,S.*J. Nat. Prod.* **2001,** *64,* 491. (d) Gewali, M. B.; Tezuka, Y.; Banskota, A. H.; Ali, M. S.; Saiki, I.; Dong, H.; Kadota, S. *Org. Lett.* **1999**, *1*, 1733. (e) Dong, H.; Chen, S.-X.; Xu, H.-X.; Kadota, S.; Namba, T. *J. Nat. Prod*. **1998**, *61*, 142. (f) Prasain, J. K.; Tezuka, Y.; Li, J.-X.; Tanaka, K.; Basnet, P.; Dong, H.; Namba, T.; Kadota, S. *Tetrahedron* **1997**, *53*, 7833.

8. (a) Tian,X.;Jaber,J. J.;Rychnovsky,S. D. *J. Org. Chem.* **2006**, *71*, 3176. (b) Tian, X.;Rychnovsky,S. D.*Org. Lett.***2007**,*9*, 4955. (c) Cakir, S. P.; Mead,K. T.*Tetrahedron Lett.***2006**, *47*, 2451.
9. (a) Yang, X.-F.; Wang, M.; Zhang, Y.; Li, C.-J. *Synlett***2005**, 1912.(b) Geng,Z.-C.; Zhang,S.-Y.; Li,N.-K.; Li,N.; Chen,J.; Li,H.-Y.; Wang,X.-W.*J. Org. Chem.***2014**, *79*, 10772.(c) Cakir,S. P.; Stokes,S.;Sygula,A.; Mead,K. T.*J. Org. Chem.***2009**, *74*, 7529. (d) Ackrill,T. D.;Sparkes,H. A.; Willis,C. L.*Org. Lett.***2015**, *17*, 3884.
10. (a) Reddy, B.V.S.; Divya, B.; Swain, M.; Rao, T. P.; Yadav, J. S.; Vishnu Vardhan, M. V. P. S. *Bioorg. Med. Chem. Lett.* **2012**, *22*, 1995. (b) Alonso, S. J.; Orellana, H. C.; Braun, A. E.; Ravelo, A. G.; Sacau, E. P.; Machín, F. *J. Med. Chem.***2008**, *51*, 6761. (c) Alonso, S. J.; Lomas, A. L. P.; Braun, A. E.; Martinez, F. M.; Orellana, H. C.; Ravelo, A. G.; Gamarro, F.; Castanys, S.; López, M. *J. Med. Chem.***2008**, *51*, 7132. (d) Periasamy, M.; Srinivas, G.; Bharathi, P. *J. Org. Chem.***1999**, *64*, 4204. (e) Bakthadoss,M.;Sivakumar, G.*Tetrahedron Lett.***2014**, *55*, 1765.
11. (a) Tietze, L. F.; Beifuss, U. *Angew. Chem.* **1993**, *105*, 137. (b) Tietze, L. F.; Beifuss, U.*Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 131. (c) Tietze, L. F. *Chem. Ind.* **1995**, 453. Waldmann, H. "*Domino Reaction*" *in Organic Synthesis Highlight II*; Waldmann, H., Ed.; VCH: Weinheim, **1995**, 193-202. (d) Hall, N. *Science* **1994**, *266*, 32.

12. (a) Tietze, L. F.; Stegelmeier, H.; Harms, K.; Brumby, T. *Angew. Chem., Int. Ed. Engl.***1982**, *94*, 868. (b) Tietze, L. F.; Stegelmeier, H.; Harms, K.; Brumby, T. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 863. (c) Tietze,L. F.; Brumby,T.; Pretor, M. *Synthesis* **1987**,*8*, 700.

13. Tietze, L. F.; Beifuss, U.; Antel, J.; Sheldrick, G. M. *Angew. Chem.* **1988***, 100*, 739.*Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 703.

14. Tietze, L. F.; Schunke, C. *Angew. Chem.* **1995**, *107*, 1901.*Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1731.

15. Safaei-Ghomi, J.;Paymard-Samani, S. *Chem. Heterocycl. Compd.***2015**,*11*, 1567-1574.

16. Tietze, L. F.; Fennen, J.; Geissler, H.; Schulz, G.; Anders, E. *Liebigs Ann. Chem.* **1995**, 1681.

17. MOiler, G. H.; Waldmann, H. *Tetrahedron Lett.* **1996**, *22*, 3833.

18. Tietze, L. F.; Rischer, M. *Angew. Chem.* **1992**, *104*, 1269. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1221.

19. Tietze, L. F.; Wichmann, J. *Angew. Chem.* **1992**, *104*, 1091. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1079.

20. Ueda, M. *Chem. Pharm. Bull.* **2014**, *62*, 845.

21. Suman, K.; Thennarasu, S.*RSC Adv.***2015**, *5*, 23291.

22. Chang, M.-Y.; Wu, M.-H.; Tai, H.-Y. *Org. Lett.***2012**, *14*, 3936.

23. (a) Pokhodylo1, N. T.; Savka1, R. D.; Obushak, M. D. *Chem. Heterocycl. Compd.***2014**,*4*, 544. (b) Saito, T.;Nagashima, M.;Karakasa, T.; Motoki, S. *J. Chem. Soc., Chem. Commun.***1990**, 1665. (c) Saito, T.; Nagashima, M.; Karakasa, T.; Motoki, S. *J. Chem. Soc., Chem. Commun.***1992**, 411.(d) Saito, T.; Kimura, H.; Sakamaki, K.; Karakasa, T.; Moriyama, S. *Chem. Commun.***1996**, 811. (e) Bellassoued-Fargeau, M.-C.;Maitte, P.*J.*

*heterocyclic chem.***1984**, *21*, 1549. (f) Lee, Y. R.; Kim, Y. M.; Kim, S. H. *Tetrahedron***2009**, *65*, 101. (g) Madda,J.;Venkatesham,A.;Bejjanki,N. K.;Kommua,N.;Pombala,S.; Ganesh Kumar,C.;Rao,T. P.;Nanubolu, J. B. *Bioorg. Med. Chem. Lett.***2014**, *24*, 4428. (h) Moghaddam,F. M.;Taheri,S.;Hojabri,L.;Pirani, P.;Maktabian, S.*J. Iran. Chem. Soc.***2011**,*8*, 265.

24. Carruthers, W.; Coldham, L *Modern Methods of Organic Synthesis*; Cambridge University Press, **2004**, 2.
25. (a) Tietze, L. F. *Chem. Rev.***1996**,*96*, 115. (b) Majumdar, K. C.; Taher, A.; Nandi, R. K. *Tetrahedron***2012**, *68*, 5693. (c) Sutariya, T. R.; Labana, B. M.; Parmar, B. D.; Parmar, N. J.; Kant, R.; Gupta, V. K. *RSC Adv.***2015**, *5*, 23519. (d) Parmar, N. J.; Parmar, B. D.; Sutariya, T. R.; Kant, R.; Gupta, V. K. *Tetrahedron Lett.***2014**, *55*, 6060. (e) Parmar, N. J.; Pansuriya, B. R.; Labana, B. M.; Sutariya, T. R.; Kant, R.; Gupta, V. K. *Eur. J. Org. Chem.* **2012**, 5953. (f) Parmar, N. J.; Patel, R. A.; Parmar, B. D.; Talpada, N. P. *Bioorg. Med. Chem. Lett.***2013**, *23*, 1656. (g) Parmar, N. J.; Barad,H. A.;Labana,B. M.; Kant, R.; Gupta, V. K. *RSC Adv.***2013**, *3*, 20719.
26. (a) Behr,A.;Eilting,J.;Irawadi,K.;Leschinski, J.; Lindner,F. *Green Chem.***2008**, *10*, 13. (b) Corma,A.;Iborra, S.;Velty,A. *Chem. Rev.***2007**, *107*, 2411. (c) Pagliaro,M.;Ciriminna,R.; Kimura,H.; Rossi, M.;Pina,C. D. *Angew. Chem., Int. Ed.***2007**, *46*, 4434. (d) Zhou,C.-H.;Beltramini,J. N.; Fan, Y.-X.; Lu,G. Q.*Chem. Soc. Rev.***2008**, *37*, 527. (e) Casilda,V. C.*Glycerol as an Alternative Solvent for Organic Reactions, Green Solvents I***2012**, 187.
27. Nelson,W. M. *Green Solvents for Chemistry: Perspectives and Practice; Oxford University Press, Oxford***2003**.

28. (a) Wolfson, A.;Dlugy,C. *Chem. Pap.***2007**, *61*, 228. (b) Wolfson,A.;Litvak,G.;Shotland, C.;Dlugy, Y.;Tavor,D. *Ind. Crops Prod.***2009**, *30*, 78. (c) Wolfson,A.;Dlugy, C.;Shotland,Y. *Environ. Chem. Lett.***2007**, *5*, 67.

29. (a) Silveira, C. C.; Mendes,S. R.; Líbero, F. M.;Lenardão, E. J.;Perin,G. *Tetrahedron Lett.***2009**, *50*, 6060. (b) Lenardão, E. J.;Trecha,D. O.; Ferreira,P. C.; Jacob, R. G.;Perin,G. *J. Braz. Chem. Soc.***2009**, *20*, 93. (c) Lenardão, E. J.; Silva,M. S.;Sachini,M.; Lara,R. G.; Jacob, R. G.;Perin,G. *Arkivoc***2009**, *xi*, 221.

30. (a) Wolfson,A.;Dlugy,C.;Shotland, Y.;Tavor,D. *Tetrahedron Lett.***2009**, *50*, 5951. (b) He,F.; Li,P.;Gu, Y.; Li,G. *Green Chem.***2009**, *11*, 1767. (c) Karam,A.;Villandier,N.;Delample,M.;Koerkamp,C. K.;Douliez,J.-P.;Granet,R.;Krausz,P.;Barrault, J.;Jérôme,F. *Chem.–Eur. J.***2008**, *14*, 10196.(d) Gu,Y.;Barrault, J.;Jérôme,F. *Adv. Synth. Catal.***2008**, *350*, 2007.

31. (a) Tan,J.-N.;Lia, M.;Gu,Y. *Green Chem.***2010**, *12*, 908. (b) Safaei,H. R.;Shekouhy,M.;Rahmanpur, S.;Shirinfeshan,A. *Green Chem.***2012**, *14*, 1696.

32. He, F.;Li, P.;Gu, Y.;Li, G.*Green Chem.* **2009***, 11*, 1767.

33. Tietze, L. F.; Brumby, T.; Pretor, M.; Remberg, G.*J. Org. Chem.* **1988**, *53*,810.

34. (a) Ciganek, E. *Org. React. (N.Y.)* **1984**, *32,* 1**.** (b) Oppolzer, W. *Angew. Chem. Int.Ed. Engl.* **1984**,*23*, 876. (c) Brieger, G.; Bennet, J. N. *Chem. Rev.* **1980**, *80*, 63.

35. (a) Hoffmann, R. W. *Chem. Rev.***1989**, *89*, 1841. (b) Tietze, L. F.; Beifuss, U.; Ruther, M.; Rühlmann, A.; Antel, J.; Sheldrick, G. M. *Angew. Chem. Int. Ed. Engl.***1988**, *27*, 1186.

36. Tietze, L. F.; Denzer, H.; Holdgrün, X.; Neumann, M. *Angew. Chem. Int. Ed. Engl.***1987**, *26*,1295.

37. Rahman, Atta-ur. In *Nuclear Magnetic Resonance: Basic Principles*; Springer International Edition, 1986; pp 75-78.