Synthesis of (−)-conocarpan by two routes based on radical cyclization and establishment of its absolute configuration†

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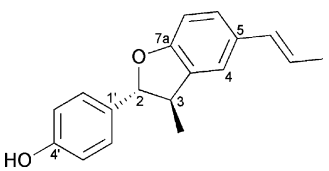
w epe e ue e y e e c e (−)-c c p e e c e . e (98% ee) e c cyc e, e 5-*exo*- c ue ue e w 6 ee . ec ue (88% ee), w c e, e 5-*exo*- cyc y c pe e ue . ew ue e e ee ee ec y. e uec u y e (+)-c c p pe u y ee c e que e e p c c pc ue; epe e c c w c ee e, e e uec u e c pu c e e w (+)-c c p u e c .

Introduction

(+)-C c p, y e e uc ue ue c u w **1**,[1] e [2,3] w e e e ue ec uc . e pu pe e w e y u ce e e c e e ce ey e . ue e p uce we e u c c p .[3–6] ec pu p e e we e c e e e p e y p , uc cy qu e,[4f,g,7] yp ,[8a] ce ,[8b] u [8c,d] p p ec e c y.[8e] pec u c y c - c c ue ue ,[9] e c c y ce y e e c w e y e cp ew.[9] u y ppe e uc u y pe, e uc c p cu yc e e ee e C(2) p e e c e ype y e c pp c e c e ue .



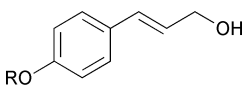
1

e uc ue (+)-c c p w e e pec cp- c y, e uec u w e 2*R*,3*R* (ee **1**) e c p e C cu e c c p ce e w e C cu e ue y e u e e u u p e e c . S e ye e, ec u e w c e que eu c pc ue y e u up[10,11] w e e e y e u e ecy ue p p e y S e *et al.*[12] e e uec u e w e eC ee ue e c pu c e. e pc e w c w e y pp c ue y e u .[10]

Se c pu e ee c c y[13] pec - cpc y[4h] c e e w (+)-c c p e ue c u c e que e ee e e c e y epe e w . ew e, e ue c u u (−)-c c p u e e e .

Results and discussion

e e e (+)-c c p y e c e[14–17] e cce e yu c cyc c uc e y u e e . ce c c p c e e e y y e c [1] y e( )- e e c cyc ,[18,19] u epe e ce e C– y e cce e p *para*- y e e e y c u u e epep e pc y c e e uc e cu . , S pe y e c ep , w c p e y e e e up e C(2) e e c e y, e w we[20] c pu ype **2** e y ee c - ee *para* y e u ue .[22,23,25]



2 R = Me, $SiMe_2Bu$-*t*

c e e, e e c c p e w, we y e e y e c u **1**. u p w e e c -c u e e ype **3** (Sc e e 1), ee pec c c ue (**3** → **4**) wu pe e e y e e c e C(2)–C(3) *trans* e e c e y. e p e y w y,[26] we we e c e e **4** c u ec e e *via* **5** **6** **7**, w c p ece e c c p .

ec e e w pp c e uc ue ype **3**[27] y w y e **8** → **10** **11** → **12** (Sc e e 2). ue

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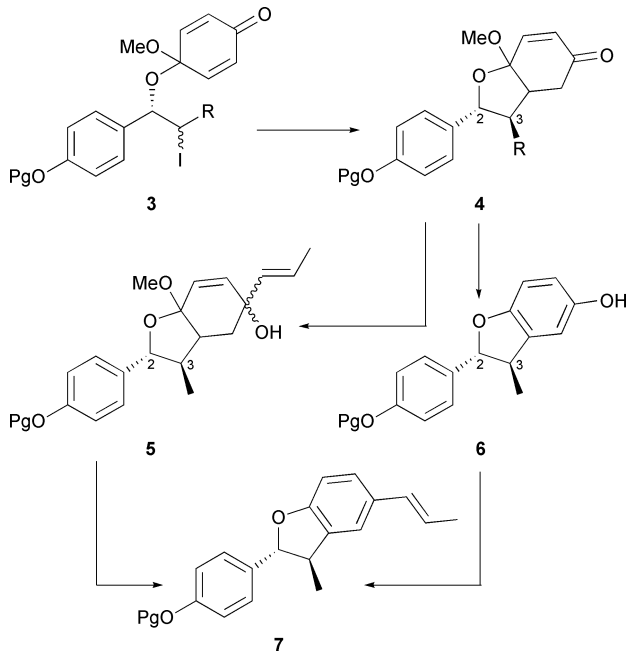
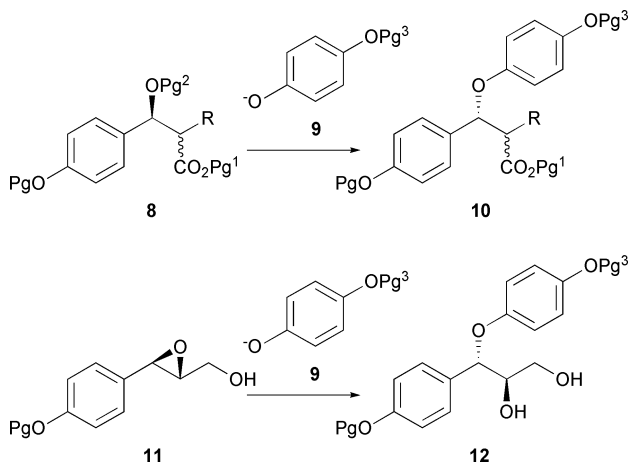
† l ec c upp e e y (I S) e: e pe- e p ce ue . See : 10.1039/ 801858



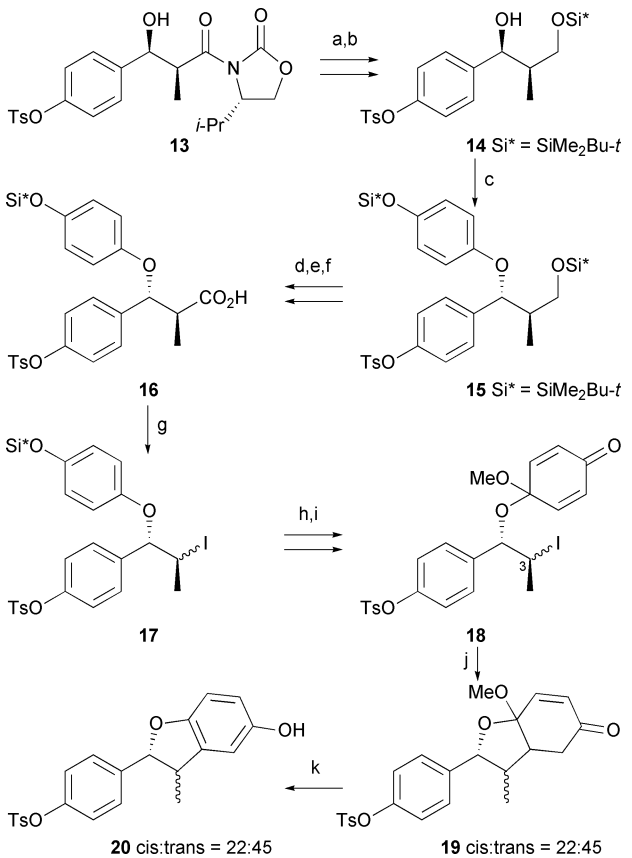
Scheme 1 = p ec up; = e upc e e.



Scheme 2 , [1], [2], [3] = p ec up ; = e up c e e.

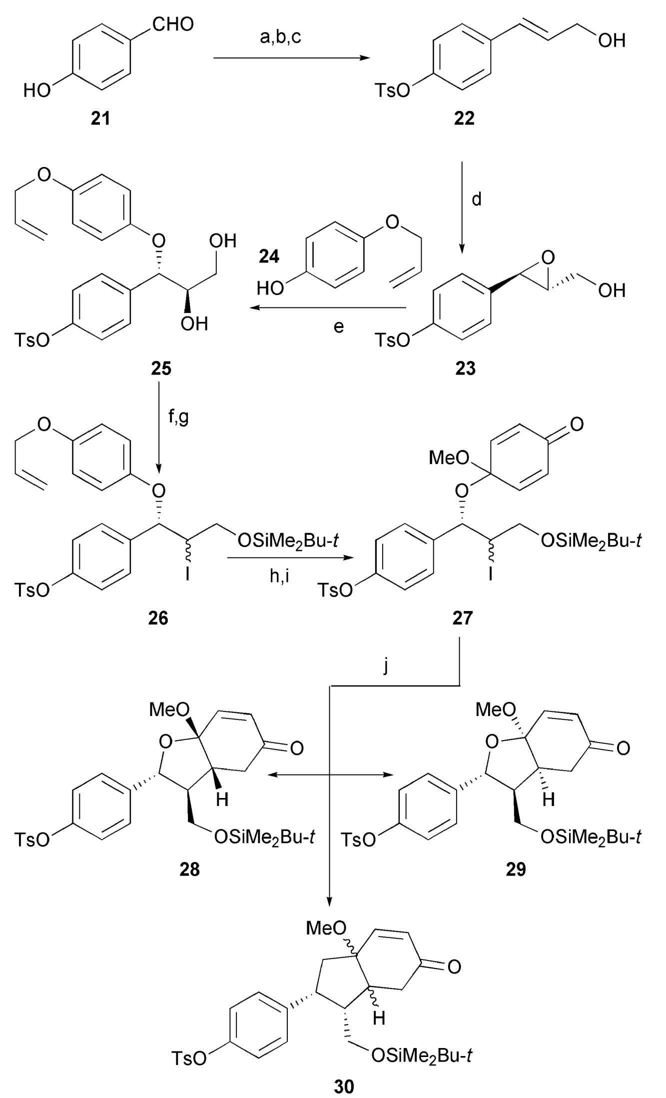
e p ce e y cc [28–30] w p e e **9** e uce p e.

Sc e e 2 , wee e **14** y u e (Sc e e 3) u e p e w e p ce e (ee **14** → **15**) e e u e u uc e y e e y c y y e e e y e. N e e e , w e e equ e p ce e p uc **15** , we e e c **16** u e -Hu ec e p ce [31] e e e **17**. e y e w (c)2 p uce e c -c u e e e **18**, u e cyc [32] (**18** → **19**) ep e e eec y , e (**19** → **20**), e *cis* : *trans* w y *ca.* 33 : 67. e p e e eec y, we p e pep e u e ype **18** w e up p ce e C(3) e y . H we e, u **14** w y CH2S 2*t*- u p ce e y, we e up e e e y c p ce e w e pec ye e e eec y.



Scheme 3 *Reagents and conditions*: ( ) H4; (b) *t*- u e2S C , H, 89% e w ep ; (c) ee e , 68% *via* e; ( ) 3. 2 (eec e ep ec e –CH2 S e2*t*- u u), 66–74%; (e) De – pe e; ( ) c , 81% e w ep ; ( ) e eec y , 43–66% e w ep ; (h) u4 , c H, 85%; ( ) (c)2, e H, 88%; ( ) u3SH, , e, 72%; (k) H H2 , 4 ecu e e , CH2C 2, 92%.

p we ec e e e ep e ype **11** (ee Sc e e 2) w e e e u equen y p ec e p y H w u y y up e ce e e - eec y e p e c cyc (ee e w). e y c c **22** w p ep e *p*-y y e e y e **21** S pe y e ce p ,[24] u (−)- p py e, e ep e **23** (Sc e e 4). e e e e ep e, c ep ce e , we e e y H N e e **23** 95 : 5. pec we u e e u e e p c pu y e c e c c e, u e ; e e e, e e y e e p c pu y c c p (ee 98%) w e u e y e e e e c H C (ee e). ec ep ew e u p e **24**[33,34] w e p uce **25**, w c we c u e e 76% yc p y. e U e c e y w **25** e e u p ep e pe ccu w e ; p e u e[35] we e p e u e ec p e u p . e c que u u ep e pe , pp e c e , ppe e ep e e e p u c . e p y y y **25** w p ec e y y e e ec- y y y w ep ce y eu 3 – 2– e



Scheme 4 *Reagents and conditions*: [illegible] 81%; (c) [illegible], 95%; [illegible], 93%; (e) [illegible], **24**, 76%; [illegible] *t*-[illegible], 96%; [illegible], 89%; [illegible], 99%; [illegible], 91%; [illegible], 80°C, 72% [illegible] **28** [illegible] **29**.

(**25** → **26**). [illegible] *5-exo-* [illegible] **27** [illegible] **28** (26%) [illegible] **29** (45%). [illegible] **30** (10.5%). [illegible] *cis* [illegible] **30**, [illegible] [36] [illegible] *cis-* [illegible] **28** [illegible] **29** [illegible] 1.

[illegible] **28** [illegible] **29** [illegible] (Scheme 5). [illegible] *E*-1-p[illegible] *t*-[illegible] *E*-1-[illegible] 99% *E*). [illegible] **31** [illegible] *E* : *Z* 97 : 3, [illegible]

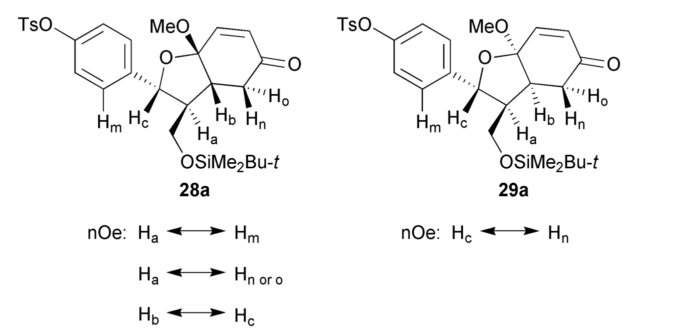
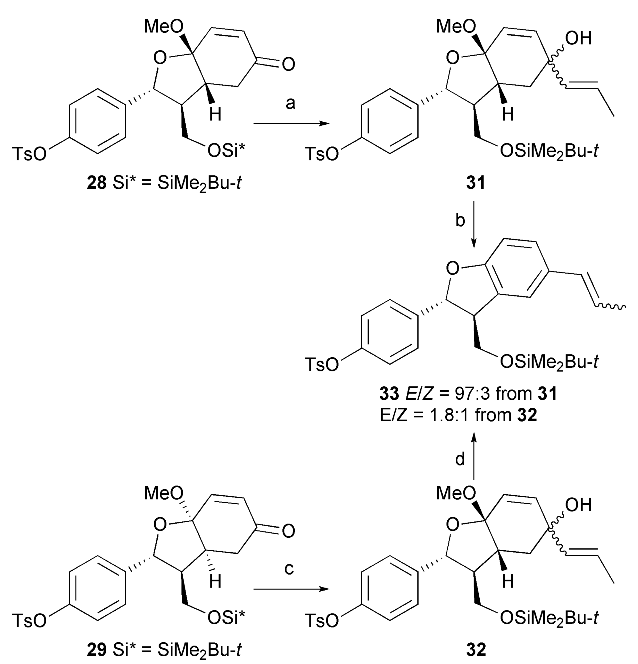


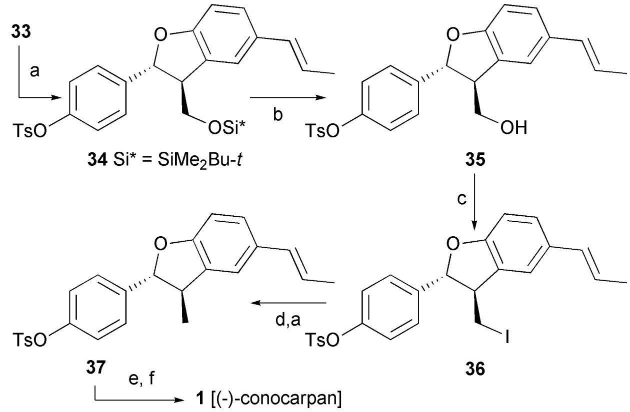
Fig. 1 [illegible]



Scheme 5 *Reagents and conditions*: ( ) *E*-1-p[illegible]; [illegible], 30 [illegible], 54% [illegible]; (c) 1-p[illegible]; ( ) [illegible], 2 [illegible], 71% [illegible].

[illegible] *E*- [illegible] **29** [illegible] 1-p[illegible] *E* : *Z* [illegible] (**32**). [illegible] (*Z* → *E*) [illegible]

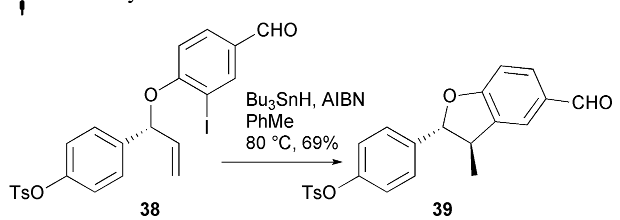
[illegible] (**31** → **33**; **32** → **33**). [illegible] *E*/*Z* [illegible] **31**, [illegible] [37] [illegible] **34** [illegible] *E* : *Z* *ca.* 97 : 3 (Scheme 6). [illegible] [38] (**34** → **35** → **36**), [illegible] [39]) [illegible] **37**. [illegible] *E* : *Z* [illegible] *Z*- [illegible] **37** [illegible] [37] 48 [illegible] (74% [illegible]



Scheme 6 *Reagents and conditions*: [illegible] 95%; [illegible] 100%; [illegible] (82%) [illegible] (85%) [illegible] 1,2- [illegible] 98%; [illegible] 95%; [illegible] 74% [illegible] **36**.

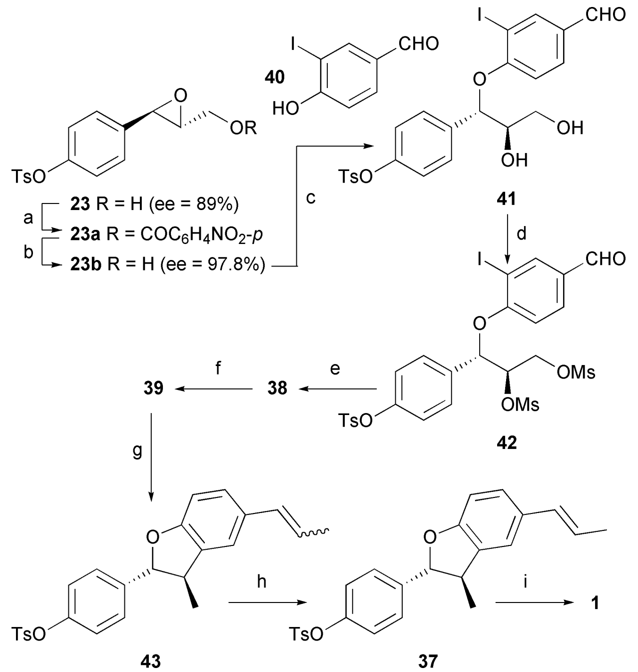
95% [illegible] [α]$_D^{22}$ −99.7 (c 1.03, [illegible]) [illegible] (+)-c[illegible] [40] [illegible] 98%; [illegible] [10] [illegible] (+)-c[illegible] (−)-c[illegible] 2*R*,3*R* [illegible] **1**. [illegible]

[illegible] *cis* : *trans* [illegible] 5-*exo*- [illegible] **38** → **39**.



[illegible] **23**, [illegible] *p*- [illegible] (**23** → **23a** → **23b**) [illegible] *ca.* 89% [illegible] 97.8% (Scheme 7).

[illegible] **23b** [illegible] **40**[41] (2 equiv.) [illegible] **41** [illegible] 83% [illegible] (100%) [illegible] [42] [illegible] 2- [illegible] **38**[43,44] [65% [illegible] 80% [illegible] (19%) [illegible] (80 °C) [illegible] *trans* [illegible] **39** [illegible] 69% [illegible] ([illegible], 300 [illegible]) [illegible] *cis* [illegible]



Scheme 7 *Reagents and conditions*: [illegible] *p*-[illegible] 70% [illegible] 62% [illegible] K$_2$C[illegible] 80% [illegible] 97%; (c) [illegible] **40**, 64% [illegible] 83% [illegible] **23b**; [illegible] 100%; [illegible] 2- [illegible] 71%; [illegible] 80 °C, 69%; [illegible] 69%; [illegible] 10 [illegible] 85%; [illegible] 95%.

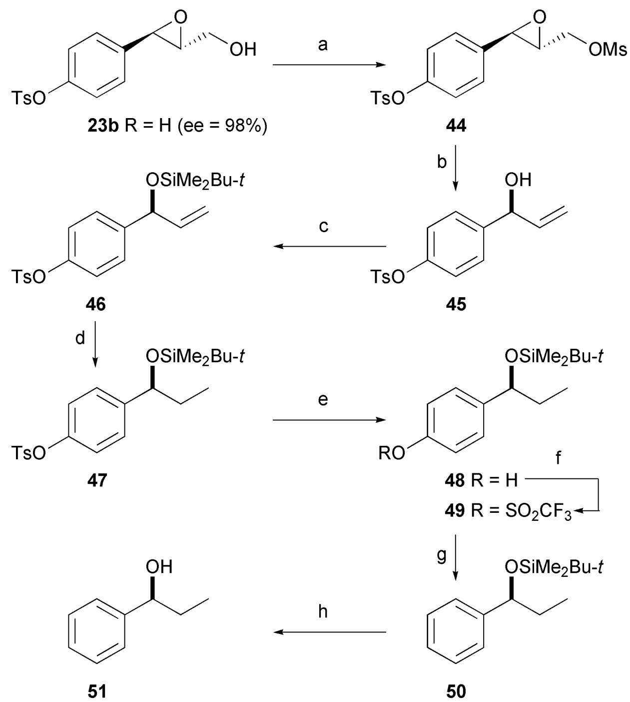
[illegible] 1-p[illegible] 3 : 1 *Z* : *E* [illegible] (**43**) [illegible] [37] 24 [illegible] (**37**) [illegible] *E*- [illegible] ($E : Z = 96.9 : 3.1$) [illegible] 10 [illegible] *Z*- [illegible] 400 [illegible] (85%) [illegible] (−)-c[illegible] (95%); [α]$_D^{22}$ −46.5 (c 0.28, [illegible])[40,45] [illegible] 88% (*i.e.* [illegible] = 94 : 6) [illegible] 99 : 1 [illegible] **23b**) [illegible] 94 : 6 [illegible] **1**), [illegible] **38** [illegible] [46] [illegible]

Proof of absolute stereochemistry

S[illegible] **1**, [illegible] [21,47] [illegible] **1**. [illegible]

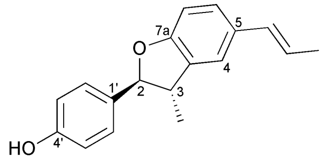
y e e e w *para* y u ue .[22] e w e u uc p u c e w u e y - y y , u p u e c y e y e e c c p ep e **23b** we e u ucce u . cc y, we u e ce e c c e ep e **23b** (*S*)-1-p y -1-p p , w e u ec u w c c e w *S*-(−) e c c .[48,49]

u e c y c e ep e **23b** w c e e e y e **44** (Sc e 8), w c **45** w y e y e w e u . y w u e u e c e e p e u e e e ep e ; e p e e e e e ep e e e, u ec c e ep e y c c y e c w e e u e e ec c c e.[50] y y p ec y y (**45** → **46**) u e y e **47**. e y upw e e y e c ( ). e e u p (**48** → **49**) we u e e p c y e y y y [51] (**49** → **50**). y, (*S*)-1-p y p p **51** w e e e y e y . e c p u $[\alpha]^{22}_{D}$ −29.3 (*c* 1.23, $CHCl_3$) [.[48] −45.6 (*c* 1.3, $CHCl_3$) , c e p ee 64%. u ep e **23b** ee 98% we y e e w c e e p c pu y; p y, ccu u e y *via* e u e c u w e e , we y u . S e e c c c y e e u e y ec c u . e u e c u e y **51** e e e[48,49] u e



Scheme 8 *Reagents and conditions*: ( ) C, ; ( ) , 1,2- e ye e, e u , 57% e w ep ; (c) *t*- u e2S S 2C 3, *sym*-c e, 100%; ( ) 5% 2 3, , 2, 99%; (e) ( ), e , 60% ec e e **47** (32%); ( ) (C 3S 2)2 , 3 , 75%; ( ) /C, 3 , 2, 100%; ( ) u4 , 71%.

e pe c e y e c ep (**22** → **23**) w e e pec e c u e; c eque y, u (+)-c c p u e e u e e e c y w **52**.



52 [(+)-conocarpan]

Conclusions

e pe w w e e c c e (+)- c c p equ e, cu e e. u y e , w c e p uc e y e e, e p cee *via* e e y c y c, e e ppe e e e c pu y. e ec ue, w c e e uc e C– , we e w ep e e e e c c p we ee. e w e 5- *exo-* c c u e e e e *cis*/*trans* e ec y, w c u e y c pe y up, e ec u e, e e e ec e.

Experimental

General methods

e *J* ue e p c e u e ec y e pec u . e pe we e e u e e p e e (2), u e e e c y. C u e e qu e e e × e . $[\alpha]_D$ ue e e 10^{-1} e ^{2} $^{-1}$.

First route

Toluene-4-sulfonic acid 4-[(2*S*,3*R*)-3-hydroxymethyloxyranyl)]-phenyl ester (23). C u e 4 ecu e e (0.5), c e >200 °C 0.3 24 , we e e u (−)- p py e (0.050 , 0.23) CH_2Cl_2 (4), e w we e c (−25 °C, C 2–CC 4). (-)4 (0.10 , 0.34) w e , we y *t*- u (3 c e, 1.6 , 4.8). e u e w e 10 **22** (728.4 , 2.390) CH_2Cl_2 (1.2 p u 0.8 e) w e pw e y y e. e u e w e 2 que c e y que u (30% w/ , 0.38) u e w C . S w c ue 10 S 4 (*ca.* 500) Ce e (*ca.* 1) we e e . e u e w we e we e e . p e e c p y e e ue e c e (2.5 × 35), u 50–60% c– e e (ep e u) 6 : 3 : 1 c– e e– e , e **23** (712.4 , 93%) w e : p 51–53 °C; ^1H (C C 3, 500) δ 1.74 (, *J* = 5.1, 7.7 , 1), 2.49 (, 3), 3.18 (, *J* = 2.3, 2.3, 3.6 , 1), 3.83 (, *J* = 3.6, 7.8, 12.6 , 1), 3.93 (, *J* = 2.0 , 1), 4.06 (, *J* = 2.5, 4.9, 12.9 , 1), 6.99 (pp p ′ ′ y , *J* = 8.7 , 2), 7.21 (pp p ′ ′ y , *J* = 8.5 , 2), 7.30 (pp p ′ ′ y , *J* = 8.3 , 2), 7.71 (pp p ′ ′ y , *J* = 8.3 , 2); ^{13}C (C C 3,

100 H) δ 22.0 ( ), 55.1 ( ), 61.3 ( ), 62.8 ( ), 122.8 ( ), 127.2 ( ), 128.7 ( ), 130.1 ( ), 132.5 ( ), 136.1 ( ), 145.7 ( ), 149.7 ( ); (CHC 3 c ; $^{-1}$) 3419, 3069, 2986, 2926, 2872, 1598, 1505, 1372, 1198, 1176, 1150; e c m/z c c $C_{16}H_{16}$ S 343.06107, 343.06134.

S p e e e e e (e e p - c y c e ep y c e c e p c c ep y c) we e p ep e y (R)-α e y-α- (u e y)p y ce y c e e u e ep y c 3 CH$_2$C$_2$. y e e e c u e e e e y H we e e e e c e e ep y c e 94 : 6. y e ep y c e c (u p ep e e e e c) y c H C [C p - H (150 × 4.6), 1 : 1 e C –w e , w 0.5 $^{-1}$, e ec 232 . e e ep c c p e; e e 11.9 14.3 we e e c e 94.7 : 5.3.

Toluene-4-sulfonic acid 4-[(1*S*,2*R*)-1-(4-Allyloxyphenoxy)-2,3-dihydroxypropyl]phenyl ester (25). p y c **23** (>88% ee, 10.94 , 34.15) w e e p e e e (70 °C) u *O*- y y qu e (12.32 , 82.04) que u H (1 , 34 , 34) w e (66), w c ue 2.5 . e u e w we c , p u e que u H (1 , 100), e ce e ee e w 2 . e c e c e we e w e w e, e (2S 4) e p e . c p y e e ue e c e (5 × 35), u 50–80% c– e e c 3 (*ca.* 3 p pe 100) (e u), e **25** (12.26 , 76%) ye w , ec e e **23** (1.09 , 10%). **25** : [α]$_D^{22}$ +46.77 (*c* 1.94, CH$_2$C$_2$); H (C C 3, 400 H) δ 2.16 (, 1 H), 2.46 (e pp , 4 H), 3.79 (, 2 H), 3.93 (, J = 5.4, 9.8 H , 1 H), 4.45 (, J = 1.5, 1.5, 5.3 H , 2 H), 5.08 (, J = 6.1 H , 1 H), 5.27 (, J = 1.4, 1.4, 1.4, 10.5 H , 1 H), 5.38 (, J = 1.6, 1.6, 1.6, 17.3 H , 1 H), 6.02 (, J = 5.3, 5.3, 10.6, 17.3 H , 1 H), 6.71–6.77 (, 4 H), 7.00 (pp p ′ ′ y , J = 8.6 H , 2 H), 7.30 (pp p ′ ′ y , J = 8.1 H , 2 H), 7.33 (pp p ′ ′ y , J = 8.6 H , 2 H), 7.69 (pp p ′ ′ y , J = 8.3 H , 2 H); ^{13}C (C C 3, 100 H) δ 21.7 (q), 62.8 ( ), 69.4 ( ), 74.5 ( ), 81.1 ( ), 115.6 ( ), 117.1 ( ), 117.6 ( ), 122.6 ( ), 128.3 ( ), 128.4 ( ), 129.7 ( ), 132.4 ( ), 133.4 ( ), 137.1 ( ), 145.4 ( ), 149.3 ( ), 151.4 ( ), 153.4 ( ); (C C 3 c ; $^{-1}$) 3400, 3069, 2924, 1597, 1505, 1373, 1212, 1199; e c m/z c c $C_{25}H_{26}$ 7S 493.12915, 493.12900.

Toluene-4-sulfonic acid 4-[(1*S*,2*S*)-3-(*tert*-butyldimethylsilanyloxy)-2-iodo-1-(1-methoxy-4-oxocyclohexa-2,5-dienyloxy)propyl]-phenyl ester (27).

(a) Toluene-4-sulfonic acid 4-[(1S,2S)-3-(e -butyldimethylsilanyloxy)-1-(4-hydroxyphenoxy)-2-iodopropyl]phenyl ester. (3)4 (269.3 , 0.2330) w e e u **26** (2.5371 , 3.652) e e (1.1353 , 8.099) H (13), w c ue 1 . p e c p y e e ue e c e (3 × 45), u 10–20% c– e e (e u), e ue e-4- u c c 4-[(1*S*,2*S*)-3-(*tert*- u y e y y y)-1-(4- y yp y)-2- p py p y e e (2.3587 , 99%) u e, w w p ce e p p y: [α]$_D^{22}$ +13.04 (*c* 1.38, CHC 3); H (C C 3, 400 H) δ 0.00 (, 3 H), 0.04 (, 3 H), 0.88 (, 9 H), 2.43 (, 3 H), 3.79 (, J = 4.5, 10.6 H , 1 H), 3.99 (, J = 8.2, 10.6 H , 1 H), 4.21 (, J = 4.3, 4.3, 8.3 H , 1 H), 5.05 (e pp w , J = 4.2 H , 2 H), 6.65–6.73 (, 4 H), 6.96 (pp p ′ ′ y , J = 8.6 H , 2 H), 7.27 (pp p ′ ′ y , J = 8.5 H , 2 H), 7.29 (pp p ′ ′ y , J = 8.7 H , 2 H), 7.65 (pp p ′ ′ y , J = 8.4 H , 2 H); ^{13}C (C C 3, 100 H) δ −5.5 (q), −5.4 (q), 18.2 ( ), 21.7 (q), 25.8 (q), 40.9 ( ), 65.7 ( ), 77.9 ( ), 115.9 ( ), 117.5 ( ), 122.4 ( ), 127.8 ( ), 128.5 ( ), 129.7 ( ), 132.0 ( ), 138.8 ( ), 145.5 ( ), 149.1 ( ), 150.2 ( ), 151.7 ( ); (CHC 3 c ; $^{-1}$) 3489, 2952, 2927, 2856, 1597, 1507, 1373, 1198, 1176, 1092, 837; e c m/z c c $C_{28}H_{35}$ 6SS 677.08606, 677.08627.

(b) Toluene-4-sulfonic acid 4-[(1S,2S)-3-(e -butyldimethylsilanyloxy)-2-iodo-1-(1-methoxy-4-oxocyclohexa-2,5-dienyloxy)-propyl]phenyl ester (27). (c)$_2$ (45.4 , 0.141) w e e p e c e (0 °C) u e e ue e-4- u c c 4-[(1*S*,2*S*)-3-(*tert*- u y e y y y)-1-(4- y yp y)-2- p py - p y e e (c *ca.* 6.5% *anti* e) (81.0 , 0.124) e H (1.3). S w c ue 30 c (10) w e . e u e w w e w u e que u HC 3 e, e (S 4) e p e . c p y e e ue e c e (1.5 × 30), u 0–20% c– e e c 3 (*ca.* 3 p pe 100) (e u), e **27** (77.3 , 91%) e , w c ppe e e e e (H , ^{13}C): [α]$_D^{22}$ +39.38 (*c* 1.49, CH$_2$C$_2$); H (C C 3, 400 H) δ 0.00 (, 3 H), 0.04 (, 3 H), 0.88 (, 9 H), 2.41 (, 3 H), 3.33 (, 3 H), 3.52 (, J = 4.2, 11.0 H , 1 H), 3.79 (, J = 6.9, 11.0 H , 1 H), 3.99 (, J = 4.3, 5.1, 6.8 H , 1 H), 4.72 (, J = 5.2 H , 1 H), 5.95 (, J = 2.1, 10.3 H , 1 H), 6.08 (, J = 2.1, 10.5 H , 1 H), 6.48 (, J = 3.2, 10.3 H , 1 H), 6.64 (, J = 3.2, 10.4 H , 1 H), 6.90 (pp p ′ ′ y , J = 8.7 H , 2 H), 7.18 (pp p ′ ′ y , J = 8.6 H , 2 H), 7.27 (pp p ′ ′ y , J = 8.5 H , 2 H), 7.64 (pp p ′ ′ y , J = 8.4 H , 2 H); ^{13}C (C C 3, 100 H) δ −5.4 (q), −5.2 (q), 18.2 ( ), 21.7 (q), 25.8 (q), 41.3 ( ), 51.5 (q), 65.5 ( ), 73.1 ( ), 93.6 ( ), 122.3 ( ), 128.2 ( ), 128.5 ( ), 129.0 ( ), 129.7 ( ), 129.8 ( ), 132.2 ( ), 139.7 ( ), 143.5 ( ), 144.2 ( ), 145.5 ( ), 149.3 ( ), 184.8 ( ); (CH$_2$C 2 c ; $^{-1}$) 3055, 2953, 2930, 2896, 2857, 1688, 1674, 1639, 1599, 1501, 1471, 1378, 1199, 1177, 1094, 867, 839; e c m/z c c $C_{29}H_{37}$ 7SS 707.09663, 707.09677. . c c $C_{29}H_{37}$ 7SS : C 50.87; H 5.45; S 4.68. : C 50.78; H 5.55; S 4.87%.

Toluene-4-sulfonic acid 4-[(2*R*,3*S*,3a*S*,7a*S*)-3-(*tert*-butyldimethylsilanyloxymethyl)-2,3,3a,4,5,7a-hexahydro-7a-methoxy-5-oxobenzofuran-2-yl]phenyl ester (29) and Toluene-4-sulfonic acid 4-[(2*R*,3*S*,3a*R*,7a*R*)-3-(*tert*-butyldimethylsilanyloxymethyl)-2,3,3a,4,5,7a-hexahydro-7a-methoxy-5-oxobenzofuran-2-yl]phenyl ester (28). u u$_3$S H (0.04 , 0.15) (6.0 , 0.037) e (3) w e e 4 e e e (80 °C) u **27** (65.4 , 0.0955) e (1) (2 p e e). e e , e w c ue 1 , e u e w

we c pe ue. p e
c py e e ue e c e
(1.5 × 30 c), u 8–20% c–e e ec 3 (*ca.*
3 pe 100), e ee c , ec ye w
. e e eu c w e e (**28**) (14.0 ;
26.3%), e eeu c w ue u w e
ee e [*i.e. cis* u u e y ee cyc e
(ee e w) (5.6 , 10.5%), e we eu c w
e ee e (**29**) (23.6 , 45.3%). e y e
e p uc u e 72%.

e e ec u weee e y e ue-
e w . 1.

e eu e **28** : [α]$_D^{22}$ −56.66 (*c* 2.49, CHC$_3$); H (C$_6$D$_6$, 400) δ 0.00 (, 6H), 0.97 (, 9H), 1.80 (, *J* = 4.3, 4.3, 8.8, 8.8 , 1H), 1.87 (, 3H), 2.48 (, *J* = 4.8, 16.6 , 1H), 2.60 (, *J* = 6.4, 16.6 , 1H), 2.93 (, *J* = 1.4, 4.9, 6.2, 9.7 , 1H), 3.28 (, 3H), 3.30 (, *J* = 4.2, 10.9 , 1H), 3.41 (, *J* = 4.6, 10.8 , 1H), 5.05 (, *J* = 8.9 , 1H), 5.95 (, *J* = 10.4 , 1H), 6.56 (, *J* = 1.4, 10.4 , 1H), 6.70 (pp e p y c , *J* = 0.6, 8.5 , 2H), 7.12 (pp e p y c , *J* = 8.7 , 2H), 7.22 (pp e p y c , *J* = 8.8 , 2H), 7.77 (pp e p y c , *J* = 0.3, 8.5 , 2H); ^{13}C (C$_6$D$_6$, 100) (w e p e c e) δ −5.6 (q), 18.3 ( ), 21.1 (q), 25.9 (e pp q), 37.9 ( ), 44.1 ( ), 49.4 (q), 55.1 ( ), 60.0 ( ), 81.8 ( ), 103.5 ( ), 122.9 ( ), 128.8 ( ), 129.7 ( ), 133.5 ( ), 140.1 ( ), 143.0 ( ), 144.8 ( ), 149.9 ( ), 196.0 ( ); , (CHC$_3$ c ; c^{-1}) 2953, 2929, 2857, 1689, 1597, 1502, 1376, 1198, 1176, 1155, 866, 837.

e w eu e **29** : [α]$_D^{22}$ −20.65 (*c* 5.88, CHC$_3$); H (C$_6$D$_6$, 400) 0.00 (, 3H), 0.01 (, 3H), 0.95 (, 9H), 1.92 (, 3H), 2.46 (, *J* = 11.7, 15.9 , 1H), 2.63 (, *J* = 4.9, 15.9 , 1H), 2.92–3.00 (, 2H, u e y 2D e pe e), 3.13 (, 3H), 3.45 (, *J* = 5.9 , 2H), 4.90 (, *J* = 9.0 , 1H), 6.04 (, *J* = 0.7, 10.5 , 1H), 6.58 (, *J* = 10.3 , 1H), 6.76 (pp e p y c , *J* = 8.1 , 2H), 7.18 (pp e p y c , *J* = 8.6 , 2H), 7.33 (pp e p y c , *J* = 8.6 , 2H), 7.80 (pp e p y c , *J* = 8.3 , 2H); ^{13}C (C$_6$D$_6$, 125) δ −5.7 (q), −5.6 (q), 18.1 ( ), 21.1 (q), 25.8 (q), 36.3 ( ), 46.6 ( ), 49.3 (q), 50.9 ( ), 59.8 ( ), 83.8 ( ), 103.8 ( ), 122.8 ( ), 128.3 ( ), 128.8 ( ), 129.65 ( ), 129.71 ( ), 133.6 ( ), 140.7 ( ), 140.9 ( ), 144.8 ( ), 150.0 ( ), 196.6 ( ); , (CHC$_3$ c ; c^{-1}) 2953, 2929, 2886, 2857, 1720, 1691, 1502, 1376, 1198, 1178, 1154, 1093, 867, 838; e c *m/z* c c C$_{29}$H$_{38}$ $_7$SS 581.19997, u 581.19977.

e c e *cis* u u p uc w e
w e e y e (y e e w
H H$_2$) w e c p uc w e c
w e p uc e e e *trans* u u-
p uc .

Toluene-4-sulfonic acid 4-[(2*R*,3*S*)-3-(*tert*-butyldimethylsilanyloxymethyl)-2,3-dihydro-5-(1*E*)-1-propenylbenzofuran-2-yl]phenyl ester (34). C$_2$(CN)$_2$ (84.6 , 0.221) w e e p e u **33** (*E* : *Z* = 1.8 : 1, 1.4696 , 2.6680) CH$_2$C$_2$ (10) e uew e 3.5 y (N$_2$ pe e), ue w ^{2} (10) ee u p (3 × 3 c), u $_2$. p e e c p y e e ue e c e (1.5 × 35 c), u 8% c–e e, e **34** (1.3980 , 95%) c e (c *ca.* 3% e *Z* e) w H e c e ep e **33**.

Toluene-4-sulfonic acid 4-[(2*R*,3*S*)-2,3-dihydro-3-iodomethyl-5-(1*E*)-1-propenylbenzofuran-2-yl]phenyl ester (36).

(a) Toluene-4-sulfonic acid 4-[(2 ,3S)-2,3-dihydro-3-(methanesulfonyloxy)methyl-5-( )-1-propenylbenzofuran-2-yl]-phenyl ester. eS$_2$C (0.025 , 0.32) w e pw e y y e e c e (0 °C) u **35** (120.0 , 0.2750) 3 (0.04 , 0.29) CH$_2$C$_2$ (3). e c w e w c ue 15 . e uew w e w e e (S$_4$). p e e c py e e ue e c e (1.5 × 30 c), u 20% c–e e, e ue e-4- u c c 4-[(2*R*,3*S*)-2,3- y -3-(e eu y y)e y -5-(1*E*)-1-p pe y e - u -2-y p e y e e (120.1 , 85%) w e , w c c e 4% e *Z* e (H): p 40–42 °C; [α]$_D^{22}$ −49.71 (*c* 6.59, CHC$_3$); H (CDC$_3$, 400) δ 1.86 (, *J* = 1.7, 6.6 , 3H), 2.45 (, 3H), 2.98 (, 3H), 3.71 (, *J* = 5.1, 5.1, 8.9 , 1H), 4.39 (, *J* = 8.4, 10.3 , 1H), 4.50 (, *J* = 5.0, 10.3 , 1H), 5.58 (, *J* = 5.2 , 1H), 6.08 (q, *J* = 6.6, 15.6 , 1H), 6.33 (, *J* = 1.6, 15.7 , 1H), 6.84 (, 8.2 , 1H), 6.97 (pp e p y c , *J* = 8.7 , 2H), 7.18 (, 1H), 7.20 (, *J* = 1.7, 8.3 , 1H), 7.29 (pp e p y c , *J* = 8.8 , 2H), 7.31 (pp e p y c , *J* = 0.5, 8.1 , 2H), 7.70 (pp e p y c , *J* = 8.4 , 2H); ^{13}C (CDC$_3$, 100) δ 18.3 (q), 21.6 (q), 37.5 (q), 50.7 ( ), 70.0 ( ), 85.7 ( ), 109.8 ( ), 121.9 ( ), 122.6 ( ), 124.0 ( ), 124.1 ( ), 126.7 ( ), 127.8 ( ), 128.4 ( ), 129.7 ( ), 130.0 ( ), 131.9 ( ), 132.2 ( ), 139.7 ( ), 145.4 ( ), 149.3 ( ), 158.5 ( ); , (CHC$_3$ c ; c^{-1}) 3024, 2937, 1503, 1490, 1360, 1198, 1176, 1154, 960, 867, 816; e c *m/z* c c C$_{26}$H$_{26}$ $_7$S$_2$ 537.10122, u 537.10121.

*(b) Toluene-4-sulfonic acid 4-[(2 ,3S)-2,3-dihydro-3-iodomethyl-5-( )-1-propenylbenzofuran-2-yl]phenyl ester (**36**).* (177.8 , 1.186) w e e u pe 3 p we (0.1681 , 2.571) ue e-4- u c c 4-[(2*R*,3*S*)-2,3- y -3-(e eu y y)e y -5-(1*E*)-1-p pe y e u -2-y p e y e e (c 4% *Z* e) (120.1 , 0.2334) y e (0.26). e ue w eue e , we c , e e u p Ce e (3 × 1.5 c). p e e c py e e ue e c e (1.5 × 30 c), u 5–8% c-e e, e e **36**.

e y e e e e uc eu y e w e e e w pw e. cue e w ee e e uce u u$_3$S H (ee e).

e e pe e , pec c y e e pep e e, (566.0 , 3.776) w e e p e u ue e-4- u c c 4-[(2*R*,3*S*)-2,3- y - 3-(e eu y y)e y -5-(1*E*)-1-p pe y e u -2-y p e y e e (c c 6% *Z* e) (403.5 , 0.7841) y e (3). e uew e ue 1.5 , we c ue w c (10). e ue w w e w e (1 × 5), u que u $_2$S$_2$ $_3$

u (1 × 5), e (1 × 5), e (S 4) e p e. c p y e e ue e c e (2 × 30 c), u 13% c–e e, e **36** (421.1 , 98%) c e , w c c e 6% e *Z* e ( ): [*α* $^{22}_{D}$ −80.22 (*c* 5.97, C C 3); (C C 3, 400) *δ* 1.88 (, *J* = 1.4, 6.6 , 3), 2.47 (, 3), 3.34 (, *J* = 9.7, 9.7 , 1), 3.53 (, *J* = 4.0, 10.2 , 1), 3.54 (, *J* = 4.0, 4.0, 8.9 , 1), 5.49 (, *J* = 4.3 , 1), 6.10 (q, *J* = 6.6, 15.6 , 1), 6.36 (, *J* = 1.2, 15.8 , 1), 6.85 (, *J* = 8.2 , 1), 6.98 (pp e p y e , *J* = 8.7 , 2), 7.21 (, 1), 7.24 (, *J* = 8.3 , 1), 7.32–7.36 (, 4), 7.73 (pp e p y e , *J* = 8.2 , 2); ^{13}C (C C 3, 100) *δ* 9.7 ( ), 18.6 (q), 22.0 (q), 53.4 ( ), 89.3 ( ), 110.2 ( ), 122.1 ( ), 122.8 ( ), 124.2 ( ), 127.0 ( ), 128.0 ( ), 128.4 ( ), 128.8 ( ), 130.1 ( ), 130.5 ( ), 132.2 ( ), 132.7 ( ), 140.3 ( ), 145.6 ( ), 149.6 ( ), 158.6 ( ); (C C 3 c ; c $^{-1}$) 3021, 2913, 2851, 1597, 1502, 1489, 1374, 1245, 1198, 1177, 1154, 1093, 966, 862, 551; e c *m/z* c c $C_{25}H_{23}$ $_4$S 569.02540, u 569.02546.

Toluene-4-sulfonic acid 4-[(2*R*,3*S*)-2,3-dihydro-3-methyl-5-(1*E*)-1-propenylbenzofuran-2-yl]phenyl ester (37). (7.9 , 0.048) w e e u cue e **36** [e y e (0.1201) u e e 0.233 u$_3$S (0.09 , 0.3) e (3.6). e c e w u e u y w $_2$ e e 80 °C. e w c ue 1 e e u we c. p e c p y e e ue e 10% K – c e[52] (1.5 × 30 c), u 5–8% c–e e (e eu), e ep e 7 : 3 u e e **37**. u e w e- ul ec e e ec , u u$_3$S (0.08) e (3.6). C p y ecue e u e e ec e **37** (67.0 , 68% e 2 ep e e y e).

p e euc p ce ue, $_3$ (1 , 3.4 , 3.4) w e pw e y y e e c e (0 °C) u **36** e *via* ep ce ue e w (923.4 , 1.690) (10). e ce w e p ce u ec e w c ue 3.5 . e (0.5) w e, we y que u (1 , 4) y $_2$ (1.5 , 30%). e u w e 20 e p e ee w e (10) $_2$ (20). e cp ew w e w e (1 × 10) e (1 × 10), e (S 4) e p e. c p y e e ue e c e (2 × 35 c), u e e 13% c–e e, e **37** (697.9 , 98%) c e w c c e 3% e *Z* e ( ): [*α* $^{22}_{D}$ −59.93 (*c* 2.24, C $_2$C $_2$); (C C 3, 400) *δ* 1.42 (, *J* = 6.9 , 3), 1.86 (, *J* = 1.7, 6.6 , 3), 2.45 (, 3), 3.34 (, 1), 5.12 (, *J* = 8.4 , 1), 6.09 (q, *J* = 6.7, 15.7 , 1), 6.36 (, *J* = 1.7, 15.7 , 1), 6.77 (, *J* = 8.8 , 1), 6.99 (pp e p y e , *J* = 8.7 , 2), 7.12 (, 1), 7.12–7.13 (, 1), 7.32 (pp e p y e , *J* = 0.7, 7.9 , 2), 7.33 (pp e p y e , *J* = 8.4 , 2), 7.72 (pp e p y e , *J* = 8.4 , 2); ^{13}C (C C 3, 100) *δ* 18.3 (q), 18.4 (q), 21.7 (q), 45.6 ( ), 91.7 ( ), 109.3 ( ), 120.8 ( ), 122.6 ( ), 123.3 ( ), 126.4 ( ), 127.2 ( ), 128.5 ( ), 129.8 ( ), 130.6 ( ), 131.6 ( ), 131.8 ( ), 132.4 ( ), 140.0 ( ), 145.4 ( ), 149.3 ( ), 158.1 ( ); (C $_2$C $_2$ c ; c $^{-1}$) 3021, 2962, 2928, 1598, 1503, 1486, 1375, 1243, 1199, 1177, 1154, 1094, 968, 868; e c *m/z* c c $C_{25}H_{24}$ $_4$S 443.12875, u 443.12864.

e w e p e c C_2(C)$_2$ w :

C_2(C)$_2$ (21 , 0.55) w e e p e u **37** (0.281 , 0.667) C $_2$C $_2$ (3) e u e 48 ($_2$ p e e), u e w $_2$ (10) e e u p (3 × 3 c), u $_2$. p e e e c p y e e ue e c e (1.5 × 35 c), u 8% c–e e, e **37** (0.2072 , 74% e e) c e ee e *Z* e (400).

Toluene-4-sulfonic acid 4-[(2*R*,3*S*)-2,3-dihydro-3-iodomethyl-5-(1*E*)-1-propenylbenzofuran-2-yl]phenyl ester (36). e (20.6 , 0.303), we y $_3$ (42.6 , 0.162) e $_2$ (46.9 , 0.185), w e e u **35** (74.0 , 0.170) e (3). e u e we 100 °C 1.5 e we c. c (10) w e e u e w w e w u e que u $_2S_2$ $_3$ u (2 × 5) e (S 4). p e e c p y e e ue e c e (1.5 × 30 c), u 13% c–e e, e **36** (75.9 , 82%) c e w pec e c e ep e e.

4-[(2*R*,3*R*)-2,3-Dihydro-3-methyl-5-(1*E*)-1-propenylbenzofuran-2-yl]phenol [(+)-conocarpan] (1). ( ) (c, 10% , 868.9 , 3.779) w e e p e u e c y pu e **37** (197.0 , 0.4685) 80% e (8), w c ue e . e u w e ec e e , u e w w e (10). e e u e e c e w $_2$ (3 × 10), y w c e que u ye w ee p uc (C c , c , 30% c–e e). e c e e ce c we e w e w e e (S 4). p e e c p y e e ue e c e (1.5 × 25 c), u 0–15% c–e e, e **1** (119.0 , 95%) w e, c y e : p 120–123 °C [.[4a] 133–135 °C; .[4g] 124–126 °C; [*α* $^{22}_{D}$ −99.7 (*c* 1.03, e), .[4a] [*α* $^{21}_{D}$ +122 (e y c c p) (*c* 1.03, e); (C C 3, 500) *δ* 1.40 (, *J* = 6.8 , 3), 1.86 (, *J* = 1.6, 6.6 , 3), 3.37–3.43 (, 1), 5.00 (, 1), 5.08 (, *J* = 8.9 , 1), 6.09 (q, *J* = 6.6, 15.6 , 1), 6.37 (, *J* = 15.6 , 1), 6.76 (, *J* = 8.1 , 1), 6.83 (pp e p y e , *J* = 8.5 , 2), 7.12–7.14 (, 2), 7.30 (pp e p y e , *J* = 8.5 , 2); ^{13}C (C C 3, 125) *δ* 17.9 (q), 18.4 (q), 45.3 ( ), 92.7 ( ), 109.3 ( ), 115.5 ( ), 120.8 ( ), 123.1 ( ), 126.3 ( ), 127.9 ( ), 130.8 ( ), 131.3 ( ), 132.4 ( ), 132.9 ( ), 155.7 ( ), 158.3 ( ); (C $_2$C $_2$ c , c c pe; c $^{-1}$) 3395, 3022, 2962, 2928, 2882, 1614, 1517, 1487, 1240, 1202, 1171, 964, 831; e c *m/z* c c $C_{18}H_{18}$ $_2$ 266.13068, u 266.13042. C y [C ce c u (0.46 × 15.0 c); 95:5 ep e– p p ; e 1 $^{-1}$; 40 °C; ec 207 .; e e 7.4 10.9 we ec p u ee 98%.

Second route

Toluene-4-sulfonic acid 4-[(1*S*,2*R*)-1-(4-formyl-2,3-dihydroxy-2-iodophenoxy)propyl]phenyl ester (41). p y c **23b** (e = 98.9 : 1.1) (1.8694 , 5.8350) w e e p e (, 70 °C) u 4-y y-3- e y e[41] (2.6359 , 10.628) u que u (1 , 5.8 , 5.8) w e (6). S 70 °C w c ue 2.5 . e ue w we c w e p ue que u (1 , 10). e que u p e w e ce w 2 ec e c e c we e w e w e (S 4). p e c p y e e ue e c e (2.5 × 35 c), u 50–80% c–e e c 3 (*ca.* 3 p pe 100) (e eu), e **41** [2.1124 , 64%, 83% e ec e **23b** (436.8 , 23%) w e, c y e : p 55–58 °C; [α_D^{22} −39.52 (*c* 5.69, CHC 3); H (CDC 3, 400) δ 2.33 (, 1H), 2.45 (, 3H), 2.75 (, 1H), 3.82 (, *J* = 3.7, 11.5H , 1H), 3.94 (, *J* = 5.2, 11.5H , 1H), 4.03–4.06 (, 1H), 5.40 (, *J* = 5.8H , 1H), 6.64 (, *J* = 8.6H , 1H), 7.03 (pp e p y e , *J* = 8.7H , 2H), 7.30 (pp e p y e , *J* = 0.6, 8.6H , 2H), 7.33 (pp e p y e , *J* = 8.6H , 2H), 7.60 (, *J* = 2.0, 8.6H , 1H), 7.69 (pp e p y e , *J* = 8.4H , 2H), 8.27 (, *J* = 2.0H , 1H), 9.76 (, 1H); ^{13}C (CDC 3, 100) δ 21.7 (q), 62.3 ( ), 74.4 ( ) 81.4 ( ), 87.4 ( ), 113.3 ( ), 122.9 ( ), 128.2 ( ), 128.3 ( ), 129.8 ( ), 131.7 ( ), 131.8 ( ), 132.3 ( ), 135.2 ( ), 140.9 ( ), 145.6 ( ), 149.6 ( ), 160.1 ( ), 189.2 ( ); (CDC 3 c ; c^{-1}) 3417, 3067, 2927, 2883, 2731, 1694, 1587, 1502, 1480, 1371, 1255, 1198, 1177, 1155, 1093, 1038, 869; e c *m/z* c c $C_{23}H_{21}$ 7S 590.99450, u 590.99454.

Toluene-4-sulfonic acid 4-[(*R*)-1-(4-formyl-2-iodophenoxy)allyl]-phenyl ester (38). (91.7 , 0.612) w e e u **42** (29.5 , 0.0408) 2-u e (2), e u e 4 , we c . e e w e p e e ue w p e e weed c u e que u 2S 3. e c e c we e w e w e, e (S 4) e p e. c p y e e ue e c e (0.5 × 20 c), u 30% c–e e, e **38** (15.7 , 71%) e : [α_D^{22} −8.88 (*c* 13.43, CH 2C 2); H (CDC 3, 500) δ 2.48 (, 3H), 5.36 (, *J* = 0.8, 10.4H , 1H), 5.50 (, *J* = 0.8, 17.1H , 1H), 5.83 (, *J* = 5.9H , 1H), 6.05 (, *J* = 5.9, 10.4, 17.0H , 1H), 6.88 (, *J* = 8.5H , 1H), 7.06 (pp e p y e , *J* = 8.6H , 2H), 7.33 (pp e p y e , *J* = 8.5H , 2H), 7.45 (pp e p y e , *J* = 8.8H , 2H), 7.73 (pp e p y e , *J* = 8.3H , 2H), 7.76 (, *J* = 2.0, 8.5H , 1H), 8.34 (, *J* = 1.9H , 1H), 9.83 (, 1H); ^{13}C (CDC 3, 125) δ 21.7 (q), 81.4 ( ), 87.8 ( ), 113.6 ( ), 117.8 ( ), 122.8 ( ), 127.8 ( ), 128.4 ( ), 129.8 ( ), 131.5 ( ), 131.6 ( ), 132.4 ( ), 136.2 ( ), 137.6 ( ), 141.2 ( ), 145.5 ( ), 149.3 ( ), 160.6 ( ), 189.2 ( ); (CH 2C 2 c ; c^{-1}) 3065, 2922, 2834, 2727, 1695, 1587, 1501, 1479, 1371, 1252, 1197, 1177, 1154, 1093, 866; e c *m/z* c c $C_{23}H_{19}$ 5S 556.98902, u 556.98890. . c c $C_{23}H_{19}$ 5S: C 51.69; H 3.58; S 6.00. u : C 51.41; H 3.65; S 5.92%.

e e pe e w epe e e c e w e e y e (2.1255 , 2.94), e ye w 65% [80% e ec e e **38** (398.1 , 19%) .

Toluene-4-sulfonic acid 4-[(2*S*,3*R*)-2,3-dihydro-5-formyl-3-methylbenzofuran-2-yl]phenyl ester (39). u u 3S H (0.62 , 2.3) (48.1 , 0.293) e (18) w e e 4 (y epu p) e e e (80 °C) u **38** (910.4 , 1.704) e (18) (2 p e e). e e ue e e u e 2 e we c . p e e p y e e ue e K – c e (10% w/w, 2.5 × 30 c), u 25% c–e e, e **39** (482.6 , 69%) ye w : [α_D^{22} −50.54 (*c* 0.77, CHC 3); H (CDC 3, 400) δ 1.40 (, *J* = 6.9H , 3H), 2.38 (, 3H), 3.31–3.38 (, 1H), 5.19 (, *J* = 8.4H , 1H), 6.88 (, *J* = 8.1H , 1H), 6.96 (pp e p y e , *J* = 8.7H , 2H), 7.24–7.27 (, 4H), 7.64–7.67 (, 4H), 9.80 (, 1H); ^{13}C (CDC 3, 100) (e pec u we c pu e) δ 18.3 (q), 21.7 (q), 44.8 ( ), 92.7 ( ), 109.8 ( ), 122.8 ( ), 124.7 ( ), 127.1 ( ) 128.5 ( ), 129.8 ( ), 131.0 ( ), 132.4 ( ), 133.1 ( ), 133.4 ( ), 138.9 ( ), 145.5 ( ), 149.6 ( ), 164.3 ( ), 190.5 ( ); (CHC 3 c ; c^{-1}) 2964, 2928, 1690, 1605, 1504, 1483, 1373, 1247, 1198, 1177, 1154, 1093, 867; e c *m/z* c c $C_{23}H_{20}$ 5S 431.09237, u 431.09242.

Toluene-4-sulfonic acid 4-[(2*R*,3*S*)-2,3-dihydro-(3-methyl-5-(1*E*)-1-propenylbenzofuran-2-yl)phenyl ester (*E*-43) and toluene-4-sulfonic acid 4-[(2*R*,3*S*)-2,3-dihydro-3-methyl-5-(1*Z*)-1-propenyl-benzofuran-2-yl]phenyl ester (*Z*-43).

(a) Use of -BuOK. *t*- u K (33.0 , 0.294) w e e u pe 3 + − (129.6 , 0.3098) 2 (2), e u e w e 0.5 . u **39** (54.2 , 0.133) 2 (1) w e y y e. e u e w e 15 e 2 (5) w e, e u e w w e ce w w e ce w e e (S 4). p e e p y e e ue e c e (1.5 × 30 c), u 5–10% c–e e (e eu), e **43** (33.9 , 62%) ye w . e e y c e y pe e e H pec u we e *E*: *Z* (e 1 : 3; p e ce, pec c e p e e ep e e **37** (*i.e.* e 97 : 3 ue e e c pu).

(b) Use of BuLi. u (1.6 e e , 0.06 , 0.096) w e e e c e (0 °C) u pe 3 + − (39.5 , 0.0944) H (2). S w c ue 15 **39** (35.7 , 0.0796) H (1.3 pu 0.3 e) w e pw e y y e. S w c ue 2 e u e que u HC 3 (0.5), p e e weed w e (5) 2 (10). e ce c w e (S 4) e p e. c p y e e ue e c e (0.5 × 30 c), u 20% c–e e c e *ca.* 1% 3, e **43** (23.2 , 69%) ye w , w c w ue *Z* *E* e.

Toluene-4-sulfonic acid 4-[(2*R*,3*S*)-2,3-dihydro-3-methyl-5-(1*E*)-1-propenylbenzofuran-2-yl]phenyl ester (37). C 2(C)2 (9.4 , 0.025) w e e u **43**

(102.3 , 0.2433) CH_2C_2 (2), w c ue 23 . $_2$ (3) w e e u w ee u p (3 × 2 c) u $_2$ (25). p e c p y e e ue e c e (1 × 30 c) u 8% c–e e c $_3$ (*ca.* 3 p pe 100), e **37** (100.9 , 99%) c e : [α]$_D^{22}$ −54.15 (*c* 5.94, CH_2C_2). e c e 3.1% e *Z* e ( ).

Isomerization with 10-day reaction time. C_2(C)$_2$ (5.3 , 0.0138) w e e u **43** (36.0 , 0.0856) CH_2C_2 (2), w c ue 10 y. e u w ee u p (1 × 1 c), u CH_2C_2 e. p e c p y e e ue e c e (0.5 × 30 c), u 13% c–e e c $_3$ (*ca.* 3 p pe 100), e **37** (30.5 , 85%) c e w pec e c ep e e ue, e cep e *Z* e c u e ece e e pec u (400).

4-[(2*R*,3*R*)-2,3-dihydro-3-methyl-5-(1*E*)-1-propenylbenzofuran-2-yl]phenol [(+)-conocarpan] (1). e u y w e y e e e e c e e ue: [α]$_D$ −46.5 (*c* 0.28, e). C y e y e c c p [C ce c u (0.46 × 15.0 c); 90 : 10 ep e– p p ; w e 0.6 $^{-1}$; 40 °C; e ec 210 .; e e e 10.69 12.60 we ec p u ee 88%.

Proof of absolute configuration

Toluene-4-sulfonic acid 4-[(*S*)-1-hydroxyallyl]phenyl ester (45). (2.42 , 16.1) w e e u **44** (p uc pe ue pe e , *ca.* 1.6) y e (8). e e ew ue w ew e ue 12 , e we c . e ue ue w c (10), w e w u e que u $_2S_2$ $_3$ (8), w e (8) e (5), e (S $_4$) e p e. c p y e e ue e c e (1.5 × 30 c), u 27% c–e e c ce (0.4–1% /) $_3$, e **45** (279.8 , 57% e 2 ep e y y ep e) c e : [α]$_D^{22}$ +4.63 (*c* 0.57, CHC_3); (C_6D_6, 300) δ 1.10 (, *J* = 3.7 , 1), 1.74 (, 3), 4.62–4.65 , 1), 4.86 (, *J* = 1.5, 10.3 , 1), 5.03 (, *J* = 1.5, 17.1 , 1), 5.64 (, *J* = 5.9, 10.3, 17.1 , 1), 6.57 (pp e p y c , *J* = 8.3 , 2), 6.92–6.98 , 4), 7.63 (pp e p y c , *J* = 8.3 , 2); ^{13}C (C_6D_6, 100) (w c c e) δ 21.2 (q), 74.4 ( ), 114.7 ( ), 122.6 ( ), 128.7 ( ), 129.8 ( ), 133.4 ( ), 140.5 ( ), 142.3 ( ), 144.9 ( ), 149.5 ( ); (CHC_3 c ; c^{-1}) 3533, 3400, 3068, 2981, 2924, 2872, 1597, 1500, 1402, 1371, 1197, 1175, 1154, 1093, 867; e c *m/z* c c C_{16} $_4$S 327.06615, u 327.06657.

c p pep e e e y e ue e [53] e c e y u e ee e ep e u e e , e ee e w 2.3 : 0.95 ( ), w e ep e ep e e 98.9 : 1.1. ewe e e ep e ec ep c c c y c H C.

Toluene-4-sulfonic acid 4-[(*S*)-1-(*tert*-butyldimethylsilanyloxy)-propyl]phenyl ester (47). $_2$ $_3$ (5% w/w, 9.7 , 0.0047) w e u **46** (30.3 , 0.0724) (1.8). e u e w e e y equ e y e cu e (u e cuu) e , equ ce e epe e w ce e. e u e w e e u e $_2$ ( ) e e e u p (0.5 × 1 c) c e, u CH_2C_2 e. p e e e **47** (30.3 , 99%) c e : [α]$_D^{22}$ −26.43 (*c* 3.03, CHC_3); (CDC_3, 400) δ 0.00 (, 3), 0.18 (, 3), 1.00 (, *J* = 7.2 , 3), 1.03 (, 9), 1.72–1.88 , 2), 2.61 (, 3), 4.70 (pp e , *J* = 5.5 , 1), 7.08 (pp e p y c , *J* = 8.6 , 2), 7.36 (pp e p y c , *J* = 8.7 , 2), 7.45 (pp e p y c , *J* = 8.6 , 2), 7.84 (pp e p y c , *J* = 8.3 , 2); ^{13}C (CDC_3, 100) δ −5.0 (q), −4.7 (q), 9.8 (q), 18.2 ( ), 21.7 (q), 25.8 (q), 33.5 ( ), 75.5 ( ), 121.9 ( ), 127.0 ( ), 128.5 ( ), 129.6 ( ), 132.3 ( ), 144.7 ( ), 145.2 ( ), 148.3 ( ); (CHC_3 c ; c^{-1}) 3034, 2957, 2929, 2857, 1598, 1501, 1472, 1463, 1378, 1257, 1198, 1175, 1155, 1094, 1060, 1014; e c *m/z* c c C_{22} $_4$SS 443.16828, u 443.16826.

4-[(*S*)-1-(*tert*-Butyldimethylsilanyloxy)propyl]phenol (48). - ( ) (815.0 , 10% , 3.543) w e e , c u y u **47** (316.4 , 0.7444) 80% e (5.4). e w u e w c ue 45 e ce , c e u . e e u e ec e e e ep y u e c p p e u e u ($_2$ $_4$, p 7, 8) $_2$ (8). S u e que u c c (2) w e e e p c u e ew e ep e. e que u ye w e ce w $_2$ (2 × 6) e c e ce c wee w e, e (S $_4$) e p e. c p y e e ue e c e (1.5 × 25 c), u 0–20% c–e e (e eu), e **48** c e (119.3 , 60%) ec ee **47** (102.3 , 32%). e **48** : [α]$_D^{22}$ −19.32 (*c* 1.41, CHC_3); (C_6D_6, 400) (p e c e e) δ −0.09 (, 3), 0.05 (, 3), 0.87 (, *J* = 6.7 , 3), 1.06 (, 9), 1.66–1.88 , 2), 4.54 (, *J* = 5.5, 7.1 , 1), 6.62 (pp e p y c , *J* = 8.8 , 2), 7.19 (pp e p y c , *J* = 0.6, 8.6 , 2); ^{13}C (C_6D_6, 100) δ −4.8 (q), −4.4 (q), 10.3 (q), 18.4 ( ), 26.1 (q), 34.1 ( ), 76.5 ( ), 115.1 ( ), 127.4 ( ), 137.7 ( ), 155.4 ( ); (CHC_3 c ; c^{-1}) 3349, 3024, 2958, 2930, 2858, 1614, 1600, 1514, 1472, 1463, 1361, 1252, 1059, 836; e c *m/z* c c C_{15} $_2$S 289.15943, u 289.15935.

Trifluoromethanesulfonic acid 4-[(*S*)-1-(*tert*-butyldimethyl-silanyloxy)propyl]phenyl ester (49). (C $_3$S $_2$)$_2$ (0.07 , 0.4) w e pw e y y e e e c e (−78 °C) u **48** (99.9 , 0.375) $_3$ (0.09 , 0.6) CH_2C_2 (1.8) (p e). S w c ue 10 e u e que u C$_3$ (0.5) w e . e c w e e e uew pue ep y u e c w e (5) CH_2C_2 (5). e uew e e (S $_4$) e p e. c p y e e ue e c e (1.5 × 20 c), u

13% ce–e e ce (0.5–1% /) e **49** (111.6 , 75%) c e : [α]$_D^{22}$ −21.08 (*c* 0.48, C HC); H (C$_6$D$_6$, 400 H) δ 0.00 (, 3H), 0.18 (3H), 0.95 (, *J* = 7.4 H , 3H), 1.12 (, 9H), 1.57–1.77 (, 2H), 4.54 (, *J* = 5.1, 6.9 H , 1H), 7.04 (pp e p y e , *J* = 8.7 H , 2H), 7.18 (pp e p y e , *J* = 0.5, 8.9 H , 2H); ^{13}C (C$_6$D$_6$, 100 H) δ −5.0 (q), −4.7 (q), 9.7 (q), 18.3 ( ), 25.9 (q), 33.6 ( ), 75.4 ( ), 119.3 (, C H$_3$ qu e , *J* = 318.6 H), 121.0 ( ), 127.7 ( ), 146.1 ( ), 148.6 ( ); (C HC$_3$ c ; c^{-1}) 2959, 2932, 2859, 1500, 1427, 1251, 1214, 1143, 890, 861, 837; e c *m/z* c c C$_{16}$H$_{25}$ $_3$ $_4$SS 421.10872, u 421.10906.

(*S*)-*tert*-Butyldimethyl(1-phenylpropoxy)silane (50). /C (10% w/w, 60.8 , 0.0571) w e u **49** (99.0 , 0.248) $_3$ (0.11 , 0.79) c (5). e e uew e e y equ y e cu e (ue cuu) e H$_2$, e p ce ue e epe e w ce e. y e e w c ec e e w c ue 3 . e e e u uew ee u p (0.5 × 1.0 c) c e,u c e. p e e **50** (62.6 , 100%) ye w : [α]$_D^{22}$ −32.21 (*c* 0.66, C HC); H (C$_6$D$_6$, 400 H) δ −0.10 (, 3H), 0.04 (, 3H), 0.87 (, *J* = 7.3 H , 3H), 0.97 (, 9H), 1.58–1.79 (, 2H), 4.51 (, *J* = 5.2, 7.0 H , 1H), 7.07 (, *J* = 1.3, 6.7 H , 1H), 7.16–7.19 (, 2H), 7.26–7.28 (, 2H); ^{13}C (C$_6$D$_6$, 100 H) δ −4.8 (q), −4.5 (q), 10.2 (q), 18.4 ( ), 26.1 (q), 34.0 ( ), 76.7 ( ), 126.2 ( ), 127.2 ( ), 128.3 ( ), 145.8 ( ); (C HC$_3$ c ; c^{-1}) 3065, 3028, 2958, 2930, 2858, 1493, 1472, 1463, 1453, 1361, 1257, 1104, 1086, 1058, 1013, 860, 837, 775, 699; e c *m/z* c c C$_{15}$H$_{26}$ S 273.16451, u 273.16448.

Acknowledgements

e e u Sc e ce ee e e c C uc C c upp .

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