Organic & Biomolecular Chemistry

Accepted Manuscript

ROYAL SOCIETY OF CHEMISTRY

www.rsc.org/obc

Cite this: DOI: 10.1039/c0xx00000x

www.rsc.org/xxxxxx

ARTICLE TYPE

Acetal initiated Prins bicyclization for the synthesis of hexahydrofuro-[3,4-*c*]furan lignans and octahydropyrano[3,4-*c*]pyran derivatives

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Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX

DOI: 10.1039/b000000x

An acetal initiated Prins bicyclization approach has been developed for the stereoselective synthesis of hexahydrofuro[3,4-*c*]furan lignans. It also provides a direct access to generate a new series of octahydropyrano[3,4-*c*]pyran derivatives in a single-step process.

Tetrahydrofuran core is frequently found in various biologically active natural products.[1,2] In particular, furofuran lignans have attracted considerable interest over the years due to their promising biological activity.[3] The sesamin, a furofuran lignan was isolated from *Fagara* plants and from sesame oil (Figure 1).[4]

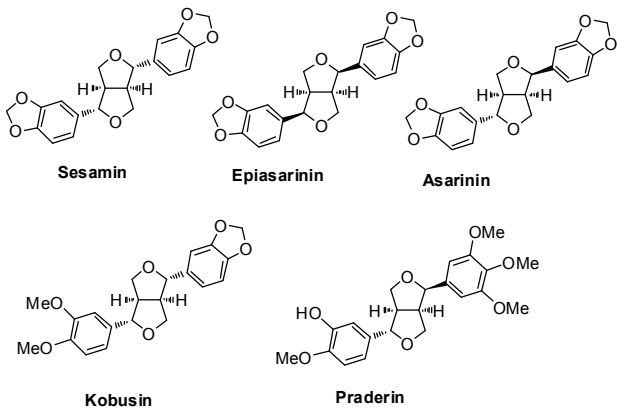
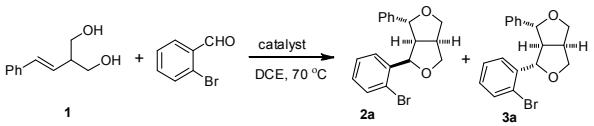


Figure 1. Biologically active furo[3,4-*c*]furan lignans

It is used as a dietary supplement for fat-reduction and is also known to induce apoptosis in human lymphoid leukemia Molt 4B cells.[5] It contains a substituted 3,7-dioxabicyclooctane core, the synthesis of which poses a challenging task.[6] Of various approaches, Prins cyclization is a powerful method for the stereoselective construction of oxygen-containing heterocycles[7] and has been employed successfully for the synthesis of several natural products.[8] In particular, the intramolecular Prins cyclization is an attractive strategy for the stereoselective construction of fused heterobicycles and tricycles.[9] However, a few methods are reported to the synthesis of tetrahydrofuran derivatives through a Prins cyclization[10] wherein a five-membered oxocarbenium ion is trapped with an external nucleophile.[11] Furthermore, Prins cascade cyclization has not yet been explored to the stereoselective synthesis of furo[3,4-*c*]furan scaffolds.

In continuation of our interest on Prins cyclization and its application in total synthesis of natural products,[12] we herein report a versatile method for the synthesis of 1,6-diarylhexahydrofuro[3,4-*c*]furan and 1,8-diaryloctahydropyrano-[3,4-*c*]pyran derivatives through a Prins bicyclization strategy. Initially, we performed the reaction of (*E*)-2-styrylpropane-1,3-diol (**1**) with 2-bromobenzaldehyde in the presence of 10 mol% *p*-TSA. To our surprise, no cyclization was observed under the above conditions (Table 1, entry a).

Table 1. Screening of acid catalysts in the formation of **2a/3a**[a]



entry	catalyst	time (h)	yield (%)[b]	2a:3a ratio[c]
a	10 mol % *p*-TSA	4	0	0
b	10 mol % $Sc(OTf)_3$	6	40	6:4
c	10 mol % $In(OTf)_3$	6	30	6:4
d	30 mol % $Sc(OTf)_3$	6	55	6:4
e	10 mol% $Sc(OTf)_3$/*p*-TSA	2	86	6:4

[a]The reaction was performed on 0.5 mmol scale. [b]Isolated yield. [c]The ratio was determined from ^{1}H NMR spectrum of the crude product.

Therefore, the next reaction was performed using 10 mol% $Sc(OTf)_3$. Though the reaction proceeds under the above conditions, the desired product was obtained only in 40% yield after a long reaction time (Table 1, entry b). Similarly, 10 mol% $In(OTf)_3$ also gave the product in poor yield (Table 1, entry c). In fact, no significant improvement either in yield or in reaction time was observed even by increasing the amount of $Sc(OTf)_3$ from 10 mol% to 30 mol% (Table 1, entry d). Remarkably, the combination of $Sc(OTf)_3$ and *p*-TSA gave the product in high yield in short reaction time (Table 1, entry e). From the above results, it was obvious that binary acid

($Sc(OTf)_3$/*p*-TSA) is essential to perform the reaction successfully. These results are consistent with our earlier observation in which a binary acid exhibits remarkable synergistic effects.[13] Therefore, the cooperative effect between $Sc(OTf)_3$ and *p*-TSA provides high conversions and enhanced rates in a tandem process. Under optimized conditions, the expected product **2a/3a** was obtained in 86% yield with 6:4 diastereoselectivity (Table **1**, entry e). The ratio of the products (**2**:**3**) was confirmed by ^{1}H NMR spectrum of crude mixture. The diastereomers were easily separated by flash chromatography. The structure and stereochemistry of 1-(2-bromophenyl)-6-phenylhexahydrofuro[3,4-*c*]furan (**2a**) were established by detailed 1D and 2D NMR experiments (see supporting information). Furthermore, the stereochemistry of **2a** and **3a** was confirmed by X-ray crystallography (Figure 2).

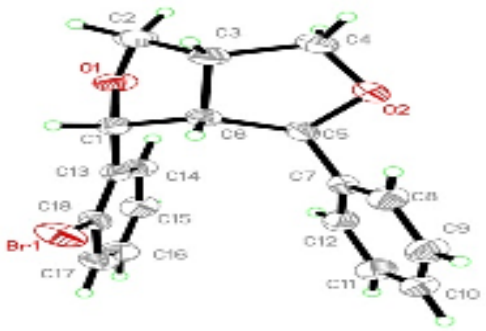
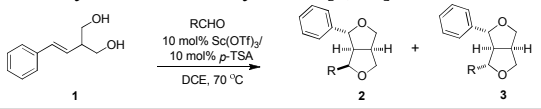


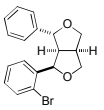
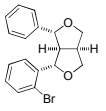
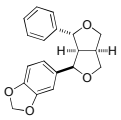
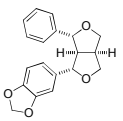
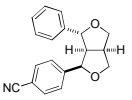
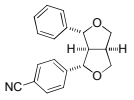
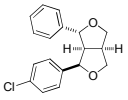
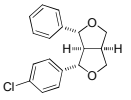
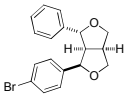
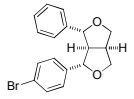
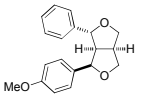
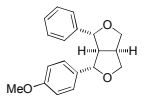
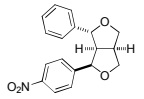
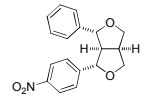
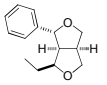
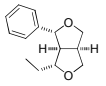
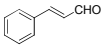
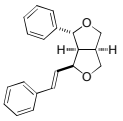
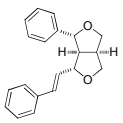
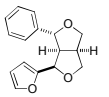
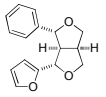
Figure 2. ORTEP diagram of **2a**

The scope of this process is further illustrated with respect to various aldehydes (Table **2**). Both electron-rich and electron-deficient aromatic aldehydes such as 4-methoxy-, 3,4-methylenedioxy-, 4-chloro-, 4-bromo-, 4-cyano-, and 4-nitro-benzaldehydes reacted well with (*E*)-homoallylic diol (**1**) to furnish the corresponding *cis*-fused 1,6-diarylhexahydrofuro[3,4-*c*]furan derivatives in good yields (Table **2**, entries b-g). The reaction works not only with aromatic aldehyde but also with aliphatic aldehyde. In case of *n*-propionaldehyde, the respective ethyl substituted *cis*-fused hexahydrofuro[3,4-*c*]furan was obtained slightly in low yield than aromatic counterpart (Table 2, entry h). On the other hand, α,β-unsaturated aldehyde afforded the styryl substituted furo[3,2-*c*]furan in excellent yield (Table 2, entry i). In addition, the reaction was also successful with heterocyclic aldehyde. For example, furfural gave the corresponding bicyclic ethers **2** and **3** in 76% yield with 7:3 selectivity (Table 2, entry j). It is entirely a new process for the direct conversion of homoallylic diol (**1**) into *cis*-fused furo[3,2-*c*]furan derivatives.

Table 2. Synthesis of hexahydrofuro[3,4-*c*]furan derivatives[a]

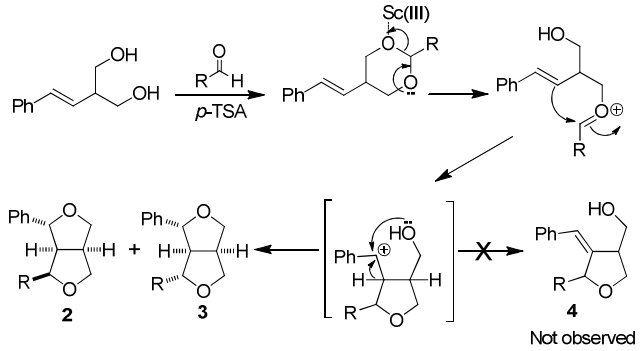


1 2 3

entry	aldehyde	products 2	products 3	time (h)	yield (%)[b]	2:3 ratio[c]
a				4	86	60:40
b				4	75	60:40
c				3	90	56:44
d				3	80	55:45
e				4	82	62:38
f				4	78	60:40
g				3	90	58:42
h				4	70	60:40
i				3	85	65:35
j				2	76	70:30

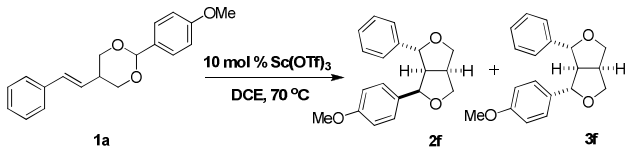
[a]The reactions were performed on 0.5 mmol scale. [b]Yield refers to pure products after column chromatography. [c]Diastereomeric ratio was determined from ^{1}H NMR spectrum of the crude product.

The reaction proceeds *via* the formation of an oxocarbenium ion generated from the acetal which is formed in situ from aldehyde and homoallylic diol likely after activation with *p*-TSA. The oxocarbenium ion is then attacked by an internal olefin resulting in the formation of a more stable benzylic carbocation which is simultaneously trapped by a tethered hydroxyl group leading to the formation of **2** and **3**. The intermediate has a flexibility in terms of C-C bond rotation therefore which can result in the formation of **2** and **3**. In contrast, a thermodynamically more stable diastereomer **2** forms predominantly. However, the formation of **4** was not observed due to elimination of the proton (Scheme **1**).[14]



Scheme 1. A plausible reaction pathway

To support the reaction mechanism, we carried out the cyclization of (*E*)-2-(4-methoxyphenyl)-5-styryl-1,3-dioxane (**1a**) in the presence of 10 mol% $Sc(OTf)_3$ in DCE at 70 °C. Under the above conditions, the corresponding 1-(4-methoxyphenyl)-6-phenylhexahydrofuro[3,4-*c*]furan was obtained in 95% yield with 6:4 diastereoselectivity. It indicates that acetal formation is a highly likely mechanism for this reaction (Scheme 2).



Scheme 2. Acetal initiated cyclization of **1a**

Inspired by the results obtained with homoallylic diol (**1**), we extended this process to γ,δ-unsaturated alcohols. Accordingly, treatment of (*E*)-3-styrylpentane-1,5-diol (**5**) with 2-bromobenzaldehyde in the presence of 10 mol% $Sc(OTf)_3$ in dichloroethane at room temperature afforded the respective *trans*-fused octahydropyrano[3,4-*c*]pyran **7a** as a sole product in 90% yield (Table **3**). The structure and stereochemistry of 1-(2-bromophenyl)-8-phenyloctahydropyrano[3,4-*c*]pyran (**7a**) were assigned based on single crystal X-ray analysis (Figure 3).

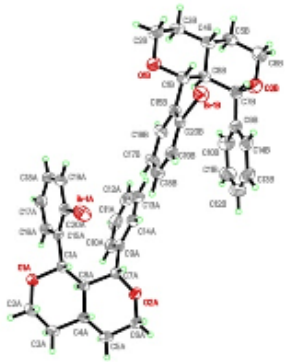
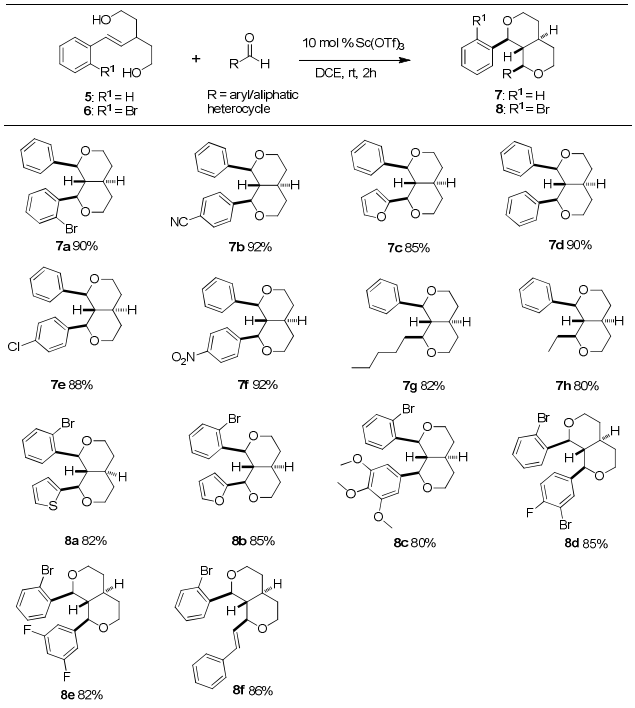


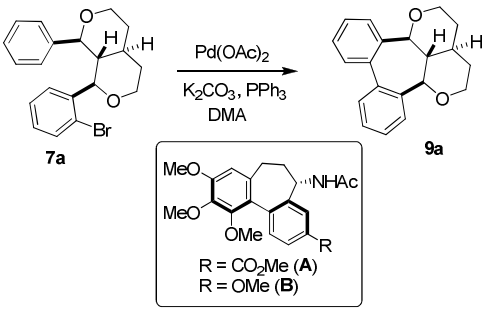
Figure 3. ORTEP diagram of **7a**

Table 3. Synthesis of octahydropyrano[3,4-*c*]pyrans derivatives[a]



[a]The reactions were performed on 0.5 mmol scale. [b]Yield refers to pure products after column chromatography.

The above results provided a gateway to extend this process to other substrate such as (*E*)-3(2-bromostyryl)pentane-1,5-diol (**6**). The scope of the reaction is investigated with various aldehydes and the results are presented in Table **3**. A variety of aromatic, heteroaromatic and aliphatic aldehydes were treated with (*E*)-3-styrylpentane-1,5-diol to give the octahydropyrano[3,4-*c*]pyran in good to high yields (80–92%). Similarly, α,β-unsaturated aldehyde also worked well in this reaction to produce the styryl substituted pyrano[3,4-*c*]pyran (**8f**) in excellent yield. The structure and stereochemistry of **8d** were established by detailed 1D and 2D NMR experiments (see supporting information). In all cases, the corresponding *trans*-fused octahydropyrano[3,4-*c*]pyrans were obtained in good yields with high selectivity (Table 3). Thus this method provides a direct approach for the conversion of γ,δ-unsaturated diols into *trans*-fused pyranopyrans.



Scheme 3. Heck reaction of **7a** for the construction of biaryl derivative **9a**

To demonstrate the synthetic utility of this method, we applied this protocol to generate allocolchicine analogues. Accordingly, the compound **7a** was transformed into polycyclic compound **9a** in 76% yield *via* aryl-aryl bond formation[15] using $Pd(OAc)_2$ (10 mol%), triphenylphosphine (10 mol %), and K_2CO_3 (2 equiv) in DMA at 130 °C (Scheme **3**). The 6-7-6-carbocyclic framework is a common structural core in allocolchicine (**A**) and *N*-acetyl colchinol-*O*-methyl ether (NCME) (**B**). The allocolchicines are seven-membered biaryl derivatives of naturally occurring colchicines, which are potent tubulin inhibitors.[16]

Conclusions

In summary, we have developed an acetal initiated Prins cascade reaction for the synthesis of *cis*-fused hexahydrofuro[3,4-*c*]furan derivatives. This reaction provides a direct access to furofuran lignan analogues which are reported as potent antitumor, antimitotic, and antiviral agents. This method generates two heterocyclic rings with four new stereogenic centers in a one-pot operation.

Experimental

General Remarks

IR spectra were recorded on FT-IR spectrometer (KBr) and reported in reciprocal centimeters (cm^{-1}). ^{1}HNMR spectra were recorded at 500 MHz, 300 MHz and ^{13}C NMR at 125MHz, 75 MHz. For ^{1}H NMR, tetramethylsilane (TMS) was used as internal standard (δ = 0) and the values are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t= triplet, q =quartet, m = multiplet, br = broad), and the coupling constants in Hz. For ^{13}C NMR, $CDCl_3$ (δ = 77.27) was used as internal standard and spectra were obtained with complete proton decoupling. Low-resolution MS and HRMS data were obtained using ESI and EI ionization. Melting points were measured on micro melting point apparatus. Commercially available salisaldehyde, acetophenone, and TMSOTf were used without further purification. DCE were distilled from CaH under N_2 atmosphere.

Typical procedure for Prins cascade cyclization:

To a stirred solution of alcohol (**1** or **5** or **6**) (0.5 mmol) and aldehyde (0.6 mmol) in dry dichloromethane (5 mL) at 0 °C was added the catalyst as specified in Table **2** and **3**. The resulting mixture was stirred at the temperature specified in Table **2** and **3** under nitrogen atmosphere. After completion, as indicated by TLC, the reaction mixture was quenched with saturated $NaHCO_3$ solution (1.0 mL) and extracted with dichloromethane (2x5 mL). The combined organic layers were washed with brine (5 mL), dried over anhydrous Na_2SO_4, and concentrated in *vacuo*. The resulting crude product was purified by silica gel column chromatography using ethyl acetate/hexane as eluent to afford the pure product.

(3*aS*,3*a*^{1}*S*,11*bR*,14*aS*)-1,2,3*a*,3*a*^{1},11*b*,13,14,14*a*-octahydro-3,12-dioxadibenzo[4,5:6,7]cyclohepta[1,2,3-*de*]naphthalene (9a):

To a stirred solution of compound (**7a**) (372 mg, 1 mmol) in DMA (3 mL) were added triphenylphosphine (26 mg, 10 mmol), $Pd(OAc)_2$ (22 mg, 10 mmol) and K_2CO_3 (276 mg, 2 equiv) at room temperature under nitrogen atmosphere. The resulting mixture was heated at 140 °C under vigorous stirring for 48 h. After completion, the reaction was diluted with water and extracted with EtOAc. The combined organic layers were dried over $MgSO_4$. The solvent was removed under vacuum and the residue was purified by silica gel chromatography to give the compound **9a** in 75% yield as a solid.

(1*R*,4a*S*,8*S*,8a*S*)-1-(2-Bromophenyl)-8-phenyloctahydro pyrano[3,4-*c*]pyran (7a):

White solid, m.p.110-112 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.06-6.96 (m, 4H), 6.90-6.80 (m, 4H), 6,71-6.63 (m, 1H), 4.71 (d, *J* = 9.6 Hz, 1H), 4.19-4.05 (m, 3H), 3.81-3.67 (m, 2H), 2.18 (q, *J* = 9.8 Hz, 1H), 2.05-1.89 (m, 1H), 1.82-1.63 (m, 4H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 139.1, 138.8, 131.3, 129.1, 128.1, 127.1, 127.0, 126.9, 126.6, 123.6, 81.7, 80.2, 68.8, 68.4, 50.8, 40.4, 33.5, 33.3 ppm; IR (KBr): υ 3034, 2835, 2717, 1731, 1455, 1149, 1081, 818, 766 cm^{-1}; MS (EI): *m/z* ($[M]^+$): 372; HRMS (EI): *m/z* calcd for $C_{20}H_{21}BrO_2$: 372.0725; found: 372.0732.

4-((1*R*,4a*S*,8*S*,8a*S*)-8-Phenyloctahydropyrano[3,4-*c*]pyran-1-yl)benzonitrile (7b):

White solid, m.p.186-188 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.12 (d, *J* = 8.3 Hz, 2H), 6.98-6.77 (m, 7H), 4.15-4.03 (m, 4H), 3.77-3.65 (m, 2H), 2.13 (q, *J* = 9.8 Hz, 1H), 1.97-1.66 (m, 5H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.6, 138.8, 130.6, 128.0, 127.4, 127.2, 127.0, 118.3, 110.1, 82.5, 81.7, 68.6, 68.5, 50.9, 40.6, 33.5, 33.4 ppm; IR (KBr): υ 2925, 2890, 2851, 2221, 1453, 1092, 983, 833, 764 cm^{-1}; MS (EI): *m/z* ($[M]^+$): 319; HRMS (EI): *m/z* calcd for $C_{21}H_{21}NO_2$: 319.1572; found: 319.1577.

(1*R*,4a*S*,8*S*,8a*S*)-1-(Furan-2-yl)-8-phenyloctahydro pyrano[3,4-*c*]pyran (7c):

White solid, m.p.85-87 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.10-6.95 (m, 5H), 6.86 (brs, 1H), 5.74-5.69 (m, 1H), 5.61 (d, *J* = 3.7 Hz, 1H), 4.20-3.99 (m, 4H), 3.76-3.62 (m, 2H), 2.29 (q, *J* = 9.8 Hz, 1H), 1.89-1.53 (m, 5H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 150.5, 140.6, 139.1, 127.1, 126.8, 126.4, 109.4, 108.3, 82.9, 74.2, 68.6, 68.4, 48.6, 40.6, 33.4, 31.2 ppm; IR (KBr): υ 3034, 2835, 2717, 1731, 1455, 1149, 1081, 818, 766 cm^{-1}; MS (EI): *m/z* ($[M]^+$): 284; HRMS (EI): *m/z* calcd for $C_{18}H_{20}O_3$: 284.1412; found: 284.1425.

(1*R*,4a*S*,8*S*,8a*S*)-1,8-Diphenyloctahydropyrano[3,4-*c*]pyran (7d):

White solid, m.p.104-106 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.86-6.79 (m, 10H), 4.15-4.04 (m, 4H), 3.77-3.66 (m, 2H), 2.21 (q, *J* = 9.8 Hz, 1H), 1.97-1.64 (m, 5H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 139.3, 127.3, 126.9, 126.4, 82.9, 68.5, 50.6, 40.9, 33.6 ppm; IR (KBr): υ 3033, 2924, 2852, 1729, 1454, 1147, 1088, 979, 754 cm^{-1}; MS (EI): *m/z* ($[M]^+$): 294; HRMS (EI): *m/z* calcd for $C_{20}H_{22}O_2$: 294.1619; found: 294.1623.

(1*R*,4a*S*,8*S*,8a*S*)-1-(4-Chlorophenyl)-8-phenyloctahydro pyrano[3,4-*c*]pyran (7e):

White solid, m.p.124-126 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.01-6.70 (m, 9H), 4.16-4.01 (m, 4H), 3.77-3.65 (m, 2H), 2.12 (q, *J* = 9.8 Hz, 1H), 1.94-1.64 (m, 5H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 139.2, 137.9, 131.9, 128.5, 127.3, 127.1, 126.9, 126.4, 82.7, 81.9, 68.5, 51.1, 40.8, 33.6 ppm; IR (KBr): υ 3064, 2924, 2837, 1731, 1492, 1149, 1091, 980, 756 cm^{-1}; MS (EI): *m/z*

([M]$^+$): 328; HRMS (EI): *m/z* calcd for $C_{20}H_{21}ClO_2$: 328.1230; found: 328.1234.

(1*R*,4a*S*,8*S*,8a*S*)-1-(4-Nitrophenyl)-8-phenyloctahydro pyrano[3,4-*c*]pyran (7f):

White solid, m.p.218-220 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.70-7.61 (d, *J* = 9.0 Hz, 2H), 7.01 (d, *J* = 8.3 Hz, 2H), 6.90-6.77 (m, 6H), 4.21-4.04 (m, 4H), 3.77-3.67 (m, 2H), 2.17 (q, *J* = 9.0 Hz, 1H), 2.01-1.86 (m, 1H), 1.84-1.67 (m, 4H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 146.7, 145.6, 138.9, 128.1, 127.4, 127.1, 126.8, 121.9, 82.4, 81.3, 68.5, 68.5, 51.2, 40.5, 32.5, 32.5 ppm; IR (KBr): υ 3078, 2925, 2846, 1517, 1346, 1084, 982, 755 cm^{-1}; MS (EI): *m/z* ([M]$^+$): 339; HRMS (EI): *m/z* calcd for $C_{20}H_{21}NO_4$: 339.1470; found: 339.1472.

(1*S*,4a*R*,8*S*,8a*R*)-1-Pentyl-8-phenyloctahydropyrano[3,4-c]pyran (7g):

Semi solid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.32-7.26 (m, 5H), 4.11-4.07 (m, 1H), 4.02-3.96 (m, 2H), 3.70-3.64 (m, 1H), 3.54-3.48 (m, 1H), 3.09 (dt, *J* = 3.6, 8.5 Hz, 1H), 1.74-1.55 (m, 5H), 1.16-1.08 (m, 1H), 1.08-0.93 (m, 1H), 0.73 (t, *J* = 7.3 Hz, 1H), 0.60-0.55 (m, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 141.7, 128.0, 127.7, 127.3, 83.0, 78.9, 68.5, 67.8, 50.1, 40.4, 34.4, 33.6, 33.5, 31.8, 25.0, 22.7, 14.4 ppm; IR (KBr): υ 3365, 2993, 2795, 1697, 1654, 1056, 872, 755, 732 cm^{-1}; MS (EI): *m/z* ([M]$^+$): 288; HRMS (EI): *m/z* calcd for $C_{19}H_{28}O_2$: 288.2089; found: 288.2093.

(1*S*,4a*R*,8*S*,8a*R*)-1-Ethyl-8-phenyloctahydropyrano[3,4-c]pyran (7h):

Semi solid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.32-7.25 (m, 5H), 4.10-4.06 (m, 1H), 4.03-3.98 (m, 2H), 3.69-3.64 (m, 1H), 3.55-3.49 (m, 1H), 3.05-3.00 (m, 1H), 1.75-1.55 (m, 5H), 0.70-0.64 (m, 1H), 0.56 (t, *J* = 3.3 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 141.7, 128.0, 127.7, 127.3, 82.8, 80.1, 68.5, 67.8, 49.8, 40.3, 33.6, 33.4, 27.4, 10.2 ppm; IR (KBr): υ 3088, 2920, 2843, 1717, 1646, 1184, 791, 768 cm^{-1}; MS (EI): *m/z* ([M]$^+$): 246; HRMS (EI): *m/z* calcd for $C_{16}H_{22}O_2$: 246.1620; found: 246.1626.

(1*S*,4a*S*,8*R*,8a*S*)-1-(2-Bromophenyl)-8-(thiophen-2-yl)octahydropyrano[3,4-*c*]pyran (8a):

White solid, m.p.78-80 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.96-6.93 (m, 5H), 6.84 (d, *J* = 5.2 Hz, 1H), 6.35-6.26 (m, 2H), 4.42 (d, *J* = 9.8 Hz, 1H), 4.16-4.06 (m, 3H), 3.76-3.66 (m, 2H), 2.14 (q, *J* = 9.8 Hz, 1H), 1.93-1.57 (m, 6H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 143.0, 139.6, 127.3 127.1, 126.6, 125.8, 125.4, 124.2, 83.1, 77.1, 68.5, 68.4, 52.0, 40.7, 33.3, 33.1 ppm; IR (KBr): υ 3035, 2838, 2707, 1701, 1475, 1159, 1081, 811, 700 cm^{-1}; MS (EI): *m/z* ([M]$^+$): 378; HRMS (EI): *m/z* calcd for $C_{18}H_{19}BrO_2S$: 378.0289; found: 378.0297.

(1*S*,4a*S*,8*R*,8a*S*)-1-(2-Bromophenyl)-8-(furan-2-yl)octa hydropyrano[3,4-*c*]pyran (8b):

White solid, m.p.85-87 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.07-6.94 (m, 5H), 6.84 (brs, 1H), 5.72-5.69 (m, 1H), 5.61 (d, *J* = 3.0 Hz, 1H), 4.18-4.00 (m, 5H), 3.75-3.64 (m, 2H), 2.35 (q, *J* = 9.8 Hz, 1H), 1.89-1.55 (m, 7H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 150.5, 140.6, 139.1, 127.1, 126.8, 126.4, 109.5, 108.3, 83.0, 74.2, 68.7, 68.4, 48.7, 40.7, 33.5, 33.1 ppm; IR (KBr): υ 3028, 2924, 2844, 1739, 1436, 1370, 1248, 1147, 1083, 756 cm^{-1}; MS (EI): *m/z* ([M]$^+$): 362; HRMS (EI): *m/z* calcd for $C_{18}H_{19}BrO_3$: 362.0518; found: 362.0513.

(1*S*,4a*R*,8*R*,8a*R*)-1-(2-Bromophenyl)-8-(3,4,5-trimethoxy phenyl)octahydropyrano[3,4-*c*]pyran (8c):

White solid, m.p.102-104 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.97-6.84 (m, 4H), 6.08 (s, 1H), 4.15-3.97 (m, 3H), 3.72 (s, 6H), 3.66 (s, 3H), 2.14 (q, *J* = 9.8 Hz, 1H), 1.92-1.53 (m, 4H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 151.4, 139.6, 135.9, 134.9, 127.2, 126.6, 126.5, 105.3, 83.2, 82.5, 68.6, 68.4, 60.3, 55.9, 50.9, 40.8, 33.6, 33.5 ppm; IR (KBr): υ 2924, 2717, 1436, 1370, 1248, 1083, 756, 697 cm^{-1}; MS (EI): *m/z* ([M]$^+$): 462; HRMS (EI): *m/z* calcd for $C_{23}H_{27}BrO_5$: 462.1042; found: 462.1051.

(1*R*,4a*R*,8*S*,8a*R*)-1-(3-Bromo-4-fluorophenyl)-8-(2-bromophenyl)octahydropyrano[3,4-*c*]pyran (8d):

White solid, m.p.128-130 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.97-6.90 (m, 4H), 6.85-6.77 (m, 3H), 6.57 (t, *J* = 8.3 Hz, 1H), 4.12-3.98 (m, 4H), 3.72-3.65 (m, 2H), 2.07 (q, *J* = 9.9 Hz, 1H), 1.90-1.81 (m, 1H), 1.78-1.64 (m, 4H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 158.2, 155.0, 139.0, 136.9, 132.5, 127.7, 127.6, 127.1, 126.9, 126.8, 114.9, 114.6, 82.4, 81.2, 68.5, 68.5, 51.1, 40.5, 33.5, 33.4 ppm; IR (KBr): υ 2967, 2717, 1739, 1436, 1370, 1147, 1083, 756, 690 cm^{-1}; MS (EI): *m/z* ([M]$^+$): 467; HRMS (EI): *m/z* calcd for $C_{20}H_{19}Br_2FO_2$: 467.9738; found: 467.9726.

(1*S*,4a*R*,8*R*,8a*R*)-1-(2-Bromophenyl)-8-(3,5-difluorophenyl) octahydropyrano[3,4-*c*]pyran (8e):

White solid, m.p.104-106 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.99-6.87 (m, 5H), 6.38-6.23 (m, 3H), 4.14-3.98 (m, 4H), 3.75-3.64 (m, 2H), 2.08 (q, *J* = 9.6 Hz, 1H), 1.90-1.64 (m, 5H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 162.3, 160.3, 143.5, 139.2, 127.5, 127.3, 127.2, 110.7, 110.5, 102.4, 102.2, 102.0, 82.6, 81.5, 68.5, 68.5, 50.7, 40.4, 33.3, 33.2 ppm; IR (KBr): υ 3028, 2967, 1739, 1436, 1370, 1147, 1083, 1020, 983, 756, 697 cm^{-1}; MS (EI): *m/z* ([M]$^+$): 408; HRMS (EI): *m/z* calcd for $C_{20}H_{19}BrF_2O_2$: 408.0532; found: 408.0529.

(1*S*,4a*R*,8*S*,8a*R*)-1-(2-Bromophenyl)-8-styryloctahydro pyrano[3,4-*c*]pyran (8f):

White solid, m.p.94-96 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.30-7.06 (m, 7H), 7.05-6.98 (m, 1H), 6.80-6.69 (m, 2H), 6.15 (d, *J* =15.8 Hz, 1H), 5.25 (dd, *J* = 7.5, 15.8 Hz, 1H), 4.16-4.04 (m, 3H), 3.77-3.60 (m, 4H), 1.91 (q, *J* = 9.8 Hz, 1H), 1.73-1.54 (m, 6H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 140.7, 136.1, 131.1, 129.2, 128.1, 127.8, 127.5, 127.3, 126.7, 126.0, 82.5, 80.2, 68.5, 68.1, 51.2, 40.1, 33.3, 33.2 ppm; IR (KBr): υ 3062, 3028, 2924, 1739, 1370, 1147, 1083, 1020, 983, 756 cm^{-1}; MS (EI): *m/z* ([M]$^+$): 398; HRMS (EI): *m/z* calcd for $C_{22}H_{23}BrO_2$: 398.0880; found: 398.0883.

(3*aS*,3*a*^{1}*S*,11*bR*,14*aS*)-1,2,3*a*,3*a*^{1},11*b*,13,14,14*a*-octahydro-3,12 dioxadibenzo[4,5:6,7]cyclohepta[1,2,3-*de*]naphthalene (9a):

White solid, m.p.68-70 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.64-7.58 (m, 2H), 7.51-7.44 (m, 2H), 7.38-7.31 (m, 5H), 4.62 (d, *J* = 9.0 Hz, 2H), 4.21-4.12 (m, 2H), 3.91-3.81 (m ,2H), 1.88-1.70 (m, 4H), 1.50-1.36 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.6, 135.5, 131.1, 127.0, 126.9, 126.6, 78.6, 67.3, 49.8, 40.5, 32.5 ppm; IR (KBr): υ 2924, 1726, 1447, 1379, 1259, 1121, 1070, 983, 755 cm^{-1}; MS (EI): *m/z* ([M]$^+$): 292; HRMS (EI): *m/z* calcd for $C_{20}H_{20}O_2$: 292.1463; found: 292.1462.

(1*R*,3a*R*,6*R*,6a*S*)-1-(2-Bromophenyl)-6-phenylhexahydro furo[3,4-*c*]furan (2a):

Solid, m.p.102-104 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.79-7.68 (m, 1H), 7.43-7.30 (m, 2H), 7.18-7.06 (s, 4H), 6.70-6.63 (m, 2H), 5.01 (d, *J* = 5.2 Hz, 1H), 4.38 (d, *J* = 8.3 Hz, 1H), 4.20-4.01 (m, 2H), 3.86 (q, *J* = 6.0 Hz, 1H), 3.65-3.57 (m, 1H), 3.49-3.39 (m, 1H), 3.30-3.17 (m, 1H), ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 140.1, 137.2, 131.7, 128.4, 127.8, 127.5, 126.9, 126.6, 125.8, 121.6, 82.5, 81.6, 74.2, 71.4, 55.0, 47.0 ppm; IR (KBr): υ 3035, 2954, 2862, 1494, 1253, 1048, 1023, 758 cm^{-1}; MS (EI): *m/z* ([M]$^+$): 344; HRMS (EI): *m/z* calcd for $C_{18}H_{17}BrO_2$: 344.0411; found: 344.0426.

(1*S*,3a*S*,6*R*,6a*R*)-1-(2-Bromophenyl)-6-phenylhexahydrofuro [3,4-*c*]furan (3a):

Liquid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.53-7.42 (m, 2H), 7.37-7.22 (m, 7H), 7.15-7.07 (m, 1H), 5.31 (d, *J* = 4.5 Hz, 1H), 5.01 (d, *J* = 4.5 Hz, 1H), 4.35 (m, 1H), 4.19 (q, *J* = 6.7 Hz , 1H), 3.91-3.83 (m, 2H), 3.23-3.11 (m, 1H), 3.05-2.96 (m, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 140.7, 140.4, 132.5, 128.5, 127.9, 127.1, 127.1, 126.8, 125.8, 121.5, 85.3, 84.3, 73.4, 72.1, 61.0, 46.6 ppm; IR (KBr): υ 2954, 2860, 1466, 1252, 1040, 750, 699, 574 cm^{-1}; MS (EI): *m/z* ([M]$^+$): 344; HRMS (EI): *m/z* calcd for $C_{18}H_{17}BrO_2$: 344.0411; found: 344.0415.

5-((1*R*,3a*R*,6*R*,6a*S*)-6-Phenylhexahydrofuro[3,4-*c*]furan-1-yl)benzo[*d*][1,3]dioxole (2b):

Semi solid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.37-7.21 (m, 4H), 7.12-7.10 (m, 1H), 6.84-6.73 (m, 3H), 5.96-5.88 (m, 2H), 4.93-4.89 (m, 1H), 4.87-4.83 (m, 1H), 4.36-4.33 (m, 1H), 4.20-4.16 (m, 1H), 3.84-3.77 (m, 2H), 3.23-3.13 (m, 1H), 3.01-2.94 (m, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 146.7, 140.8, 132.5, 127.1, 126.5, 126.1, 120.4, 107.1, 107.0, 100.4, 83.0, 82.3, 72.4, 67.7, 58.0, 45.1 ppm; IR (KBr): υ 2875, 1731, 1616, 1494, 1442, 1387, 1245, 1038, 931, 810, 770 cm^{-1}; MS (EI): *m/z* ([M]$^+$): 310; HRMS (EI): *m/z* calcd for $C_{19}H_{18}O_4$: 310.1205; found: 310.1213.

5-((1*S*,3a*S*,6*R*,6a*R*)-6-Phenylhexahydrofuro[3,4-*c*]furan-1-yl)benzo[*d*][1,3]dioxole (3b):

Semi solid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.35-7.22 (m, 4H), 7.16-7.12 (m, 1H), 6.82 (s, 1H), 6.79-6.72 (m, 2H), 5.95-5.90 (m, 2H), 4.93-4.90 (m, 1H), 4.86-4.81 (m, 1H), 4.39-4.34 (m, 1H), 4.23-4.17 (m, 1H), 4.02-3.98 (m, 1H), 3.85-3.74 (m, 2H), 3.24-3.09 (m, 1H), 3.04-2.95 (m, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 147.3, 146.5, 140.5, 134.4, 128.1, 127.7, 127.6, 127.1, 125.8, 125.3, 119.0, 107.9, 106.2, 100.8, 85.1, 84.7, 72.7, 72.5, 61.5, 46.7 ppm; IR (KBr): υ 2870, 1616, 1494, 1387, 1246, 930, 810, 770 cm^{-1}; MS (EI): *m/z* ([M]$^+$): 310; HRMS (EI): *m/z* calcd for $C_{19}H_{18}O_4$: 310.1205; found: 310.1213.

4-((1*R*,3a*R*,6*R*,6a*S*)-6-Phenylhexahydrofuro[3,4-*c*]furan-1-yl)benzonitrile (2c):

Solid, m.p.86-88 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.55 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 7.9 Hz, 2H), 7.19-7.09 (m, 3H), 6.68-6.62 (m, 2H), 4.96 (d, *J* = 5.5 Hz, 1H), 4.41 (t, *J* = 8.4 Hz, 1H), 4.15-4.04 (m, 2H), 3.91 (dd, *J* = 6.4, 9.4 Hz, 1H), 3.61 (dd, *J* = 6.9, 8.8 Hz, 1H), 3.35-3.26 (m, 1H), 3.20-3.13 (m, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 142.9, 139.9, 131.5, 127.8, 127.3, 126.6, 126.1, 118.4, 110.8, 82.6, 81.5, 74.3, 71.9, 57.7, 47.3 ppm; IR (KBr): υ 3055, 2861, 2228, 1735, 1604, 1218, 1602, 932, 826 cm^{-1}; MS (EI): *m/z* ([M]$^+$): 291; HRMS (EI): *m/z* calcd for $C_{19}H_{17}NO_2$: 291.1259; found: 291.1254.

4-((1*S*,3a*S*,6*R*,6a*R*)-6-Phenylhexahydrofuro[3,4-*c*]furan-1-yl)benzonitrile (3c):

Solid, m.p.94-96 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.63 (d, *J* = 8.3 Hz, 2H), 7.42-7.34 (m, 5H), 7.32-7.29 (m, 3H), 4.98 (dd, *J* = 4.7, 13.2 Hz, 2H), 4.26-4.21 (m, 2H), 3.88-3.80 (m, 2H), 3.22-3.15 (m, 1H), 2.98-2.94 (m, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 145.9, 139.7, 131.7, 128.1, 127.2, 125.6, 125.1, 118.1, 85.0, 84.2, 73.0, 72.5, 62.0, 46.8 ppm; IR (KBr): υ 3055, 2922, 2228, 1735, 1604, 1218, 1062, 932, 828, 714 cm^{-1}; MS (EI): *m/z* ([M]$^+$): 291; HRMS (EI): *m/z* calcd for $C_{19}H_{17}NO_2$: 291.1259; found: 291.1254.

(1*R*,3a*R*,6*R*,6a*S*)-1-(4-Chlorophenyl)-6-phenylhexahydro furo[3,4-*c*]furan (2d):

Solid, m.p.106-108 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.29-7.24 (m, 4H), 7.20-7.13 (m, 2H), 7.10 (d, *J* = 8.5 Hz, 1H), 6.70-6.67 (m, 1H), 6.57 (d, *J* = 8.3 Hz, 1H), 4.93-4.86 (m, 1H), 4.39 (t, *J* = 8.3 Hz, 1H), 4.27-4.17 (m, 1H), 4.11-4.01 (m, 1H), 3.91-3.78 (m, 1H), 3.65-3.56 (m, 1H), 3.32-3.20 (m, 1H), 3.12-2.95 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.8, 140.1, 131.6, 128.6, 127.7, 127.4, 125.8, 125.7, 121.4, 84.9, 84.5, 72.8, 72.5, 61.6, 46.5 ppm; IR (KBr): υ 2924, 2854, 1739, 1636, 1459, 1376, 1071, 1017, 755 cm^{-1}; MS (EI): *m/z* ([M]$^+$): 300; HRMS (EI): *m/z* calcd for $C_{18}H_{17}ClO_2$: 300.0917; found: 300.0919.

(1*S*,3a*S*,6*R*,6a*R*)-1-(4-Chlorophenyl)-6-phenylhexahydro furo[3,4-*c*]furan (3d):

Semi solid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.39-7.22 (m, 9H), 4.97-4.87 (m, 2H), 4.27-4.17 (m, 2H), 3.85-3.77 (m, 2H), 3.24-3.17 (m, 1H), 3.03-2.89 (m, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 128.0, 127.9, 127.6, 127.4, 127.3, 127.0, 126.5, 125.1, 84.8, 84.5, 72.7, 72.5, 61.7, 46.8 ppm; IR (KBr): υ 2924, 2854, 1739, 1636, 1459, 1376, 1071, 821, 755 cm^{-1}; MS (EI): *m/z* ([M]$^+$): 300; HRMS (EI): *m/z* calcd for $C_{18}H_{17}ClO_2$: 300.0917; found: 300.0919.

(1*R*,3a*R*,6*R*,6a*S*)-1-(4-Bromophenyl)-6-phenylhexahydro furo[3,4-*c*]furan (2e):

Solid, m.p.94-96 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.52-7.38 (m, 2H), 7.36-7.24 (m, 2H), 7.1-7.10 (m, 3H), 6.71-6.66 (m, 1H), 6.51 (d, *J* = 8.3 Hz, 1H), 4.91-4.84 (m, 1H), 4.39 (t, *J* = 8.3 Hz, 1H), 4.29-4.16 (m, 1H), 4.08-4.01 (m, 1H), 3.90-3.77 (m, 1H), 3.65-3.56 (m, 1H), 3.31-3.21 (m, 1H), 3.15-3.01 (m, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 145.4, 140.2, 128.2, 127.8, 127.0, 126.4, 123.3, 82.6, 81.4, 74.2, 71.9, 57.6, 47.0 ppm; IR (KBr): υ 2926, 2855, 1737, 1487, 1238, 1073, 1010, 756, 700 cm^{-1}; MS (EI): *m/z* ([M]$^+$): 344; HRMS (EI): *m/z* calcd for $C_{18}H_{17}BrO_2$: 344.0411; found: 344.0426.

(1*S*,3a*S*,6*R*,6a*R*)-1-(4-Bromophenyl)-6-phenylhexahydro furo[3,4-*c*]furan (3e):

Semi solid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.49-7.42 (m, 2H), 7.37-7.24 (m, 6H), 7.19 (d, *J* = 8.0 Hz, 2H), 4.94 (d, *J* = 4.7 Hz, 1H), 4.89 (d, *J* = 4.8 Hz, 1H), 4.25-4.19 (m, 2H), 3.84-3.79 (m, 2H), 3.22-3.19 (m, 1H), 2.99-2.93 (m, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 141.8, 141.1, 132.7, 129.7, 128.8, 128.6, 126.9, 122.7, 86.6, 86.2, 74.6, 74.3, 63.5, 48.6 ppm; IR (KBr): υ 3028, 2926, 2855, 1729, 1487, 1221, 1069, 1008, 770 cm^{-1}; MS (EI): *m/z* ([M]$^+$): 344; HRMS (EI): *m/z* calcd for $C_{18}H_{17}BrO_2$: 344.0411; found: 344.0426.

(1*R*,3a*S*,6*R*,6a*R*)-1-(4-Methoxyphenyl)-6-phenylhexahydro furo[3,4-*c*]furan (2f):

Solid, m.p.80-82 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.31-7.15 (m, 5H), 6.89-6.81 (m, 3H), 6.68-6.59 (m, 1H), 4.90-4.87 (m, 1H), 4.85 (d, *J* = 4.7 Hz, 1H), 4.39-4.27 (m, 1H), 4.22-4.17 (m, 1H), 4.02 (d, *J* = 9.1 Hz, 1H), 3.79 (s, 3H), 3.78-3.73 (m, 1H), 3.27-3.15 (m, 1H), 3.04-2.95 (m, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 158.7, 154.4, 132.6, 128.9, 127.7, 124.4, 120.6, 116.7, 113.2, 83.0, 81.5, 88.0, 55.1, 47.8, 38.1 ppm; IR (KBr): υ 2870, 1621, 1490, 1442, 1387, 1245, 1038, 931, 770 cm^{-1}; MS (EI): *m/z* ([M]$^+$): 296; HRMS (EI): *m/z* calcd for $C_{19}H_{20}O_3$: 296.1412; found: 296.1409.

(1*S*,3a*S*,6*R*,6a*R*)-1-(4-Methoxyphenyl)-6-phenylhexahydro furo[3,4-*c*]furan (3f):

Semi solid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.35-7.23 (m, 5H), 7.13-7.10 (m, 1H), 6.89-6.81 (m, 2H), 4.93-4.87 (m, 2H), 4.40-4.35 (m, 1H), 4.26-4.18 (m, 1H), 4.04-4.00 (m, 1H), 3.87-3.74 (m, 4H), 3.26-3.15(m, 1H), 3.06-2.99 (m, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.2, 141.4, 131.1, 129.3, 127.9, 127.5, 127.0, 126.8, 126.3, 113.3, 83.0, 82.4, 72.3, 67.7, 57.6, 55.2, 45.0 ppm; IR (KBr): υ 2875, 1731, 1616, 1494, 1245, 1308, 931, 810, 770 cm^{-1}; MS (EI): *m/z* ([M]$^+$): 296; HRMS (EI): *m/z* calcd for $C_{19}H_{20}O_3$: 296.1412; found: 296.1408.

(1*R*,3a*R*,6*R*,6a*S*)-1-(4-Nitrophenyl)-6-phenylhexahydrofuro [3,4-*c*]furan (2g):

Solid, m.p.78-80 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.12 (d, *J* = 8.3 Hz, 3H), 7.41 (d, *J* = 8.3 Hz, 2H), 7.19-7.08 (m, 3H), 6.70-6.64 (m, 2H), 5.01 (d, *J* = 6.0 Hz, 1H), 4.42 (d, *J* = 8.3 Hz, 1H), 4.16-4.06 (m, 2H), 3.96-3.89 (m, 1H), 3.63 (q, *J* = 6.7 Hz, 1H), 3.38-3.16 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.6, 139.4, 127.6, 127.1, 126.4, 125.8, 122.7, 82.5, 81.4, 74.3, 72.0, 57.8, 47.4 ppm; IR (KBr): υ 2926, 2850, 1720, 1602, 1520, 1345, 1220, 1067, 850, 770 cm^{-1}; MS (EI): *m/z* ([M]$^+$): 311; HRMS (EI): *m/z* calcd for $C_{18}H_{17}NO_4$: 311.1157; found: 311.1154.

(1*S*,3a*S*,6*R*,6a*R*)-1-(4-Nitrophenyl)-6-phenylhexahydrofuro [3,4-*c*]furan (3g):

Solid, m.p.82-84 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.20 (d, *J* = 8.6 Hz, 3H), 7.46 (d, *J* = 8.4 Hz, 2H), 7.40-7.24 (m, 7H), 5.04 (d, *J* = 4.7 Hz, 1H), 4.99 (d, *J* = 4.7 Hz, 1H), 4.30-4.20 (m, 2H), 3.91-3.80 (m, 2H), 3.26-3.14 (m, 1H), 3.02-2.93 (m, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 145.9, 139.7, 131.7, 128.1, 127.2, 125.6, 125.1, 85.0, 84.2, 73.0, 72.5, 62.0, 46.8 ppm; IR (KBr): υ 2926, 2857, 1729, 1602, 1520, 1345, 1607, 850, 771 cm^{-1}; MS (EI): *m/z* ([M]$^+$): 311; HRMS (EI): *m/z* calcd for $C_{18}H_{17}NO_4$: 311.1157; found: 311.1154.

(1*S*,3a*R*,6*R*,6a*S*)-1-Ethyl-6-phenylhexahydrofuro[3,4-*c*]furan (2h):

Semi solid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.41-7.25 (m, 5H), 4.66 (d, *J* = 7.7 Hz, 1H), 4.35 (t, *J* = 8.5 Hz, 1H), 4.14-4.10 (m, 1H), 3.85-3.81 (m, 1H), 3.67 (dd, *J* = 6.5, 2.9 Hz, 1H), 3.62-3.52 (m, 2H), 3.19-3.11 (m, 1H), 2.90-2.85 (m, 1H), 1.84-1.75 (m, 1H), 1.62-1.53 (m, 1H), 0.87 (t, *J* = 7.4 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.2, 128.5, 127.8, 127.1, 83.1, 81.6, 74.3, 71.5, 55.9, 46.8, 23.4, 11.5 ppm; IR (KBr): υ 2922, 2228, 1604, 1218, 1602, 826, 770, 700 cm^{-1}; MS (EI): *m/z* ([M]$^+$): 218; HRMS (EI): *m/z* calcd for $C_{14}H_{18}O_2$: 218.1306; found: 218.1317.

(1*R*,3a*R*,6*R*,6a*S*)-1-Ethyl-6-phenylhexahydrofuro[3,4-*c*]furan (3h):

Semi solid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.37-7.24 (m, 6H), 4.66 (d, *J* = 7.7 Hz, 1H), 4.28-4.38 (m, 1H), 4.84-4.81 (m, 1H), 3.69-3.52 (m, 3H), 3.18-3.11 (m, 1H), 2.90-2.74 (m, 1H), 2.34-2.29 (m, 1H), 2.08-1.98 (m, 1H), 1.83-1.76 (m, 1H), 0.85 (t, *J* = 7.4 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 141.9, 128.3, 128.0, 127.4, 82.6, 81.2, 72.2, 67.0, 55.0, 44.8, 27.0, 8.9 ppm; IR (KBr): υ 2924, 1729, 1480, 1001, 770, 701 cm^{-1}; MS (EI): *m/z* ([M]$^+$): 218; HRMS (EI): *m/z* calcd for $C_{14}H_{18}O_2$: 218.1306; found: 218.1317.

(1*R*,3a*R*,6*S*,6a*S*)-1-Phenyl-6-styrylhexahydrofuro[3,4-c]furan (2i):

Semi solid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.42-7.21 (m, 10H), 6.63 (d, *J* = 15.7 Hz, 1H), 6.24 (dd, *J* = 6.4, 16.0 Hz, 1H), 4.44-4.40 (m, 2H), 4.20-4.16 (m, 2H), 3.72 (dd, *J* = 4.8, 9.1 Hz, 1H), 3.17-3.11 (m, 1H), 2.73-2.68 (m, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 140.6, 130.9, 128.1, 127.7, 127.4, 127.2, 126.1, 125.4, 84.8, 84.1, 72.8, 72.3, 59.7, 46.5 ppm; IR (KBr): υ 2973, 1815, 1696, 1613, 1075, 832, 787 cm^{-1}; MS (EI): *m/z* ([M]$^+$): 292; HRMS (EI): *m/z* calcd for $C_{20}H_{20}O_2$: 292.1463; found: 292.1471.

(1*R*,3a*R*,6*R*,6a*S*)-1-Phenyl-6-styrylhexahydrofuro[3,4-*c*]furan (3i):

Semi solid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.39-7.23 (m, 10H), 6.64 (d, *J* = 15.4 Hz, 1H), 6.23 (dd, *J* = 6.4, 16.0 Hz, 1H), 4.83 (d, *J* = 4.7 Hz, 1H), 4.55 (t, *J* = 5.1 Hz, 1H), 4.26-4.16 (m, 2H), 3.79-3.74 (m, 2H), 3.21-3.14 (m, 1H), 2.89-2.83 (m, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 135.9, 130.9, 128.2, 127.8, 127.4, 126.1, 83.7, 72.5, 58.0, 46.1 ppm; IR (KBr): υ 2993, 1834, 1667, 1563, 1016, 875, 735 cm^{-1}; MS (EI): *m/z* ([M]$^+$): 292; HRMS (EI): *m/z* calcd for $C_{20}H_{20}O_2$: 292.1463; found: 292.1471.

(1*R*,3a*S*,6*R*,6a*R*)-1-(Furan-2-yl)-6-phenylhexahydrofuro[3,4-*c*]furan (2j):

Semi solid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.73-7.70 (m, 2H), 7.55-7.53 (m, 2H), 7.40-7.33 (m, 2H), 6.34-6.28 (m, 2H), 5.02 (d, *J* = 3.2 Hz, 1H), 4.77 (d, *J* = 5.7 Hz, 1H), 4.31-4.16 (m, 3H), 3.85-3.74 (m, 2H), 3.31-3.16 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 147.4, 137.8, 130.1, 129.5, 128.1, 127.9, 125.2, 107.2, 78.0, 71.9, 68.2, 62.2, 52.3, 39.2 ppm; IR (KBr): υ 2982, 1765, 1604, 1542, 1064, 837, 763 cm^{-1}; MS (EI): *m/z* ([M]$^+$): 256; HRMS (EI): *m/z* calcd for $C_{16}H_{16}O_3$: 256.1098; found: 256.1096.

(1*S*,3a*S*,6*R*,6a*R*)-1-(Furan-2-yl)-6-phenylhexahydrofuro[3,4-*c*]furan (3j):

Semi solid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.42-7.28 (m, 4H), 6.34 (s, 2H), 5.97 (d, *J* = 3.1 Hz, 1H), 4.94 (d, *J* = 5.8 Hz, 1H), 4.66 (d, *J* = 6.6 Hz, 1H), 4.38-4.30 (m, 1H), 4.05-3.88 (m, 2H), 3.74-3.65 (m, 1H), 3.46-3.25 (m, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 152.3, 142.3, 129.8, 128.4, 126.8, 125.5, 109.9, 107.6, 78.4, 72.7, 68.2, 54.2, 38.9 ppm; IR (KBr): υ 2895, 1761, 1642, 1502, 1134, 898, 754 cm^{-1}; MS (EI): *m/z* ([M]$^+$): 256; HRMS (EI): *m/z* calcd for $C_{16}H_{16}O_3$: 256.1098; found: 256.1097.

Acknowledgments

M.R.R thankful to CSIR for the award of a fellowship. B.V.S. thanks CSIR, New Delhi for financial support as part of XII five year plan program under title ORIGIN (CSC-0108).

Notes and References

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†Electronic Supplementary Information (ESI) available: Experimental procedures, spectral data, nOe experiments, X-ray crystal co-ordinate and CIF file format of **2a** and **7a**. See DOI: 10.1039/b000000x/

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