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Supramolecular carbohydrate scaffold-catalyzed synthesis of tetrahydroquinolines

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ABSTRACT

Natural supramolecular carbohydrate scaffold-catalyzed synthesis of tetrahydroquinoline derivatives by the reaction of aromatic amine and cyclic enol ether in excellent yield with high diastereoselectivity has been developed. Carbohydrates, cellulose, and starch were converted into their sulfonic acid derivative and these scaffolds exhibit efficient catalytic properties, along with excellent cost effectivity and recyclability.

Recently due to environmental and social pressure on industry, there has been a strong shift towards green technology.[1] Chemists have to dedicate numerous efforts to the development of clean technologies either by replacing a conventional solvent with an ecofriendly solvent or by developing a new ecofriendly catalyst.[2] The major challenge in this area is the development of lucrative, highly active, and stable solid acid catalyst as a substitute of homogeneous catalysts, such as HF, $AlCl_3$, and H_2SO_4. Even though these homogeneous catalysts are very successful, they produce highly corrosive media with chemically reactive waste streams. Indeed, the solid catalysts have many advantages; they are noncorrosive and environmentally benign, presenting fewer disposal problems. Their reuse is possible and their separation from liquid products is much easier. Furthermore, they can be designed to give higher activity, selectivity, and longer catalytic life. In this regard natural biopolymers are attractive candidates as new solid support catalysts.[3,4]

As a part of our continual efforts toward the development of environmentally benign synthetic procedures for multicomponent reactions,[5] we have initiated exploration of ecofriendly natural supramolecular carbohydrates as catalyst for the synthesis of bioactive tricylic tetrahydroquinoline scaffolds.

The tricylic tetrahydroquinoline moieties are widely distributed in nature and reveal a broad range of biological activities. Tricylic tetrahydroquinoline moieties are found in many alkaloids (Fig. 1) such as flindersine, oricine, veprisine, and skimmianine.[6,7] These alkaloids possess important biological activities such as antiallergic,[8] psychotropic,[9] anti-inflammatory,[10] and estrogenic.[11]

A plethora of procedures for the formation of tetrahydroquinoline is precedented in the literature, catalyzed by Lewis acid,[12–17]

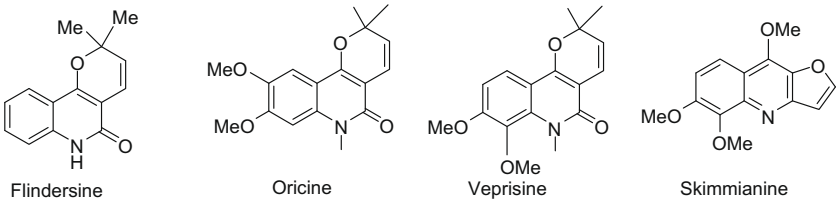

Figure 1. Bioactive tricyclic tetrahydroquinoline.

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metal triflates,[18–20] and protonic acids, such as HCl and trifluoroacetic acid. Also Chao-Jun Li et al. have reported that indium(III) chloride catalyzed pyranoquinoline in water.[21] The *aza*-Diels–Alder reaction catalyzed by Lewis acid is the most explored method for the synthesis of pyrano-/furano-quinoline derivatives. All these methodologies involve costly and hazardous catalyst as well as cumbersome work-up procedure.

We wish to report here an efficient synthesis of tricyclic tetrahydroquinoline using natural supramolecular carbohydrates as catalyst via cycloaddition of aromatic amine and cyclic enol ether. Carbohydrates are considered as the most abundant molecules of the biomass and we have selected two most generous supramolecular carbohydrates: cellulose and starch molecules, for catalytic activity, because these are very cost-effective, biodegradable, and are obtained from renewable resources. In order to achieve effective catalytic properties, cellulose and starch were converted to their sulfonic acid derivatives (Fig. 2).

We herein describe the diastereoselective synthesis of tricyclic tetrahydroquinoline by cellulose sulfuric acid (CellSA) or starch sulfuric acid (StarSA) as catalyst from aromatic amine and cyclic enol ether.

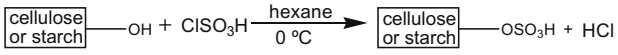
The reaction of aromatic amine with 2 equiv of cyclic enol ether in the presence of CellSA or StarSA in acetonitrile at room temperature furnished the corresponding pyranoquinoline and furanoquinoline in good to excellent yields. The cis and trans isomers are formed in almost all the cases. However cis-isomer is preferentially formed with a high diastereoselectivity. Furanoquinolines showed a better diastereoselectivity than pyranoquinolines[22] (Scheme 1). This reaction is categorized as ABB′ type multicomponent reaction because cyclic enol ether (B) component is chemodifferentially incorporated in two distinct manners (B and B′).[23] The cyclic enol ether serves a dual role: as an aldehyde and as a cyclic enol ether.

CellSA or StarSA can be easily prepared by the reaction of an inexpensive cellulose or starch with chlorosulfonic acid[24] (Scheme 2).

This white homogeneous solid acid is very stable and is not affected by air, water, or light. Sulfur content of the samples by conventional elemental analysis was 0.55 and 0.12 mmol/g for cellulose sulfuric acid and starch sulfuric acid, respectively. The number of H^+ sites of cellulose–SO_3H and starch–SO_3H determined by acid–base titration was 0.50 and 0.10 mequiv/g, respectively. This value corresponds to about 90% and 83% of the sulfur content, indicating that most of the sulfur species on both the samples are in the form of the sulfonic acid group.

The cellulose–SO_3H catalyst has an excellent catalytic property which is attributed to the high hydrothermal stability and strong acid sites of sulfo functional groups. Due to low solubility and high stability, cellulose is more suitable as a support relative to starch.

We explored the 1:2 coupling of substituted anilines with electron-rich alkene under different conditions and found that cellulose sulfuric acid (cellSA) was the most efficient catalyst for tetrahydroquinoline synthesis in CH_3CN at room temperature.



Scheme 2. The preparation of a catalyst.

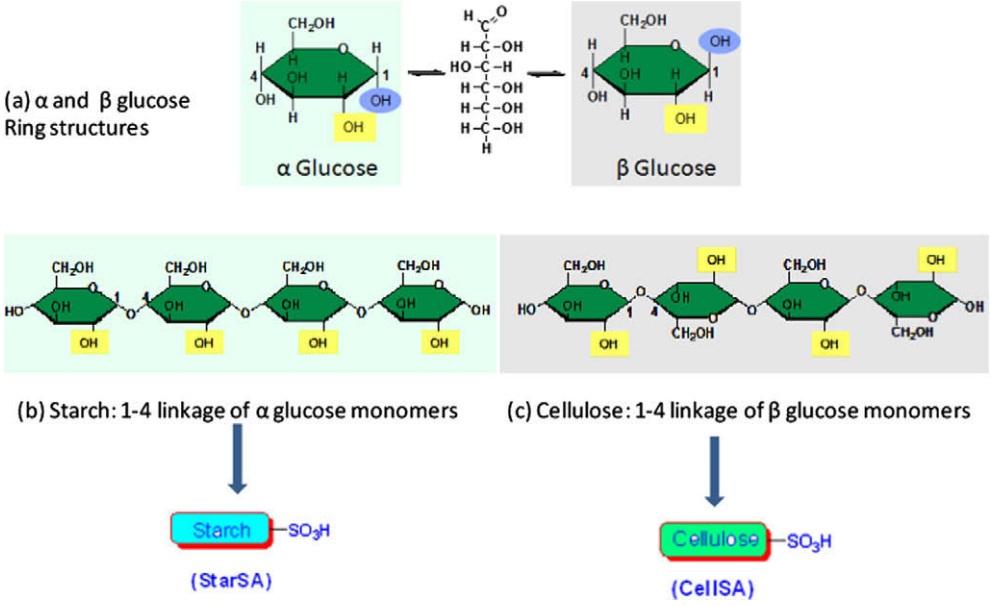
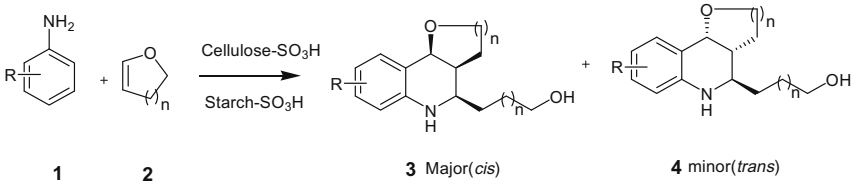


Figure 2. Natural supramolecular carbohydrate catalyst.



Scheme 1. Synthesis of pyranoquinoline and furanoquinoline.

In the reaction of aniline (5 mmol) with pyran (10 mmol) in the presence of 0.01 g of cellulose sulfuric acid in CH_3CN, only a trace amount of desired product is formed in 24 h. To optimize the reaction conditions, we carried out the reaction with 0.02, 0.03, 0.04, and 0.05 g of CellSA and StarSA. The best results were obtained with CellSA (0.03 g) in terms of yields and reaction time (Fig. 3).

One of the advantages of solid acid catalysts is their recyclability. We were able to separate cellulose or starch sulfuric acid from the reaction medium smoothly by washing with CH_2Cl_2. After drying, it was reused for successive reactions (at least 3–4 runs). Thus, this process could also be interesting for large-scale synthesis. CellSA was found to be more efficient in recyclability than StarSA (Fig. 4).

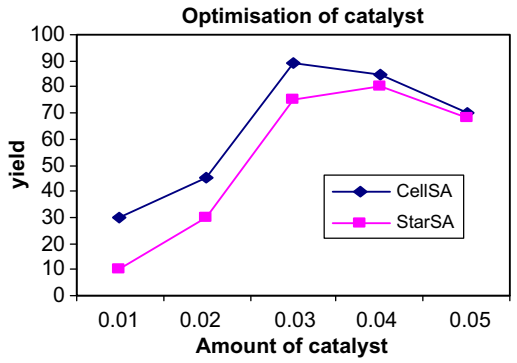


Figure 3. Catalyst optimization plot.

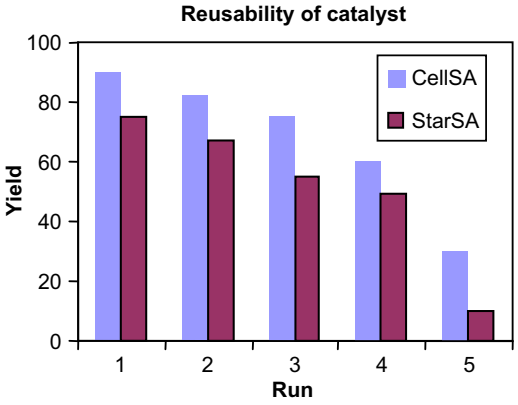


Figure 4. Reusability of catalyst.

We also carried out the reaction without any catalyst, where cellulose and starch with aniline and 3,4-dihydro-*2H*-pyran were reacted at room temperature in CH_3CN for two days but no reaction was observed. In order to see the solvent effect on this reaction, we have performed the reaction in acetonitrile, DMF, and THF. Acetonitrile was found to be the best solvent with respect to yields, reaction time, and selectivity. Reaction of aniline with 3,4-dihydro-*2H*-pyran in acetonitrile in the presence of cellulose sulfuric acid (0.03 g) gave pyranoquinolines in good yield (89%)

Table 1
Reaction optimization with catalyst and solvent

Catalyst	*g*	Solvent	Time (h)	Yield[a]	*cis*/*trans*[b]
None	—	CH_3CN	48	Trace	—
Cellulose	0.03	CH_3CN	48	Trace	—
Starch	0.03	CH_3CN	48	Trace	—
StarSA	0.03	CH_3CN	4	75	—
StarSA	0.04	CH_3CN	5	80	—
StarSA	0.05	CH_3CN	4.5	77	—
CellSA	0.01	CH_3CN	24	Trace	—
CellSA	0.02	CH_3CN	8	20	—
CellSA	0.03	CH_3CN	8	89	85:15
CellSA	0.03	THF	8	58	68:32
CellSA	0.03	DMF	8	50	60:40
CellSA	0.04	CH_3CN	4	78	85:15
CellSA	0.05	CH_3CN	4	70	85:15

[a] (%) Isolated yield.
[b] *Cis*/*trans* ratio was determined by ^1H NMR.

Table 2
Cellulose sulfuric acid-catalyzed pyranoquinoline and furanoquinoline

Entry	R	*n*	Reaction time (h)	Yield[a] (%)	*cis*/*trans*[b]
a	H	2	4.0	89	85:15
b	*p*-OCH_3	2	4.5	74	79:21
c	*o*-OCH_3	2	4.0	85	82:18
d	*p*-CH_3	2	5.5	83	80:20
e	*p*-F	2	6.0	72	75:25
f	*p*-Cl	2	5.0	65	78:22
g	*p*-Br	2	6.5	79	89:13
h	*m*-NO_2	2	5.5	60	67:33
i	H	1	4.5	78	89:11
j	*p*-Cl	1	6.0	95	82:18
k	*p*-CH_3	1	4.5	90	90:10
l	*p*-OCH_3	1	4.0	89	87:13
m	*p*-Br	1	4.4	90	91:09

Reaction conditions: 5 mmol (aromatic amine) 10 mmol (cyclic enol ether).
[a] Isolated yield.
[b] cis/trans ratio determined by ^1H NMR.

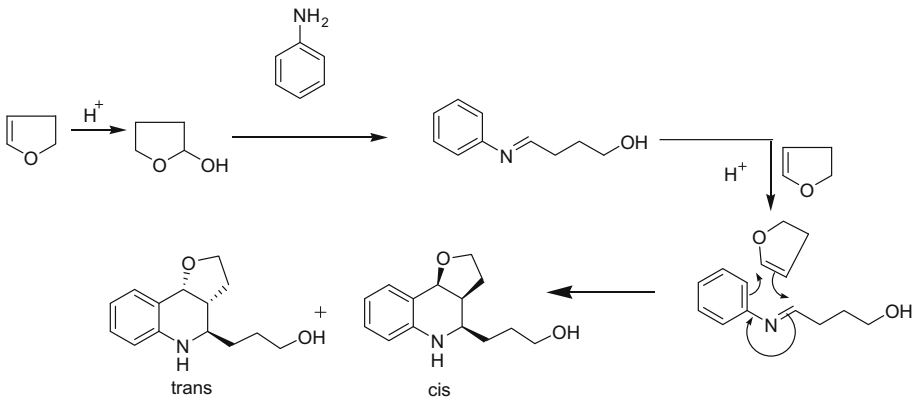


Figure 5. The proposed reaction mechanism for CellSA-catalyzed furanoquinoline derivative.

with high cis selectivity (Table 1). Compound 3a (cis product) was obtained as a major product, whereas **4a (trans** product) was obtained as a minor product. The optimized conditions of pyranoquinolines were applied for the synthesis of furanoquinolines. The selectivity and yield of furanoquinolines were better than those of the corresponding pyranoquinolines.

Using these optimized reaction conditions, the efficiency of the catalyst was studied for the synthesis of a wide variety of aromatic amines, and the results are summarized in[25] Table 2. The substituent on aniline has a marked effect on the reaction. Aniline with an electron-donating group favors the reaction more than with an electron-withdrawing group.

A proposed mechanism for the formation of furanoquinolines is given in Figure 5.

In summary, cellulose sulfuric acid, a recyclable and easily handled solid-supported acid catalyst, has been demonstrated as a new reagent for the synthesis of tricyclic tetrahydroquinoline. This novel methodology allows for the first time the preparation of tricyclic tetrahydroquinoline, a transformation that only proceeded previously with extremely poor yields and diastereoselectivity. The synthetic efficacy of this protocol has been further extended.

Acknowledgment

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References and notes

1. (a) Anastas, P. T.; Warner, J. C. *Green Chemistry Theory and Practice*; Oxford Univ. Press: Oxford, 1998; (b)*Green Chemistry: Frontiers in Chemical Synthesis and Processes*; Anastas, P. T., Williamson, T. C., Eds.; Oxford Univ. Press: Oxford, 1998; (c)*Benign by Design: Alternative Synthetic Design for Pollution Prevention*; Anastas, P. T., Farris, C. A., Eds.ACS Symp. Ser. nr. 577; ACS: Washington, DC, 1994.
2. (a) Sheldon, R. A. *Chem tech,* March, 1994, pp 38–47.; (b) Sheldon, R. A. *Chem. Ind. (London)* **1992**, *903*; (c) Sheldon, R. A. *Chem. Ind. (London)* **1997**, *12*; (d) Sheldon, R. A. *J. Chem. Tech. Biotechnol.* **1997**, *68*, 381; (e) Sheldon, R. A. *J. Mol. Catal. A: Chem.* **1996**, *107*, 75.
3. (a) Breslow, R. *Acc. Chem. Res.* **1980**, *13*, 170; (b) Clark, J. H.; Macquarrie, D. J. *Green Chemistry and Technology*; Blackwell: Abingdon, 2002.
4. (a) Ahmad, S.; Ali, M. *Appl. Catal., A* **2007**, *331*, 149; (b) Ahmad, S.; Ali, M.; Jafar, R.; Ebrahim, S. *Chem. Pharm. Bull.* **2007**, *55*, 957; (c) Ahmad, S.; Abbas, R.; Zahra, B. *Catal. Commun.* **2008**, *9*, 13.
5. (a) Kumar, A.; Maurya, R. A. *Tetrahedron Lett.* **2008**, *49*, 5471–5474; (b) Kumar, A.; Maurya, R. A. *Tetrahedron* **2008**, *64*, 3471–3482; (c) Kumar, A.; Maurya, R. A. *Tetrahedron Lett.* **2007**, *48*, 3887–3890; (d) Kumar, A.; Maurya, R. A. *Tetrahedron* **2007**, *63*, 1946–1952.
6. (a) Anzino, M.; Cappelli, A.; Vomero, S.; Cagnatto, A.; Scorupska, M. *Med. Chem. Res.* **1993**, *3*, 44; (b) Quraishi, M. A.; Thakur, V. R.; Dhawan, S. N. *Indian J. Chem., Sect. B* **1989**, *28B*, 891.
7. (a) Ramesh, M.; Mohan, P. S.; Shanmugam, P. *Tetrahedron* **1984**, *40*, 4041–4049; (b) Abe, M. O. *Phytochemistry* **1971**, *10*, 3328–3330; (c) Khalid, S. A. *Phytochemistry* **1981**, *20*, 2761–2763; (d) Sejourne, M.; Viel, C.; Bruneton, J.; Rideau, M.; Chenieux, J. C. *Phytochemistry* **1981**, *20*, 353–355.
8. (a) Takahashi, K.; Arai, Y.; Kadowaki, S.; Shono, T.; Yuki, S.; Kanayama, T.; Nishi, H.; Sugasawa, K.; Iwakura, M. *Oyo Yakuri* **1986**, *32*, 233 (Jpn); (b) Takahashi, K.; Arai, Y.; Kadowaki, S.; Shono, T.; Yuki, S.; Kanayama, T.; Nishi, H.; Sugasawa, K.; Iwakura, M. *Chem. Abstr.* **1986**, *105*, 218691j; (c) Yamada, N.; Kadowaki, S.; Takahashi, K.; Umezu, K. *Biochem. Pharmacol.* **1992**, *44*, 121.
9. Nesterova, I. N.; Alekseeva, L. M.; Andreeva, L. M.; Andreeva, N. I.; Golovira, S. M.; Granik, V. G. *Khim.-Farm. Zh.* **1995**, *29*, 31 (Russ); Nesterova, I. N.; Alekseeva, L. M.; Andreeva, L. M.; Andreeva, N. I.; Golovira, S. M.; Granik, V. G. *Chem. Abstr.* **1996**, *124*, 117128t.
10. Faber, K.; Stueckler, H.; Kappe, T. *J. Heterocycl. Chem.* **1984**, *21*, 1177.
11. Khodzhaeva, Kh. S. A.; Bessonova, I. A. *Dokl. Akad. Nauk Uzh. SSR.* **1982**, 34–36. Russ; Khodzhaeva, Kh. S. A.; Bessonova, I. A. *Chem. Abstr.* **1983**, *98*, 83727q.
12. Povarov, L. S. *Russ. Chem. Rev.* **1967**, *36*, 656.
13. Babu, G.; Perumal, P. T. *Tetrahedron Lett.* **1998**, *39*, 3225.
14. Yadav, J. S.; Reddy, B. V. S.; Srinivas, R.; Madhuri, Ch.; Ramalingam, T. *Synlett* **2001**, 240.
15. Yadav, J. S.; Reddy, B. V. S.; Madhuri, Ch.; Sabitha, G. *Synthesis* **2001**, 1065.
16. Babu, G.; Perumal, P. T. *Tetrahedron Lett.* **1997**, *38*, 5025.
17. Qian, Y. Ma. C.; Xie, M.; Sun, J. *J. Org. Chem.* **1999**, *64*, 6462.
18. Weinreb, S. M.. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Paquette, L. A., Eds.; Pergamon: Oxford, 1991; Vol. 5, pp 401–449.
19. Boger, D. L.; Weinreb, S. M. *Hetero Diels–Alder methodology in Organic Synthesis*; Academic: San Diego, 1987. Chapters 2 and 9.
20. Kobayashi, S.; Araki, M.; Ishitani, H.; Nagayama, S.; Hachiya, I. *Synlett* **1995**, 233.
21. Zhang, J.; Li, C.-J. *J. Org. Chem.* **2002**, *67*, 3969–3971.
22. *Typical experimental procedure for tetrahydroquinoline*: A mixture of substituted aniline (5 mmol), cyclic enol ether (10 mmol), and cellulose sulfuric acid or starch sulfuric acid (0.03 g) was taken in acetonitrile (5 ml) and stirred at room temperature for 4–6 h. After completion of the reaction, as indicated by TLC, the reaction was quenched with water and extracted with ethyl acetate. The organic phase was dried (Na_2SO_4), filtered, and concentrated under vacuum The product was purified by silica gel column chromatography (100:2, hexane/ethyl acetate) to afford the pure pyrano/furanoquinoline derivatives. All the products were characterized by ^1H and ^{13}C NMR spectroscopy.
23. Tejedor, D.; García-Tellado, F. *Chem. Soc. Rev.* **2007**, *36*, 484–490.
24. *Preparation of cellulose or starch sulfuric acid*: To a magnetically stirred mixture of 5.00 g of cellulose (DEAE for column chromatography, Merck) or starch 5.00 g (Merck) in 20 ml of *n*-hexane, 1.0 g of chlorosulfonic acid (9 mmol) was added dropwise at 0 °C over 2 h. HCl gas was removed from the reaction vessel immediately. After the addition was complete, the mixture was stirred for 2 h. Then, the mixture was filtered, washed with 30 ml of acetonitrile, and dried at room temperature to obtain 5.47 g cellulose sulfuric acid as a white powder or 5.06 g starch sulfuric acid as a cream powder.
25. *Spectral data of selected compound* Table 2 **3a** *cis-isomer*: MS (ES^+): m/z = 262.2 $[M+1]^+$. ^1H NMR (200 MHz, $CDCl_3$): δ 1.32–1.70 (m, 10H), 2.0 (dddd, J = 3.0, 5.4, 7.1, 12.1 Hz, 1H), 3.34 (dt, J = 2.2, 7.0 Hz, 1H), 3.39 (dt, J = 2.3, 11.4 Hz, 1H), 3.6 (ddt, J = 1.6, 4.4, 11.4 Hz, 1H), 3.67 (t, J = 6.3 Hz, 2H), 4.98 (d, J = 5.7 Hz, 1H), 6.38 (d, J = 7.5 Hz, 1H, Ar-H), 6.67 (t, J = 7.5 Hz, 1 H, Ar-H), 6.96 (t, J = 7.5 Hz, 1H, Ar-H), 7.31 (d, J = 7.5 Hz, 1H, Ar-H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 17.86, 22.14, 25.41, 31.96, 32.59, 35.52, 54.13, 60.63, 62.47, 72.41, 113.79, 117.74, 120.02, 127.51, 127.85, 145.01. Compound **4a** trans-isomer: ^1H NMR (200 MHz, $CDCl_3$): δ 1.32–1.70 (m, 10H), 1.90 (m, 1H), 3.58 (m, 1H), 3.66 (m, 3H), 3.90 (m, 1H), 4.42 (d, J = 3.2 Hz, 1H), 6.42 (d, J = 7.5 Hz, 1H, Ar-H), 6.60 (t, J = 7.5 Hz, 1H, Ar-H), 6.96 (t, J = 7.5 Hz, 1H, Ar-H), 7.21 (d, J = 7.5 Hz, 1H, Ar-H). Compound **3b** cis-isomer: MS (ES^+): m/z = 292 5 $[M+1]^+$. ^1H NMR (300 MHz, $CDCl_3$): δ 1.32–1.70 (m, 10H), 2.00 (dddd, J = 3.0, 5.4, 7.1, 12.1 Hz, 1H), 3.30 (dt, J = 2.6, 7.3 Hz, 1H), 3.62 (m, 2H), 3.68 (t, J = 6.3 Hz, 2H), 3.74 (s, 3 H, OCH_3), 5.00 (d, J = 5.4 Hz, 1H), 6.48 (d, J = 8.0 Hz, 1H, Ar-H), 6.66 (dd, J = 2.6, 8.0 Hz, 1H, Ar-H), 6.90 (d, J = 2.6 Hz, 1H, Ar-H). Compound **4b** trans-isomer: ^1H NMR (300 MHz, $CDCl_3$): δ 1.32–1.70 (m, 10H), 1.96 (m, 1H), 3.48 (m, 1H), 3.68 (m, 3H), 3.72 (s, 3H, OCH_3), 3.92 (m, 1H), 4.44 (d, J = 5.4 Hz, 1H), 6.50 (d, J = 8.0 Hz, 1H, Ar-H), 6.68 (dd, J = 2.6, 8.0 Hz, 1 H, Ar-H), 6.80 (d, J = 2.6 Hz, 1H, Ar-H). Compound **3f** cis-isomer: MS (ES^+): m/z = 296.2 $[M+1]^+$. ^1H NMR (300 MHz, $CDCl_3$): δ 1.32–1.70 (m, 10H), 2.02 (dddd, J = 3.0, 5.4, 7.1, 12.1 Hz, 1H), 3.34 (dt, J = 2.2, 7.0 Hz, 1H), 3.50 (dt, J = 2.3, 11.4, 1H), 3.65 (ddt, J = 1.6, 4.4, 11.4 Hz, 1H), 3.70 (t, J = 6.3 Hz, 2H), 5.00 (d, J = 5.5 Hz, 1H), 6.42 (d, J = 8.0 Hz, 1H, Ar-H), 6.96 (dd, J = 2.6, 8.0 Hz, 1H, Ar-H), 7.30 (d, J = 2.6 Hz, 1H, Ar-H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 17.87, 21.28, 22.68, 23.03, 24.10, 32.97, 36.09, 50.19, 66.67, 72.98, 115.33, 122.52, 123.50, 128.82, 129.53, 143.58. Compound **4f** trans-isomer: ^1H NMR (300 MHz, $CDCl_3$): δ 1.32–1.70 (m, 10H), 1.88 (m, 1H), 3.50 (m, 1H), 3.65 (m, 3H), 3.86 (m, 1H), 4.42 (d, J = 3.0 Hz, 1H), 6.44 (d, J = 8.0 Hz, 1H, Ar-H), 6.98 (dd, J = 2.6, 8.0 Hz, 1H, Ar-H,), 7.18 (d, J = 2.6 Hz, 1H, Ar-H). Compound **3i** cis-isomer: MS (ES^+): m/z = 234.0 $[M+1]^+$. ^1H NMR (300 MHz, $CDCl_3$): δ 1.55–1.90 (m, 5 H), 2.03 (m, 1H), 2.64 (1H, OH), 2.63 (m, 1H), 3.44 (m, 1H), 3.70 (m, 2H), 3.79 (m, 2H), 5.11 (d, J = 8.0 Hz, 1H), 6.30 (d, J = 8.0 Hz, 1H, Ar-H), 6.76 (m, 1H, Ar-H), 7.04 (m, 1H, Ar-H), 7.29 (d, J = 7.6 Hz, 1H, Ar-H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 24.22, 29.21, 30.93, 42.69, 52.68, 62.52, 66.81, 76.02, 114.86, 118.94, 122.84, 128.55, 130.25, 145.24. Compound **4i** trans isomer: .^1H NMR (300 MHz, $CDCl_3$): δ 1.50–1.90 (m, 5H), 2.20 (m, 1H), 2.64 (1H, OH), 2.82 (m, 1H), 3.70 (m, 2H), 3.79 (m, 2H), 3.95 (m, 1H), 4.56 (d, J = 5.6 Hz, 1H), 6.64 (d, J = 8.0 Hz, 1H, Ar-H), 7.09 (m, 1H, Ar-H), 6.76 (m, 1H, Ar-H), 7.34 (d, J = 7.6 Hz, 1H, Ar-H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 28.79, 29.37, 30.09, 41.39, 52.16, 62.64, 65.76, 76.10, 115.08, 118.42, 120.48, 129.10, 131.20, 145.16. Compound **3k** cis-isomer: MS (ES^+): m/z = 248.2 $[M+1]^+$. ^1H NMR (300 MHz, $CDCl_3$): δ 1.55–1.90 (m, 5H), 2.04 (m, 1H), 2.23 (s, 3H, CH_3), 2.62 (m, 1H), 3.40 (m, 1H), 3.70 (m, 2H), 3.80 (m, 2H), 5.08 (d, J = 8.0 Hz, 1H), 6.46 (d, J = 8.0 Hz, 1H, Ar-H), 6.86 (dd, J = 2.0 Hz, 8.0 Hz, 1H, Ar-H), 7.11 (d, J = 2.0 Hz, 1H, Ar-H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.80, 24.28, 29.28, 30.97, 42.80, 53.00, 62.50, 66.89, 76.14, 115.00, 122.87, 128.17, 129.32, 130.51, 140.77. Compound **4k** trans isomer: ^1H NMR (300 MHz, $CDCl_3$): δ 1.55–1.90 (m, 5H), 2.20 (m, 1H), 2.24 (s, 3H, CH_3), 2.79 (m, 1H), 3.70 (m, 2H), 3.80 (m, 2H), 3.95 (m, 1H), 4.54 (d, J = 5.2 Hz, 1 H), 6.58 (d, J = 8.0 Hz,1 H, Ar-H), 6.91 (dd, J = 2.0 Hz, 8.0 Hz,1H, Ar-H), 7.17 (d, J = 2.0 Hz, 1H, Ar-H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.73, 28.86, 29.45, 30.17, 41.65, 52.55, 62.65, 65.87, 76.14, 115.24, 120.74, 127.74, 129.81, 131.33, 142.77.