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Gluconic acid aqueous solution: a task-specific bio-based solvent for ring-opening reactions of dihydropyrans

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ABSTRACT

Gluconic acid aqueous solution (GAAS) that is a largely available bio-based chemical was proved to be an effective task-specific medium for ring-opening reactions of dihydropyrans. In the presence of nucleophiles, such as indoles, 1,3-cyclohexanediones, *N*,*N*-dimethylaniline, *N*-methylaniline, 2-naphthol, and resorcin, a series of 2-substituted 1, 3-dicarbonyl compounds were synthesized in good to excellent yields. The first example of ring-opening of oxa-Pictet–Spengler product with nucleophiles was also described. These results not only demonstrate the feasibility of using GAAS as a sustainable solvent, but also offer an effective way for the ring-opening reactions of dihydropyrans with nucleophiles. Because these reactions proceeded with excellent atom-economy in a sustainable bio-based solvent, the present method was thus characterized by many properties of green chemistry, such as green solvent, atom-economy, and utilization of bio-based chemicals.

1. Introduction

Solvents play a pivotal role in many processes such as chemical reactions, separation, and product purification procedures.[1] Currently, there are only two kinds of solvents that can be used in chemistry: solvents obtained from petroleum industry (petro-based solvents) and solvents of agricultural origin (bio-based solvents). Today, many of the most widely used solvents are petro-based chemicals, which may be classified as volatile organic compounds, and thus they are important atmospheric pollutants considering their known contributions to effects such as ozone depletion or global warming.[2] Chemicals from agricultural origin are generally safe and easy to degrade in the environment. Therefore, compared with the most of petro-based solvents, bio-based solvents are more eco-friendly. For this reason, replacement of conventional organic solvents with bio-based one has gained much attention recently.[3]

According to the solvent properties, bio-based solvents can be classified as polar and non-polar. Polar bio-based solvents generally contain at least one hydroxyl group in the structure, which makes them behave like an alcohol or even water. Glycerol is a typical polar bio-based solvent,[4] and three hydroxyl groups in its structure lead this solvent to be highly hydrophilic. Some other polar bio-based chemicals, such as lactates[5] and polyhydroxyalkanoate,[6] have also been used as alternative solvents. Non-polar bio-based solvents are normally obtained from natural fatty compounds, for example, biodiesel,[7] or terpenes, such as D-limonene.[8] In order to push the bio-based solvents easily acceptable for industry, some non-polar compounds that possess a solvent property close to commonly used THF, were also selected as alternative solvents, such as 2-methyltetrahydrofuran.[9] Because this compound could be now prepared from bio-based chemicals, it actually falls into the catalog of non-polar bio-based solvents.

In view of the explosive growth in research on this area, bio-based solvents may be the best candidate for acting as the next generation of green solvents after successful developments of the first generation involving water, ionic liquids, supercritical fluids, perfluorocarbon, and polyethylene glycol.[10] Today, although the great advantages of bio-based solvents have been well elucidated by some pioneering studies, owing to the fact that this topic is still in its infancy. Particularly, we viewed that it should be very interesting to develop a bio-based solvent that has a specific capacity by means of rationally utilizing its structure. Our recent interest is particularly focusing on development of new methods with bio-based solvents for sustainable organic synthesis.[11] In connection with this research program, we started, some time ago, a research on exploration of bio-based chemicals, which possess a functional group that might be able to assist progress of an organic reaction. During our investigation, we are attracted by D-gluconic acid (GA), which is a bio-based chemical and largely available in the market as a 50% of aqueous solution.[12] Under

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normal conditions, gluconic acid aqueous solution (50 wt %, GAAS) exhibits an equilibrium, in which about 5% of glucono-δ-lactone is present in the solution at room temperature. Particularly, dissociation of proton from GA molecule resulted in the aqueous solution to be slightly acidic. This allowed us to directly use GAAS as a bio-based solvent for promoting some organic reactions that need assistance of a weak acid. Out of these considerations, we have recently examined some organic reactions, including Friedel–Crafts alkylations of indoles with benzyl alcohols and α,β-unsaturated ketones, in GAAS.[13] Although the results obtained are promising, owing to these reactions are rather simple, validity and necessity of using GAAS as solvent for organic reactions have not been fully demonstrated. Therefore, applications of GAAS solvent in other organic reactions are appealingly needed at this moment.

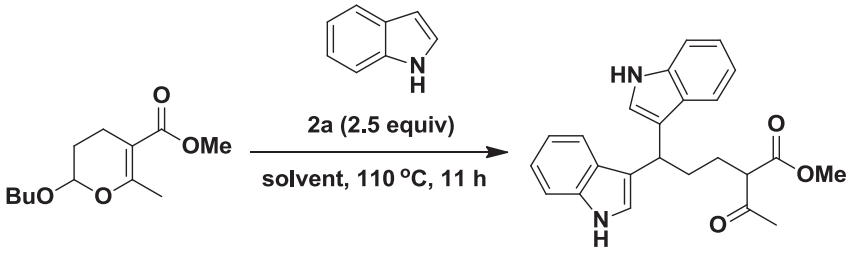
On the other hand, the use of simple heterocycles as substrate in organic synthesis has gained much attention because heterocycles displayed in organic transformations a great productivity in creation of molecular complexicity and diversity.[14] Dihydropyran derivatives, which are among the most investigated heterocycles in the past decade, are widely present in nature-occurring products.[15] We have recently reported a novel ring-opening reaction of 2-alkoxy- or 2-aryl-3,4-dihydropyrans with nucleophiles,[16] which generated a variety of 2-substituted 1,3-dicarbonyl compounds in high yields. However, these reactions are quite sensitive to the acid strength of catalyst, and therefore, only mild Lewis acid catalysts, such as $MnCl_2$ and $MnBr_2$ could be applied in these reactions. This resulted in two disadvantages to this type of reactions including (i) the reaction has to be conducted in organic solvent, such as nitromethane that is a volatile, toxic, and explosive solvent, and (ii) difficulty of recycling the metal Lewis acid catalyst. In view of these facts, we envisaged that performing the reaction in GAAS solvent might be an ideal choice for overcoming these problems. In this paper, we disclose the successful outcome of this endeavor, in which 2-alkoxy-3,4-dihydropyrans, 2-aryl-3,4-dihydropyrans, and an oxa-Pictet–Spengler adduct reacted readily with many nucleophiles, such as indoles, 1,3-cyclohexanediones, *N*,*N*-dimethylaniline, *N*-methylaniline, 2-naphthol, and resorcin, affording excellent yields of the corresponding ring-opening products in GAAS solvent.

2. Results and discussion

Initially, we studied whether solvent could promote the reaction of a 2-butoxy-3,4-dihydropyran **1a** with indole. As shown in Table 1, no product was obtained under solvent-free condition (entry 1), and also in toluene, DCE, nitromethane, DMF, DMSO, polyethylene glycol 400, glycerol, and water (entries 2–9). Because the mechanism of the model reaction most likely involves an acid-assisted nucleophilic substitution, an acidic medium should be appropriate for this reaction. We, thus, then examined acetic acid, and in this case, a product, **3a**, was obtained in 79% after 11 h of reaction at 110 °C (entry 10). However, in order to isolate **3a**, acetic acid has to be neutralized by aqueous NaOH solution at the end of the reaction. This step generates thus a lot of wastes. As a result, performing the model ring-opening reaction in acetic acid is not perfect from the viewpoints of economy and the concept of green chemistry. We therefore decided to search for an alternative solvent to acetic acid. Very interestingly, when another acidic medium, GAAS, was used, **3a** was also formed with a high selectivity, and the reaction yield reached to 82% (entry 11). Further investigation revealed that the ring-opening reaction of **1a** with **2a** in GAAS also affected by temperature and reaction time, and the optimal condition should be 110 °C and 11 h (entries 12 and 13). It should be noted that, because of the immiscibility of GAAS with non-polar organic solvent, the formed product could be easily extracted from the GAAS phase with an appropriate organic solvent. This method for isolating the reaction product not only simplifies the operation procedure, but also offers an easy way for recycling the GAAS. In the model reaction, the recovered GAAS could be reused at least four times without significant loss of activity (entry 14).

With the optimized system in hand, we probed the scope of the reaction with respect to both the indole and the dihydropyran components. As evidenced by the results in Table 2, indoles with

Table 1
Ring-opening reaction of dihydropyran **1a** with indole in different solvents[a]

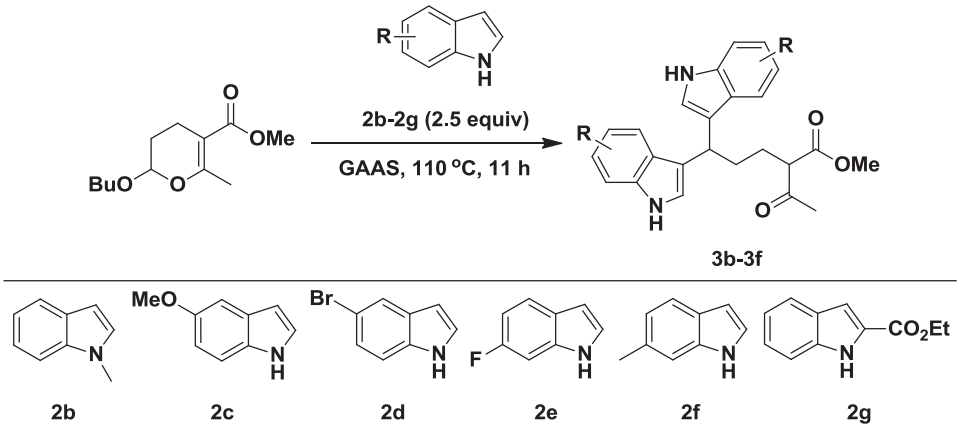


1a 3a

Entry	Solvent	Temp (°C)	Time (h)	Yield (%)
1	No solvent	110	11	0
2	Toluene	110	11	0
3	DCE	110	11	0
4	CH_3NO_2	110	11	0
5	DMF	110	11	0
6	DMSO	110	11	0
7	PEG 400	110	11	0
8	Glycerol	110	11	0
9	H_2O	110	11	0
10	CH_3CO_2H	100	11	79
11	GAAS	110	11	82
12	GAAS	80	11	56
13	GAAS	110	6	72
14[b]	GAAS	110	11	82

[a] Solvent: 1.0 mL, **1a**: 0.25 mmol, **2a**: 0.63 mmol.
[b] GAAS was reused in the fourth time.

Table 2
Ring-opening reaction of **1a** with different indoles in GAAS[a]



Entry	Indole	Product	Yield (%)
1	**2b**	**3b**	71
2	**2c**	**3c**	85
3	**2d**	**3d**	80
4	**2e**	**3e**	78
5	**2f**	**3f**	86
6	**2g**	—	0

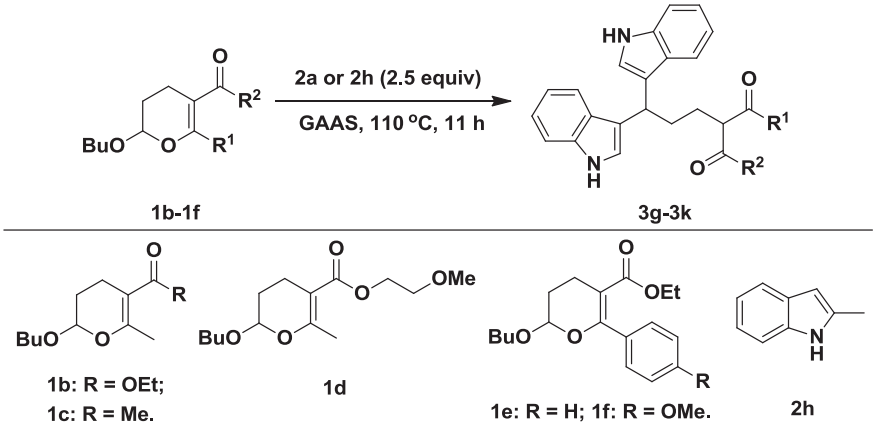
[a] GAAS: 1.0 mL, **1a**: 0.25 mmol, indole: 0.63 mmol, 110 °C, 11 h.

different substituent groups smoothly reacted with **1a**, producing the corresponding 2-substituted 1,3-dicarbonyl compounds in generally good yields (entries 1–5). However, an indole **2g** that contains a strongly electron-withdrawing group, ethoxycarbonyl, failed to participate in the reaction (entry 6).

The scope of the reaction with respect to 2-butoxy-3,4-dihydropyran was found also to be very good. As Table 3 illustrates, a range of functional groups could be employed without significantly affecting the reaction yields (entries 1–5). Thus, dihydropyrans containing an acetyl, phenyl, and methoxy functionality readily participated in the reaction. A reaction in preparative scale (10 mmol) was also examined, and it was found that the reaction proceeds very well, indicating the usefulness of our method for practical synthesis (entry 6).

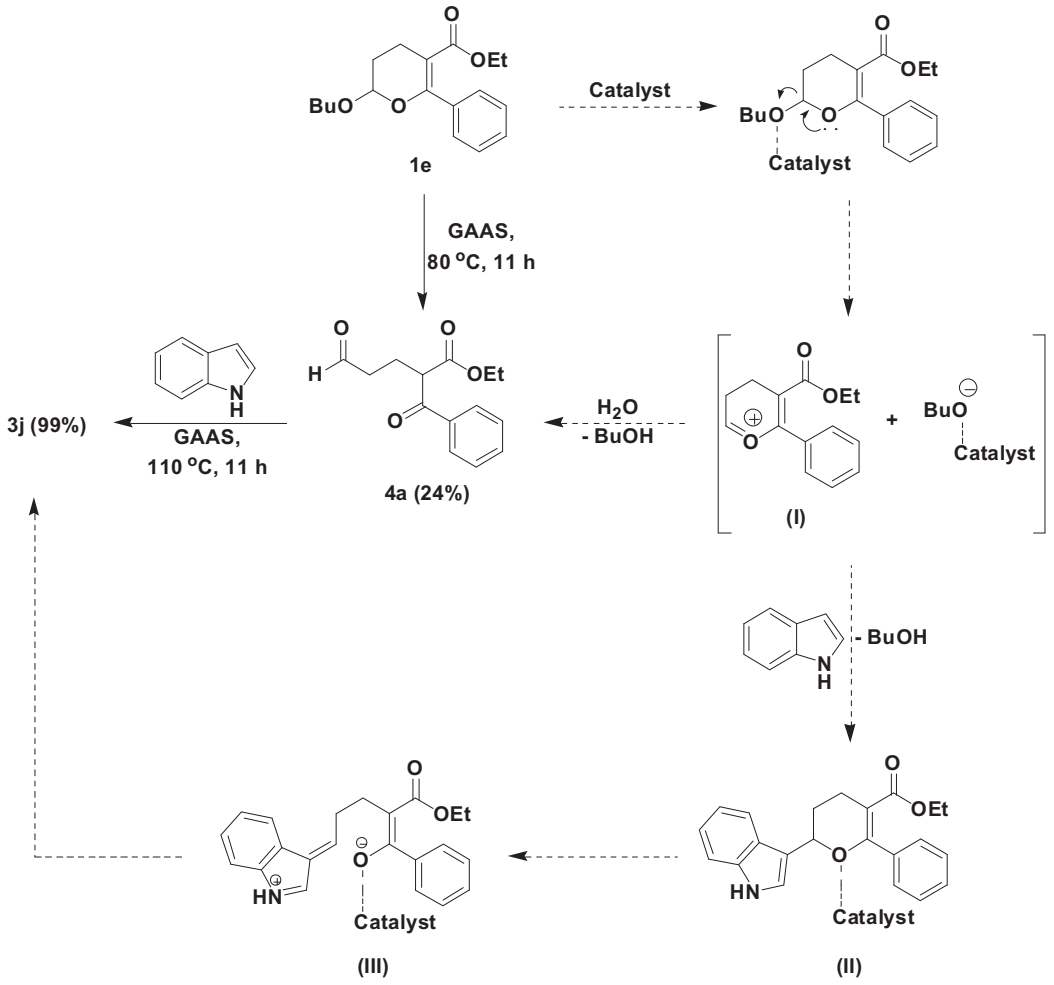
To probe the mechanism of the ring-opening reaction, we treated a dihydropyran, **1e**, in GAAS in the absence of indole. As shown in Scheme 1, an aldehyde, **4a**, was obtained in 24% of yield after 11 h of reaction at 80 °C. It should be noted that **4a** is the only product in this reaction, and the low yield mainly resulted from incomplete conversion of **1e**. Following treatment of the isolated **4a** with **1a** in GAAS resulted in a quantitative formation of **3j**. On the basis of these results, we thus believe that the model reaction should proceed in

Table 3
Ring-opening reaction of different 2-butoxy-3,4-dihydropyrans with indoles in GAAS[a]



Entry	3,4-Dihydropyran	Indole	Product	Yield (%)
1[b]	**1b**	**2h**	**3g**	72
2	**1c**	**2a**	**3h**	66
3	**1d**	**2a**	**3i**	71
4[b]	**1e**	**2h**	**3j**	76
5	**1f**	**2h**	**3k**	76
6[c]	**1a**	**2a**	**3a**	81

[a] GAAS, 1.0 mL, dihydropyran: 0.25 mmol, indoles: 0.63 mmol, 110 °C, 11 h.
[b] Reaction time: 24 h.
[c] The reaction was performed in 10 mmol scale.

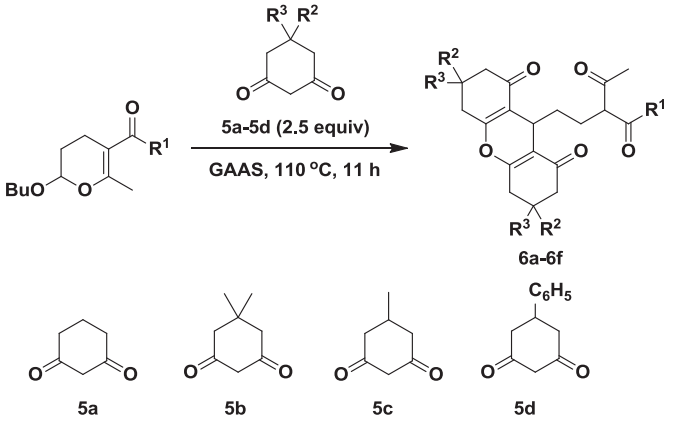


Scheme 1. Plausible mechanism of the model reaction.

a same reaction pathway that we have proposed in the reaction catalyzed by $MnCl_2 \cdot 4H_2O$.[16c] In the beginning of the reaction, dihydropyran **1e** was activated with the aid of GAAS to form a cyclic oxocarbenium ion intermediate (**I**). This step was generally catalyzed by acid.[17] The formation of a linear oxocarbenium ion could be also possible through a cleavage of C–O bond in the ring, but compared with the cyclic one, it should be much less stable because of a lack of conjugation effect. Once (**I**) was formed, it tended to react with water to form an aldehyde **4a** that can further interact with indole to generate **3j**. Additionally, interaction of one molecule of indole and intermediate (**I**) might form an intermediate (**II**). With the aid of GAAS, intermediate (**II**) underwent the cleavage of C–O bond to form a ring-opening intermediate (**III**) that tended to react with next indole to generate the final product **3j**.

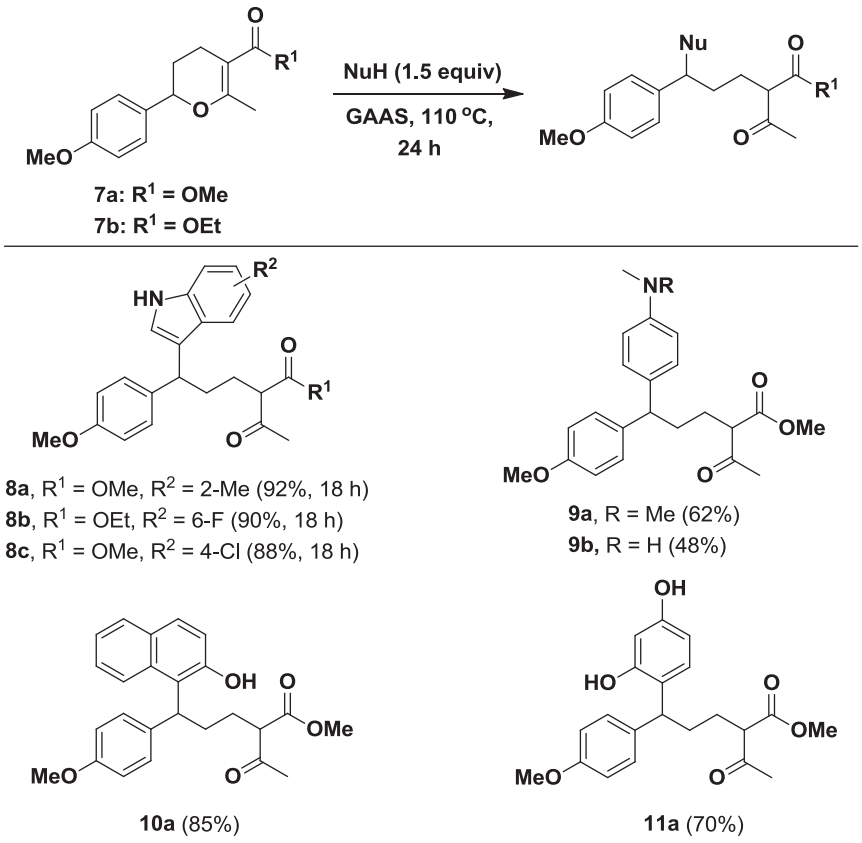
Interestingly, GAAS-mediated ring-opening reaction of the 3,4-dihydropyran showed also a good generality with respect to nucleophiles. As shown in Table 4, 1,3-cyclohexanedione derivatives could be successfully used, and a new class of products that contain both moieties of 3,4,5,6,7,9-hexahydro-1*H*-xanthene-1,8(2*H*)-dione and 1,3-dicarbonyl compound were obtained in good yields (entries 1–6). Scheme 2 also shows ring-opening reactions of 2-aryl-3,4-dihydropyrans, **7a** and **7b**, in GAAS with some nucleophiles, such as indoles, *N*,*N*-dimethylaniline, *N*-methylaniline, 2-naphthol, and resorcin. It should be noted that these ring-opening reactions proceeded in a manner of 100% of atom-economy, thus conferring to this system a salient feature of green chemistry. All these examples demonstrated that GAAS is, indeed, a very efficient

Table 4
Ring-opening of 2-butoxy-3,4-dihydropyran **1a** with 1,3-cyclohexanediones in GAAS[a]



Entry	3,4-Dihydropyran	Cyclohexanedione	Product	Yield (%)
1	**1a**	**5a**	**6a**	74
2	**1a**	**5b**	**6b**	98
3	**1a**	**5c**	**6c**	80
4	**1b**	**5b**	**6d**	96
5	**1b**	**5c**	**6e**	85
6	**1f**	**5d**	**6f**	73

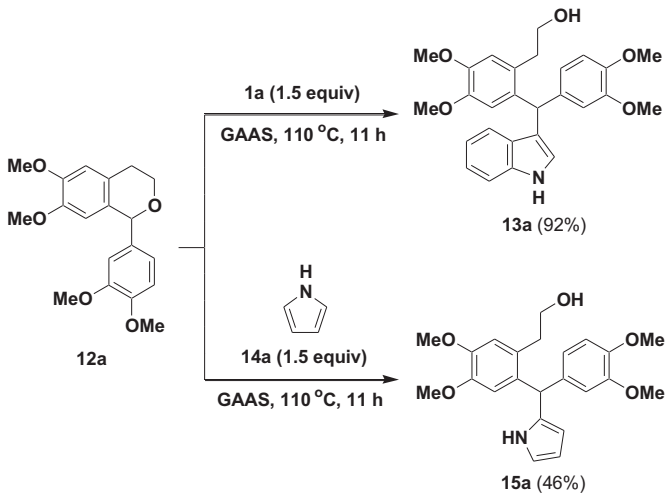
[a] GAAS: 1.0 mL, 3, 4-dihydropyrane: 0.25 mmol, cyclohexanedione: 0.63 mmol, 110 °C, 11 h.



Scheme 2. Ring-opening reactions of 2-aryl-3,4-dihydropyrans with other nucleophiles.

promoting medium for the ring-opening reactions of 2-substituted 3,4-dihydropyrans with nucleophiles.

Inspired by the above-mentioned results, we then investigated another type of ring-opening reaction by using GAAS as a promoting medium. As shown in Scheme 3, an oxa-Pictet–Spengler reaction product, **12a**, could react smoothly with indole and pyrrole in GAAS to give the ring-opening products in moderate to excellent yields.[18] It should be noted that this type of ring-opening reaction has not been reported before. By using GAAS as a promoting medium, we thus realized the first example of ring-opening of oxa-Pictet–Spengler product with nucleophile.



Scheme 3. Ring-opening reactions of oxa-Pictet–Spengler product **12a** with indole or pyrrole in GAAS.

3. Conclusion

In summary, GAAS that is a largely available bio-based chemical was proved, for the first time, to be an effective task-specific medium for the ring-opening reaction of 2-substituted 3,4-dihydropyrans with many nucleophiles including indoles, 1,3-cyclohexanediones, *N*,*N*-dimethylaniline, *N*-methylaniline, 2-naphthol, and resorcin, which generated a series of 2-substituted 1,3-dicarbonyl compounds in moderate to excellent yields. These results not only demonstrate the feasibility and necessity of using GAAS as a sustainable solvent, but also offer an effective way for the ring-opening reaction of 2-substituted 3,4-dihydropyrans with nucleophiles. Furthermore, the first example of ring-opening of oxa-Pictet–Spengler product with nucleophile was also described. In addition to the above-mentioned salient features, GAAS system also showed good recoverability and recyclability in the ring-opening reaction, which conferred the present method more significant property on the eco-friendliness. Moreover, because these reactions proceeded with excellent atom-economy in a sustainable bio-based solvent, the present method was thus characterized by many properties of green chemistry, such as green solvent, atom-economy, and utilization of bio-based chemicals.

4. Experimental section

4.1. General

All reactions were conducted in a 10 mL of V-type flask equipped with triangle magnetic stirring. In a typical reaction, gluconic acid aqueous solution (1.0 mL) was mixed with **1a** (57.1 mg, 0.25 mmol) and indole (**1a**, 73.2 mg, 0.63 mmol) under air. The mixture was stirred for 11 h at 110 °C. After reaction, the mixture

was cooled to room temperature and the reaction mixture was extracted with a mixed solution composed of ethyl acetate and *n*-heptane (v/v=2:1, 6 mL×3). And the desired product, **3a**, was obtained by preparative TLC using a mixed solution of ethyl acetate and petro ether (bp=60–90 °C) as eluting solvent (the ratio of ethyl acetate/petroleum ether is 1:6); 79.4 mg, yield=82%. Tests for substrate scope, reaction in preparative scale, and experiments concerning the mechanism were all performed according to the above-mentioned analogous procedure. The ring-opening reactions of **7a** and **7b** were also performed according to the above-mentioned analogous procedure.

4.2. Spectroscopic data of new compounds

*4.2.1. Ethyl 2-butoxy-6-phenyl-3,4-dihydro-2H-pyran-5-carboxylate (**1f**).*[19] Colorless liquid; ^{1}H NMR ($CDCl_3$): 0.93 (t, *J*=7.6 Hz, 3H), 1.01 (t, *J*=6.8 Hz, 3H), 1.39 (sext, *J*=7.6 Hz, 2H), 1.61 (quint, *J*=6.8 Hz, 2H), 1.83–1.93 (m, 1H), 1.93–2.02 (m, 1H), 2.47–2.57 (m, 2H), 3.61 (td, J_a=6.8 Hz, J_b=9.6 Hz, 1H), 3.81 (s, 3H), 3.91 (td, J_a=6.4 Hz, J_b=9.2 Hz, 1H), 3.97 (q, *J*=7.2 Hz, 2H), 5.19 (dd, J_a=2.8 Hz, J_b=4.0 Hz, 1H), 6.87 (td, J_a=1.6 Hz, J_b=8.8 Hz, 2H), 7.29 (td, J_a=2.4 Hz, J_b=8.8 Hz, 2H); ^{13}C NMR ($CDCl_3$): 13.9, 13.9, 18.8, 19.4, 26.2, 31.7, 55.3, 59.8, 68.6, 98.5, 103.8, 113.0, 129.3, 130.0, 159.6, 160.1, 168.6; IR (cm^{-1}): 2958, 2935, 2872, 1710, 1690, 1629, 1608, 1578, 1511, 1463, 1371, 1339, 1293, 1248, 1175, 1155, 1125, 1057, 954, 905, 833, 784, 759; HRMS *m*/*z* (ESI) calcd for $C_{19}H_{26}NaO_5$ $[M+Na]^+$ 357.1678; found 357.1669.

*4.2.2. Methyl 2-acetyl-5,5-bis(6-methyl-1H-indol-3-yl)pentanoate (**3f**).* Brown liquid; ^{1}H NMR ($CDCl_3$): 1.82–2.00 (m, 2H), 2.07–2.17 (m, 2H), 2.37 (s, 6H), 3.41 (t, *J*=7.2 Hz, 1H), 3.62 (s, 3H), 4.36 (t, *J*=7.2 Hz, 1H), 6.66 (dd, J_a=1.6 Hz, J_b=7.2 Hz, 2H), 6.83 (d, *J*=8.4 Hz, 2H), 6.95 (s, 2H), 7.39 (d, *J*=8.0 Hz, 2H), 7.69 (s, 2H); ^{13}C NMR ($CDCl_3$): 21.8, 27.2, 28.9, 33.3, 34.1, 52.5, 59.8, 111.4, 119.0, 119.2, 120.9, 121.3, 124.8, 124.9, 131.5, 137.2, 170.6, 203.9; IR (cm^{-1}): 3406, 2951, 2920, 1738, 1709, 1625, 1455, 1359, 1340, 1279, 1224, 1153, 1093, 802, 732; HRMS *m*/*z* (ESI) calcd for $C_{26}H_{28}N_2NaO_3$ $[M+Na]^+$ 439.1998; found 439.1983.

*4.2.3. Ethyl 2-acetyl-5,5-bis(2-methyl-1H-indol-3-yl)pentanoate (**3g**).* Brown liquid; ^{1}H NMR ($CDCl_3$): 1.18 (t, *J*=7.2 Hz, 3H), 1.87–1.95 (m, 2H), 2.08 (s, 3H), 2.19 (s, 3H), 2.20 (s, 3H), 2.34–2.46 (m, 2H), 3.43 (t, *J*=7.6 Hz, 1H), 4.10 (q, 7.2 Hz, 2H), 4.38 (t, *J*=7.6 Hz, 1H), 6.96 (t, *J*=7.2 Hz, 2H), 6.99 (t, *J*=7.6 Hz, 2H), 7.13 (d, *J*=7.6 Hz, 2H), 7.59 (d, *J*=7.6 Hz, 2H), 7.76 (d, *J*=2.8 Hz, 2H); 12.6, 12.6, 14.1, 27.1, 28.7, 32.3, 34.9, 60.0, 61.4, 110.3, 114.0, 119.1, 119.2, 119.2, 120.5, 128.2, 128.2, 131.1, 131.1, 135.2, 170.0, 203.6; IR (cm^{-1}): 3394, 2933, 2869, 1732, 1708, 1618, 1583, 1523, 1488, 1461, 1362, 1325, 1301, 1225, 1152, 1096, 1016, 744; HRMS *m*/*z* (ESI) calcd for $C_{27}H_{30}N_2NaO_3$ $[M+Na]^+$ 453.2154; found 453.2149.

*4.2.4. Ethyl 2-benzoyl-5,5-di(2-methyl-1H-indol-3-yl)pentanoate (**3j**).* Brown solid; mp: 150–152 °C; ^{1}H NMR ($CDCl_3$): 1.08 (t, *J*=7.2 Hz, 3H), 1.84–2.01 (m, 1.5H), 22.04–2.11 (m, 1.5H), 2.14 (d, *J*=5.2 Hz, 6H), 2.43–2.53 (m, 1H), 4.06 (q, *J*=7.2 Hz, 2H), 4.27–4.36 (m, 1H), 4.39 (t, *J*=8.0 Hz, 1H), 6.93 (t, *J*=7.6 Hz, 2H), 6.99 (t, *J*=7.2 Hz, 2H), 7.11 (t, *J*=7.6 Hz, 2H), 7.34 (t, *J*=8.0 Hz, 2H), 7.47–7.52 (m, 1H), 7.70 (d, *J*=8.0 Hz, 2H), 7.73 (d, *J*=8.0 Hz, 2H), 7.81 (dd, J_a=0.8 Hz, J_b=8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$): 12.5, 12.5, 14.0, 19.2, 18.4, 30.6, 32.4, 34.9, 54.4, 61.4, 65.7, 110.4, 113.9, 114.0, 119.0, 119.0, 119.2, 120.4, 120.4, 128.2, 128.6, 128.7, 128.9, 131.2, 133.4, 135.2, 136.2, 170.2, 195.7; IR (cm^{-1}): 3394, 2957, 2930, 1727, 1678, 1618, 1581, 1489, 1461, 1326, 1300, 1243, 756, 742, 698; HRMS *m*/*z* (ESI) calcd for $C_{32}H_{32}N_2NaO_3$ $[M+Na]^+$ 515.2311; found 515.2295.

*4.2.5. Ethyl 2-(4-methoxy)benzoyl-5,5-di(2-methyl-1H-indol-3-yl) pentanoate (**3k**).* Brown solid; mp: 92–94 °C; ^{1}H NMR ($CDCl_3$): 1.08 (t, *J*=7.2 Hz, 3H), 2.07 (d, *J*=5.6 Hz, 6H), 1.80–2.06 (m, 2H), 2.10–2.25 (m, 1H), 2.47 (q, *J*=7.2 Hz, 1H), 3.77 (s, 3H), 4.05 (q, *J*=7.2 Hz, 2H), 2.04–2.30 (m, 1H), 4.36 (t, *J*=8.0 Hz, 1H), 6.78 (d, *J*=8.8 Hz, 2H), 6.92 (t, *J*=8.0 Hz, 2H), 6.98 (t, *J*=7.6 Hz, 2H), 7.07 (t, *J*=6.8 Hz, 2H), 7.57 (d, *J*=8.0 Hz, 2H), 7.71 (d, *J*=7.6 Hz, 2H), 7.79 (d, *J*=8.8 Hz, 2H); ^{13}C NMR ($CDCl_3$): 12.4, 12.5, 14.0, 28.5, 32.5, 34.9, 54.2, 55.5, 61.4, 110.4, 113.9, 114.0, 118.9, 119.0, 119.2, 120.3, 120.4, 128.1, 128.2, 129.1, 131.0, 131.3, 135.2, 163.8, 170.5, 194.2; IR (cm^{-1}): 3394, 2960, 2934, 1729, 1672, 1599, 1575, 1512, 1461, 1424, 1302, 1260, 1172, 1027, 843, 743; HRMS *m*/*z* (ESI) calcd for $C_{33}H_{34}N_2NaO_4$ $[M+Na]^+$ 545.2416; found 545.2402.

*4.2.6. Methyl 2-acetyl-4-(1,8-dioxo-2,3,4,5,6,7,8,9-octahydro-1H-xanthen-9-yl)butanoate (**6a**).* Yellow pale liquid; ^{1}H NMR ($CDCl_3$): 1.40–1.48 (m, 2H), 1.57–1.65 (m, 2H), 1.98–2.09 (m, 4H), 2.22 (s, 3H), 2.33 (ddd, J_a=6.4 Hz, J_b=10 Hz, J_c=16.4 Hz, 2H), 2.43–2.54 (m, 4H), 2.60 (dt, J_a=5.2 Hz, J_b=17.6 Hz, 2H), 3.47 (t, *J*=7.2 Hz, 1H), 3.70 (s, 3H), 3.80 (t, *J*=4.8 Hz, 1H); ^{13}C NMR ($CDCl_3$): 20.4, 23.7, 24.9, 27.1, 27.2, 29.5, 31.4, 37.0, 52.3, 58.8, 115.3, 115.3, 165.7, 165.8, 170.1, 197.2, 197.3, 203.3; IR (cm^{-1}): 2953, 2873, 1743, 1715, 1665, 1620, 1454, 1432, 1383, 1201, 1174, 1131, 1063, 1011, 957, 899, 534; HRMS *m*/*z* (ESI) calcd for $C_{20}H_{24}NaO_6$ $[M+Na]^+$ 383.1471; found 383.1464.

*4.2.7. Methyl 2-acetyl-4-(3,3,6,6-tetramethyl-1,8-dioxo-2,3,4,5,6,7,8,9-octahydro-1H-xanthen-9-yl)butanoate (**6b**).* White solid; mp: 114–116 °C; ^{1}H NMR ($CDCl_3$): 1.12 (d, *J*=8.4 Hz, 12H), 1.47–1.55 (m, 2H), 1.59–1.67 (m, 2H), 2.20 (s, 3H), 2.25 (d, *J*=16 Hz, 2H), 2.32 (d, *J*=16 Hz, 2H), 2.38 (d, *J*=17.6 Hz, 2H), 2.44 (d, *J*=17.6 Hz, 2H), 3.46 (t, *J*=7.2 Hz, 1H), 3.69 (s, 3H), 3.77 (t, *J*=4.4 Hz, 1H); ^{13}C NMR ($CDCl_3$): 24.0, 25.0, 27.3, 27.3, 29.3, 31.2, 31.9, 40.8, 40.8, 50.8, 52.2, 58.8, 114.0, 114.1, 164.1, 164.2, 170.0, 197.0, 197.1, 203.0; IR (cm^{-1}): 2959, 2934, 1727, 1657, 1620, 1443, 1384, 1291, 1241, 1203, 1164, 1143, 1065, 1004, 899, 830, 577; HRMS *m*/*z* (ESI) calcd for $C_{24}H_{32}NaO_6$ $[M+Na]^+$ 439.2097; found 439.2081.

*4.2.8. Methyl 2-acetyl-4-(3,6-dimethyl-1, 8-dioxo-2,3,4,5,6,7,8,9-octahydro-1H-xanthen-9-yl)butanoate (**6c**).* Colorless liquid; ^{1}H NMR ($CDCl_3$): 1.12 (t, *J*=5.6 Hz, 6H), 1.39–1.51 (m, 2H), 1.52–1.63 (m, 2H), 2.0–2.5 (m, 1H), 2.07–2.10 (m, 1H), 2.20 (t, *J*=3.6 Hz, 3H), 2.22–2.41 (m, 4H), 2.45–2.62 (m, 4H), 3.39–3.49 (m, 1H), 3.69 (t, *J*=2.0 Hz, 3H), 3.78 (t, *J*=4.4 Hz, 1H); ^{13}C NMR ($CDCl_3$): 20.7, 20.8, 23.6, 23.7, 23.7, 24.8, 25.1, 28.0, 28.0, 28.3, 29.4, 29.5, 30.8, 30.8, 31.5, 34.8, 34.8, 35.3, 35.3, 35.4, 45.0, 45.3, 52.3, 58.7, 58.8, 58.8, 58.9, 114.4, 114.5, 114.5, 114.8, 114.9, 114.9, 164.6, 164.7, 164.7, 165.4, 164.5, 164.6, 170.1, 170.1, 197.1, 197.2, 197.2, 197.3, 203.2, 203.3; IR (cm^{-1}): 2956, 1743, 1715, 1667, 1621, 1455, 1433, 1384, 1359, 1290, 1187, 1134, 1004, 946, 917, 885, 732, 648, 596, 550; HRMS *m*/*z* (ESI) calcd for $C_{22}H_{28}NaO_8$ $[M+Na]^+$ 411.1784; found 411.1764.

*4.2.9. Ethyl 2-acetyl-4-(3,3,6,6-tetramethyl-1, 8-dioxo-2,3,4,5,6,7,8,9-octahydro-1H-xanthen-9-yl)butanoate (**6d**).* Yellow pale liquid; ^{1}H NMR ($CDCl_3$): 1.12 (d, *J*=9.6 Hz, 12H), 1.24 (t, *J*=7.2 Hz, 3H), 1.49–1.55 (m, 2H), 1.58–1.66 (m, 2H), 2.20 (s, 3H), 2.23–2.34 (m, 4H), 2.34–2.46 (m, 4H), 3.41 (t, *J*=3.2 Hz, 1H), 3.78 (t, *J*=4.4 Hz, 1H), 4.14 (dd, J_a=7.2 Hz, J_b=14.4 Hz, 2H); ^{13}C NMR ($CDCl_3$): 14.0, 23.9, 25.1, 27.4, 29.3, 29.3, 31.0, 32.0, 40.8, 50.9, 59.1, 61.2, 114.0, 114.1, 164.1, 164.2, 169.6, 197.0, 197.1, 203.2; IR (cm^{-1}): 2960, 2251, 1739, 1715, 1664, 1624, 1467, 1453, 1426, 1382, 1337, 1290, 1243, 1197, 1163, 1138, 1002, 916, 861, 732; HRMS *m*/*z* (ESI) calcd for $C_{25}H_{34}NaO_6$ $[M+Na]^+$ 453.2253; found 453.2237.

*4.2.10. Ethyl 2-acetyl-4-(3,6-dimethyl-1,8-dioxo-2,3,4,5,6,7,8,9-octahydro-1H-xanthen-9-yl)butanoate (**6e**).* Yellow pale liquid; ^{1}H NMR ($CDCl_3$): 1.12 (t, *J*=5.6 Hz, 6H), 1.24 (tt, J_a=1.2 Hz, J_b=7.2 Hz, 3H), 1.37–1.52 (m, 2H), 1.52–1.63 (m, 2H), 2.03 (dd, J_a=12.8 Hz,

J_b=16.4 Hz, 1H), 2.14–2.19 (m, 1H), 2.20 (t, J=3.6 Hz, 3H), 2.22–2.42 (m, 4H), 2.44–2.64 (m, 4H), 3.34–3.45 (m, 1H), 3.78 (dd, J_a=3.6 Hz, J_b=7.6 Hz, 1H), 4.10–4.19 (m, 2H); ^{13}C NMR ($CDCl_3$): 14.0, 20.6, 20.8, 23.5, 23.6, 24.9, 25.1, 28.0, 28.0, 28.3, 29.3, 29.4, 30.7, 31.4, 34.7, 34.8, 35.3, 35.3, 45.0, 45.3, 59.0, 59.0, 59.1, 59.1, 61.2, 114.4, 114.4, 114.8, 114.8, 114.9, 164.5, 164.6, 165.3, 165.4, 165.5, 169.5, 169.6, 169.6, 197.0, 197.1, 197.2, 203.2, 203.3; IR (cm^{-1}): 2958, 2932, 1740, 1714, 1667, 1622, 1455, 1431, 1384, 1290, 1239, 1187, 1135, 1005, 946, 863, 732, 649, 605, 570, 551; HRMS m/z (ESI) calcd for $C_{23}H_{30}NaO_6$ $[M+Na]^+$ 425.1940; found 425.1932.

*4.2.11. Ethyl 4-(1,8-dioxo-3,6-diphenyl-2,3,4,5,6,7,8,9-octahydro-1H-xanthen-9-yl)-2-(4-methoxybenzoyl)butanoate (**6f**).* White solid; mp: 75–77 °C; ^{1}H NMR ($CDCl_3$): 1.17 (q, 7.2 Hz, 3H), 1.50–1.99 (m, 4H), 2.50–2.99 (m, 8H), 3.30–3.51 (m, 2H), 3.84 (d, J=6.8 Hz, 3H), 3.94 (br s, 1H), 4.07–4.33 (m, 3H), 6.94 (dd, J_a=2.8 Hz, J_b=8.8 Hz, 2H), 7.20–7.30 (m, 7H), 7.35 (q, J=6.4 Hz, 3H), 7.97 (dt, J_a=2.0 Hz, J_b=13.2 Hz, 2H); ^{13}C NMR ($CDCl_3$): 14.1, 19.2, 24.5, 25.6, 25.8, 30.1, 30.6, 31.2, 34.3, 34.4, 34.9, 38.3, 38.4, 38.7, 39.0, 43.9, 44.0, 44.1, 53.6, 55.5, 55.5, 61.3, 61.3, 113.9, 114.9, 115.0, 126.7, 126.7, 126.7, 127.1, 127.2, 128.8, 128.9, 129.2, 129.3, 131.1, 142.1, 142.2, 142.2, 142.3, 163.9, 163.9, 164.4, 165.1, 165.2, 165.2, 169.9, 170.0, 193.8, 196.2, 196.5; IR (cm^{-1}): 2935, 1735, 1667, 1600, 1511, 1453, 1423, 1385, 1258, 1181, 1134, 1028, 991, 914, 843, 764, 700; HRMS m/z (ESI) calcd for $C_{39}H_{38}NaO_7$ $[M+Na]^+$ 641.2515; found 641.2497.

*4.2.12. Methyl 2-acetyl-5-(2-methyl-1H-indol-3-yl)-5-(p-methoxyphenyl)pentanoate (**8a**).* Red oil; ^{1}H NMR ($CDCl_3$): 1.66–1.96 (m, 2H), 1.97–2.07 (m, 2H), 2.09 (d, J=6.4 Hz, 1H), 2.12–2.25 (m, 2H), 2.29 (d, J=6.0 Hz, 3H), 3.32–3.48 (m, 1H), 3.61 (d, J=6.4 Hz, 1.5H), 3.66 (d, J=6.0 Hz, 1.5H), 3.70 (d, J=6.0 Hz, 2.7H), 3.77 (d, J=5.6 Hz, 0.3H), 4.04–4.16 (m, 1H), 6.76 (t, J=2.4 Hz, 2H), 6.97 (dd, J_a=5.2 Hz, J_b=12.0 Hz, 1H), 7.03 (q, J=6.8 Hz, 1H), 7.12–7.30 (m, 3H), 7.46 (br s, 1H); ^{13}C NMR ($CDCl_3$): 12.2, 12.3, 27.2, 27.3, 28.6, 29.0, 32.2, 32.3, 41.1, 41.2, 52.4, 52.4, 55.3, 59.6, 59.8, 110.5, 113.4, 113.5, 113.7, 119.1, 119.2, 119.2, 120.8, 127.6, 127.7, 128.5, 128.6, 131.6, 131.6, 135.5, 137.1, 137.1, 157.7, 170.4, 203.4, 203.4; IR (cm^{-1}): 3399, 2953, 1739, 1712, 1612, 1582, 1511, 1489, 1460, 1436, 1359, 1300, 1246, 1179, 1152, 1034, 971, 911, 831, 742, 596, 533; HRMS m/z (ESI) calcd for $C_{24}H_{27}NNaO_4$ $[M+Na]^+$ 416.1838; found 416.1825.

*4.2.13. Ethyl 2-acetyl-5-(6-fluoro-1H-indol-3-yl)-5-(p-methoxyphenyl)pentanoate (**8b**).* Brown liquid; ^{1}H NMR ($CDCl_3$): 1.22 (dd, J_a=7.2 Hz, J_b=12.4 Hz, 3H), 1.76–2.01 (m, 3H), 2.02–2.12 (m, 1H), 2.14 (d, J=9.2 Hz, 3H), 3.44 (q, J=7.6 Hz, 1H), 3.71 (s, 3H), 4.06 (t, J=6.4 Hz, 1H), 4.16 (q, J=6.8 Hz, 2H), 6.70–6.82 (m, 3H), 6.91 (d, J=2.0 Hz, 1H), 6.95 (d, J=5.6 Hz, 2H), 7.14 (d, J=7.2 Hz, 2H), 7.22–7.29 (m, 1H), 8.27 (br s, 1H); ^{13}C NMR ($CDCl_3$): 14.1, 14.1, 26.8, 26.9, 28.7, 29.0, 33.7, 33.9, 41.9, 42.0, 55.2, 59.8, 59.9, 61.5, 97.3, 97.6, 107.7, 108.0, 113.9, 119.6, 119.7, 120.0, 120.1, 121.5, 121.5, 123.5, 123.5, 128.7, 128.7, 136.5, 136.6, 136.8, 158.0, 158.7, 161.1, 169.9, 170.0, 203.6; IR (cm^{-1}): 3413, 2934, 1734, 1711, 1626, 1611, 1589, 1551, 1510, 1457, 1343, 1302, 1248, 1178, 1142, 1034, 952, 912, 834, 806, 733; HRMS m/z (ESI) calcd for $C_{24}H_{26}FNNaO_4$ $[M+Na]^+$ 434.1744; found 434.1736.

*4.2.14. Methyl 2-acetyl-5-(4-chloro-1H-indol-3-yl)-5-(p-methoxyphenyl)pentanoate (**8c**).* Yellow liquid; ^{1}H NMR ($CDCl_3$): 1.78–2.00 (m, 3H), 2.05–2.13 (m, 1H), 2.13 (s, 1.5H), 2.17 (s, 1.5H), 3.47 (dd, J_a=6.8 Hz, J_b=14.4 Hz, 1H), 3.67 (s, 1.5H), 3.70 (s, 1.5H), 3.73 (d, J=0.8 Hz, 3H), 4.77 (t, J=8.0 Hz, 1H), 6.79 (dd, J_a=2.8 Hz, J_b=8.8 Hz, 2H), 6.88 (d, J=2.4 Hz, 0.5H), 6.92 (d, J=2.0 Hz, 0.5H), 6.97–7.02 (m, 2H), 7.13–7.21 (m, 3H), 8.44 (br s, 1H); ^{13}C NMR ($CDCl_3$): 27.0, 27.1, 28.8, 29.0, 35.5, 35.7, 41.3, 41.4, 52.4, 52.4, 55.2, 59.6, 59.8, 110.1, 113.8, 113.8, 120.3, 120.6, 120.7, 122.4, 123.0, 123.5, 123.6, 126.1, 129.1, 129.1, 136.9, 137.1, 138.0, 157.9, 157.9, 170.3, 170.4, 203.5, 203.5, 203.6; IR (cm^{-1}): 3394, 2954, 2933, 1738, 1712, 1611, 1583, 1511, 1484, 1456, 1433, 1358, 1339, 1300, 1248, 1181, 1148, 1112, 1036, 936, 910, 821, 779, 739; HRMS m/z (ESI) calcd for $C_{23}H_{24}ClNNaO_4$ $[M+Na]^+$ 436.1292; found 436.1289.

*4.2.15. Methyl 2-acetyl-5-(4-methoxyphenyl)-5-(4-dimethylnophenyl) pentanoate (**9a**).* Yellow liquid; ^{1}H NMR ($CDCl_3$): 1.68–2.00 (m, 4H), 2.14 (s, 3H), 2.87 (s, 6H), 3.42 (t, J=7.2 Hz, 1H), 3.69 (s, 3H), 3.69–3.78 (m, 4H), 6.65 (dd, J_a=1.2 Hz, J_b=8.4 Hz, 2H), 6.79 (dd, J_a=1.6 Hz, J_b=8.4 Hz, 2H), 7.05 (quint, J=3.2 Hz, 2H), 7.11 (quint, J=3.2 Hz, 2H); ^{13}C NMR ($CDCl_3$): 27.0, 28.7, 33.7, 40.8, 49.4, 52.4, 55.2, 59.7, 59.7, 112.9, 113.9, 128.2, 128.3, 128.3, 128.6, 128.6, 132.7, 132.9, 137.3, 137.5, 149.2, 157.9, 170.2, 203.1; IR (cm^{-1}): 2998, 2953, 2801, 1743, 1715, 1612, 1583, 1514, 1445, 1353, 1247, 1210, 1178, 1035, 948, 815, 547; HRMS m/z (ESI) calcd for $C_{23}H_{29}NnaO_4$ $[M+Na]^+$ 406.1994; found 406.1989.

*4.2.16. Methyl 2-acetyl-5-(4-methoxyphenyl)-5-(4-N-methylaminophenyl)pentanoate (**9b**).* Yellow liquid; ^{1}H NMR ($CDCl_3$): 1.62–1.80 (m, 2H), 1.80–1.95 (m, 2H), 2.09 (s, 3H), 2.73 (s, 3H), 3.37 (t, J=7.2 Hz, 1H), 3.56 (br s, 1H), 3.65 (s, 3H), 3.67 (s, 1H), 3.70 (s, 3H), 6.47 (d, J=8.4 Hz, 2H), 6.74 (d, J=8.4 Hz, 2H), 6.95 (dd, J_a=3.6 Hz, J_b=8.4 Hz, 2H), 7.05 (dd, J_a=3.2 Hz, J_b=8.8 Hz, 2H); ^{13}C NMR ($CDCl_3$): 13.8, 19.2, 26.9, 28.7, 28.7, 30.6, 30.9, 33.7, 49.4, 52.4, 55.2, 59.7, 59.7, 65.6, 112.6, 113.9, 128.4, 128.4, 128.6, 128.6, 128.9, 130.9, 133.3, 133.5, 137.3, 137.5, 147.7, 157.9, 170.2, 203.1; IR (cm^{-1}): 3414, 2953, 2933, 1741, 1714, 1613, 1583, 1513, 1454, 1439, 1358, 1247, 1179, 1151, 1035, 821, 556; HRMS m/z (ESI) calcd for $C_{22}H_{27}NNaO_4$ $[M+Na]^+$ 392.1838; found 392.1831.

*4.2.17. Methyl 2-acetyl-5-(2-hydroxynaphthalen-1-yl)-5-(p-methoxyphenyl)pentanoate (**10a**).* Brown liquid; ^{1}H NMR ($CDCl_3$): 1.60–1.94 (m, 2H), 2.04 (s, 1.6H), 2.06 (s, 1.4H), 2.21–2.45 (m, 2H), 3.40 (t, J=7.2 Hz, 0.45H), 3.50 (t, J=7.6 Hz, 0.55H), 3.62 (s, 1.5H), 3.66 (s, 1.5H), 3.71 (d, J=2.4 Hz, 3H), 4.98 (br s, 1H), 5.82 (br s, 1H), 6.78 (dd, J_a=4.0 Hz, J_b=8.8 Hz, 2H), 7.00 (d, J=8.8 Hz, 1H), 7.21–7.33 (m, 3H), 7.38 (s, 1H), 7.60 (d, J=8.8 Hz, 1H), 7.74 (d, J=8.0 Hz, 1H), 7.98 (br s, 1H); ^{13}C NMR ($CDCl_3$): 13.8, 19.2, 22.6, 26.8, 27.0, 28.5, 28.9, 29.7, 29.9, 30.6, 43.8, 52.4, 52.4, 55.2, 59.4, 59.8, 65.7, 114.0, 118.9, 119.0, 121.6, 121.8, 123.0, 126.4, 127.9, 128.5, 128.8, 128.9, 129.7, 129.8, 130.9, 131.0, 133.4, 133.4, 135.9, 152.0, 152.1, 157.9, 170.4, 170.4, 203.8; IR (cm^{-1}): 3416, 3002, 2954, 1735, 1711, 1671, 1623, 1609, 1583, 1511, 1457, 1437, 1360, 1248, 1180, 1149, 1034, 911, 815, 733; HRMS m/z (ESI) calcd for $C_{25}H_{26}NaO_5$ $[M+Na]^+$ 429.1678; found 429.1663.

*4.2.18. Ethyl 2-acetyl-5-(2,4-dihydroxyphenyl)-5-(4-methoxyphenyl) pentanoate (**11a**).* Colorless liquid; ^{1}H NMR ($CDCl_3$): 1.20 (t, J=7.2 Hz, 3H), 1.85 (m, 4H), 2.13 (d, 3.6 Hz, 3H), 3.46 (dd, J_a=16.4 Hz, J_b=6.8 Hz, 1H), 4.12 (m, 3H), 6.26 (s, 1H), 6.34 (dd, J_a=14.8 Hz, J_b=8.4 Hz, 2H), 6.58 (s, 1H), 6.76 (d, J=8.4 Hz, 2H), 7.12 (d, J=8.4 Hz, 2H); ^{13}C NMR: 13.7, 14.0, 14.1, 19.1, 26.6, 26.7, 28.8, 28.9, 30.5, 32.5, 42.1, 42.3, 55.2, 59.6, 59.7, 60.7, 61.8, 65.9, 103.3, 107.6, 107.7, 107.8, 113.8, 123.1, 123.3, 128.6, 128.8, 128.9, 130.3, 131.1, 136.2, 136.4, 154.3, 154.4, 154.9, 157.0, 157.7, 170.2, 170.3, 204.9; IR (cm^{-1}): 3401, 3033, 2959, 2935, 2870, 2837, 1727, 1699, 1607, 1511, 1456, 1369, 1302, 1246, 1212, 1178, 1149, 1112, 1033, 974, 910, 839, 732, 632, 552; HRMS m/z (ESI) calcd for $C_{22}H_{26}NaO_6$ $[M+Na]^+$ 409.1627; found 409.1619.

*4.2.19. 3-[(3,4-Dimethoxyphenyl)(4,5-dimethoxy-2-hydroxyethylphenyl)methyl]-1H-indole (**13a**).* Red oil; ^{1}H NMR ($CDCl_3$): 1.73 (br s, 1H), 2.89 (dt, J_a=1.2 Hz, J_b=6.4 Hz, 2H), 3.54 (s, 3H), 3.69–3.76 (m, 5H), 3.83 (s, 3H), 3.85 (s, 3H), 5.79 (s, 1H), 6.47 (d, J=1.2 Hz, 1H), 6.59 (s, 1H), 6.64 (dd, J_a=2.0 Hz, J_b=8.4 Hz, 1H), 6.72–6.78 (m, 3H), 6.96 (t, J=7.6 Hz, 1H), 7.13 (t, J=8.0 Hz, 1H), 7.21 (d, J=8.0 Hz, 1H), 7.29 (d, J=8.0 Hz, 1H), 8.28 (s, 1H); ^{13}C NMR ($CDCl_3$): 35.7, 43.9, 55.8, 55.8,

55.9, 63.5, 110.8, 111.2, 112.4, 113.2, 113.3, 119.3, 119.8, 120.0, 121.0, 122.1, 124.3, 126.9, 128.5, 134.8, 136.6, 136.8, 147.2, 147.4, 148.7; HRMS *m*/*z* (ESI) calcd for $C_{27}H_{29}NNaO_5$ $[M+Na]^+$ 470.1943; found 470.1946.

*4.2.20. 2-[(3,4-Dimethoxyphenyl)(4,5-dimethoxy-2-hydroxyethylphenyl)methyl]-1H-pyrrole (**15a**).* Red oil; ^1H NMR: 1.65 (s, 1H), 2.74–2.82 (m, 1H), 2.84–2.92 (m, 1H), 3.65 (d, *J*=2.8 Hz, 3H), 3.68 (t, *J*=3.2 Hz, 2H), 3.76 (d, *J*=2.8 Hz, 3H), 3.85 (dd, J_a=2.8 Hz, J_b=5.2 Hz, 6H), 5.64 (s, 1H), 5.75 (s, 1H), 6.11 (t, *J*=2.8 Hz, 1H), 6.50 (d, *J*=2.8 Hz, 1H), 6.61 (d, *J*=8 Hz, 1H), 6.67 (s, 1H), 6.70 (s, 1H), 6.72 (d, *J*=2.8 Hz, 1H), 6.77 (dd, J_a=2.8 Hz, J_b=8 Hz, 1H), 7.98 (s, 1H); ^{13}C NMR ($CDCl_3$): 35.4, 45.6, 55.9, 55.9, 63.5, 107.8, 108.3, 111.0, 112.2, 112.8, 113.2, 117.1, 120.9, 128.8, 134.0, 134.1, 135.6, 147.5, 147.6, 147.7, 148.9; HRMS *m*/*z* (ESI) calcd for $C_{23}H_{27}NNaO_5$ $[M+Na]^+$ 420.1787; found 420.1778.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at http://dx.doi:10.1016/j.tet.2012.11.076.

References and notes

1. (a) Schäffner, B.; Schäffner, F.; Verevkin, S. P.; Börner, A. *Chem. Rev.* **2010**, *110*, 4554–4581; (b) Estevez, C. Sustainable Solutions—Green Solvents for Chemistry. In *Sustainable Solutions for Modern Economies. RSC Green Chemistry Series*; The Royal Society of Chemistry: Cambridge, 2009; Vol. 4, pp 407–424.
2. Clark, J. H.; Tavener, S. J. *Org. Process Res. Dev.* **2007**, *11*, 149–155.
3. (a) Kerton, F. M. Alternative Solvents for Green Chemistry. In *RSC Green Chemistry Series*; Clark, J., Ed.; The Royal Society of Chemistry: Cambridge, 2009; (b) Leitner, W. *Green Chem.* **2007**, *9*, 923; (c) Leitner, W. *Green Chem.* **2009**, *11*, 603.
4. (a) Gu, Y.; Jerome, F. *Green Chem.* **2010**, *12*, 1127–1138; (b) A. E.Díaz-Álvarez, J. Francos, B. Lastra-Barreira, P. Crochet, V.Cadierno, Chem. Commun. 6208–6227.
5. (a) Aparicio, S.; Alcalde, R. *Green Chem.* **2009**, *11*, 65–78; (b) Aparicio, S.; Alcalde, R. *J. Phys. Chem. B* **2009**, *113*, 14257–14269; (c) Pereira, C. S. M.; Silva, V. M. T. M.; Rodrigues, A. E. *Green Chem.* **2011**, *13*, 2658–2671.
6. Reddy, C. S. K.; Ghai, R.; Rashmi; Kalia, V. C. *Bioresource Technol.* **2003**, *87*, 137–146.
7. Salehpour, S.; Dube, M. A. *Green Chem.* **2008**, *10*, 321–326.
8. Kulkarni, P. S.; Brazinha, C.; Afonso, C. A. M.; Crespo, J. G. *Green Chem.* **2010**, *12*, 1990–1994.
9. (a) Simeó, Y.; Sinisterra, J. V.; Alcántara, A. R. *Green Chem.* **2009**, *11*, 855–862; (b) Shanmuganathan, S.; Natalia, D.; van den Wittenboer, A.; Kohlmann, C.; Greiner, L.; de María, P. D. *Green Chem.* **2010**, *12*, 2240–2245.
10. Sheldon, R. A. *Green Chem.* **2005**, *7*, 267–278.
11. (a) He, F.; Li, P.; Gu, Y.; Li, G. *Green Chem.* **2009**, *11*, 1768–1773; (b) Li, M.; Chen, C.; He, F.; Gu, Y. *Adv. Synth. Catal.* **2010**, *352*, 519–530; (c) Tan, J.-N.; Li, H.; Gu, Y. *Green Chem.* **2010**, *12*, 1772–1782; (d) Tan, J.-N.; Li, M.; Gu, Y. *Green Chem.* **2010**, *12*, 908–914.
12. (a) Tan, X.; Deng, W.; Liu, M.; Zhang, Q.; Wang, Y. *Chem. Commun.* **2009**, 7179–7181; (b) Onda, A.; Ochi, T.; Yanagisawa, K. *Catal. Commun.* **2011**, *12*, 421–425.
13. Zhou, B.; Yang, J.; Li, M.; Gu, Y. *Green Chem.* **2011**, *13*, 2204–2211.
14. (a) Ismabery, N.; Lavila, R. *Chem.—Eur. J.* **2008**, *14*, 8444–8454; (b) Alcaide, B.; Almendros, P.; Aragoncillo, C. *Curr. Opin. Drug Discov. Dev.* **2010**, *13*, 685–697; (c) Dondoni, A. *Org. Biomol. Chem.* **2010**, *8*, 3366–3385; (d) Rodriguez, F.; Fananas, F. J. *Target in Heterocyclic Systems*; The Royal Society of Chemistry: Cambridge, 2009; Vol. 13; pp 273–302.
15. (a) Gupta, K. C.; Gupta, P.; Singh, P.; Singh, S. V.; Agarwal, S. Chemistry of Natural Dyes In *Natural Dyes: Scope and Challenges*; Daniel, M., Ed.; Scientific: Jodhpur, India, 2006; pp 7–34; (b) Marco, J. A.; Carda, M.; Murga, J.; Falomir, E. *Tetrahedron* **2007**, *63*, 2929–2958; (c) Rodriguez, R.; Moses, J. E.; Adlington, R. M.; Baldwin, J. E. *Org. Biomol. Chem.* **2005**, *3*, 3488–3495; (d) Cheung, A. K.; Murelli, R.; Snapper, M. L. *J. Org. Chem.* **2004**, *69*, 5712–5719.
16. (a) Li, M.; Tang, C.; Li, T.; Gu, Y. *Chem. Commun.* **2011**, 4529–4531; (b) Li, M.; Li, H.; Gu, Y. *Org. Lett.* **2011**, *13*, 1064–1067; (c) Li, M.; Yang, J.; Gu, Y. *Adv. Synth. Catal.* **2011**, *353*, 1551–1564; (d) Li, M.; Gu, Y. *Tetrahedron* **2011**, *67*, 8314–8320.
17. *Examples of acid catalyzed formation of oxocarbenium ions from acetals:* (a) Cossy, J.; Rakotoarisoa, H.; Kahn, P.; Desmurs, J.-R. *Tetrahedron Lett.* **2000**, *41*, 7203–7205; (b) Saraswathy, V. G.; Sankararaman, S. *J. Chem. Soc., Perkin Trans. 2* **1996**, 29–31; (c) Jensen, J. L.; Wuhrman, W. B. *J. Org. Chem.* **1983**, *48*, 4686–4691.
18. *Compound **12a** was obtained according to a reported method*: Saeed, A. *Chin. Chem. Lett.* **2010**, *21*, 261–264.
19. *Compound **1f** was obtained according to a reported method*: Gu, Y.; De Sousa, R.; Frapper, G.; Bachmann, C.; Barrault, J.; Jérôme, F. *Green Chem.* **2009**, *11*, 1968–1972.