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Stereoselective synthesis of *C*-fused pyranoindoles, pyranobenzofurans and pyranobenzothiophene scaffolds using *oxa*-Pictet Spengler type reaction of vinylogous carbonates

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***C*-fused pyranoheterocycles can be readily assembled using intramolecular *oxa*-Pictet-Spengler type reaction of vinylogous carbonates in highly stereoselective manner. Required indole and benzofuran rings tethered to vinylogous carbonates are prepared by a tandem Sonogashira coupling - nucleopalladation reaction. The entire process can also be carried out in a 'one-pot' manner starting from homopropargyl alcohol. The *C*-fused pyranoindoles could be converted to spirooxindoles as well as ring expanded products under oxidative conditions.**

Heterocyclic indole is considered a 'privileged' scaffold in medicinal chemistry. Pyran ring fused to heterocycles such as indole, benzofurans or benzothiophenes can give structures, which are very useful pharmacophores. Etodolac and pemedolac bearing a tetrahydropyrano[3,4-*b*]indole skeleton, are found to be potent anti-inflammatory and analgesic agents.[1] Tetrahydropyrano[3,4-*b*]indole skeleton is also found in many other compounds, which are inhibitors of hepatitis *C* virus (HCB) NS5B polymerase.[2] On the other hand, 3,4-dihydro-1*H*-pyrano[3,4-*b*]benzofuran and 3,4-dihydro-1*H*-benzo[4,5]thieno-[2,3-*c*]pyran derivatives proved to be a novel class of HCV NS5B RNA dependent RNA polymerase inhibitors.[3] Further, pyran ring *N*-fused to the indole ring found in oxazinoindoles is known to exhibit antidepressant activity.[3c-e]

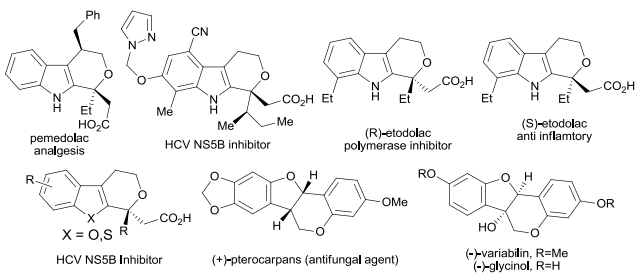
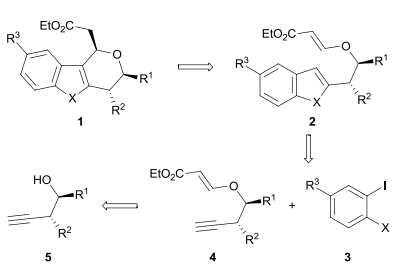


Fig. 1 Biologically important pyranoheterocycles.

Oxa-Pictet-Spengler reaction is a powerful tool for the synthesis of fused *hetero*cycles.[4] However, stereoselective synthesis of *C*-fused pyranoindole, pyranobenzofuran and pyranobenzothiophenes using this reaction has received relatively less attention.[5] Moreover, methods for the steroselective synthesis of tetrahydropyrano[4,3-*b*]indole skeleton and corresponding pyranobenzofuran and pyranobenzothiophenes are rarely encountered.[6] This is particularly surprising given the biological activity of this class of molecules. In continuation of our interest on the stereoselective synthesis of *oxa*- and *aza*-cyclic compounds using vinylogous carbonates and carbamates,[7,8] herein we describe a rapid, highly stereoselective method for assembling *C*-fused pyranoheterocycles employing a tandem Sonogashira coupling-nucleopalladation reaction followed by intramolecular *oxa*-Pictet-Spengler reaction to vinylogous carbonates. We further demonstrate that the entire sequence can be carried out in a 'one-pot' fashion. The products can be further functionalized to spirooxindoles as well as ring expanded lactam under oxidative conditions.

We envisioned that various *C*-fused pyranoheterocycles **1** could be readily assembled by Lewis acid mediated intramolecular *oxa*-Pictet-Spengler cyclization of vinylogous carbonate **2**. The vinylogous carbonates **2**, in turn, could be obtained by palladium-catalysed Sonogashira coupling-nucleopalladation reaction of *o*-iodophenols or *N*-tosyl protected iodoanilines **3** with terminal alkynes **4** (Scheme 1).[9] The known homopropargyl alcohols **5** would be the appropriate precursors for the synthesis of the alkynes **4**.[10]

Scheme 1 Retrosynthesis of *C*-fused pyranoheterocycles.



In order to test the hypothesis, synthesis of vinylogous carbonate **2a** bearing benzofuran as the heterocyclic ring was initiated. Thus, reaction of known homopropargyl alcohol **5a** with ethyl propiolate in the presence of *N*-methyl morpholine (NMM) furnished the vinylogous carbonate **4a**. The alkynyl vinylogous carbonate **4a** on tandem Sonogashira coupling/nucleopalladation reaction with *o*-iodophenol (**3a**) resulted in benzofuran derivative **2a** bearing vinylogous carbonate tethered at C2 position (Scheme 2).

Scheme 2 Synthesis of vinylogous carbonate precursor **2a**.

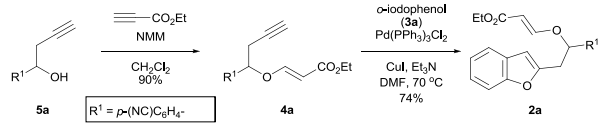
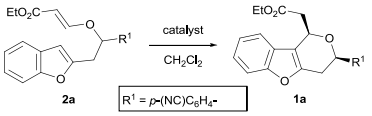


Table 1 Optimization of oxa-Pictet-Spengler reaction of vinylogous carbonate



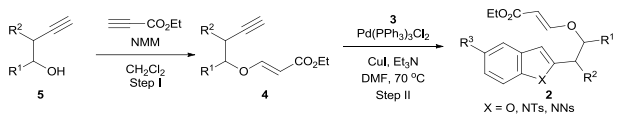
Entry	Catalyst	Equiv.	Temp. (°C)	Time (h)	Yield (%)[a]	dr[b]
1	$BF_3{\cdot}OEt_2$	1	0-rt	10	64	69:31
2	TMSOTf	1.1	0-rt	5	70	75:25
3	TMSOTf	1.1	-70	15	0[c]	-
4	TMSOTf	1.1	-25	24	64	83:17
5	TMSOTf	2.1	-25	11	72	83:17
6	***TMSOTf***	***2.0***	***-40***	***16***	***83***	***90:10***
7	$FeCl_3$	1.1	0-rt	24	0[c]	-
8	(±)-BPA	1.1	0-rt	24	0[c]	-

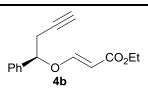
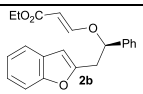
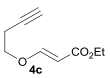
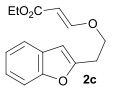
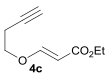
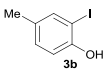
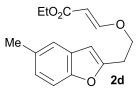
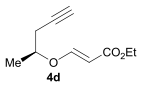
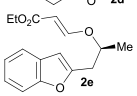
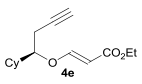
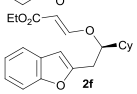
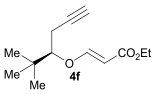
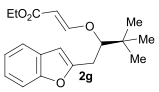
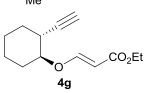
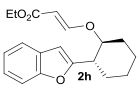
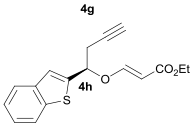
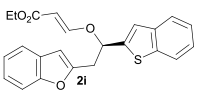
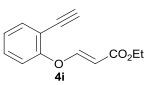
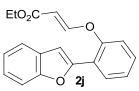
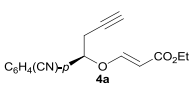
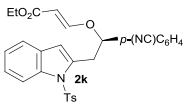
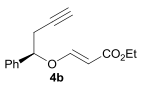
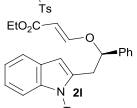
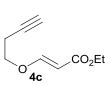
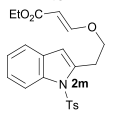
[a]Isolated yield. [b]In all the cases, dr was determined on the crude reaction mixtures by ^{1}H NMR. [c] No reaction, starting material recovered.

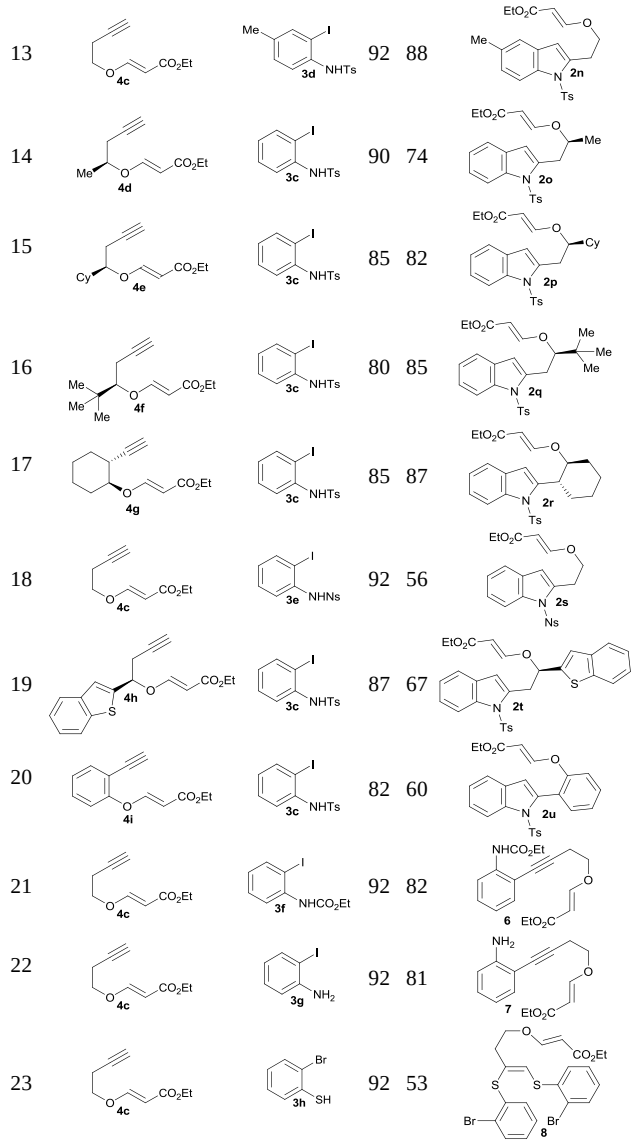
The feasibility of intramolecular *oxa*-Pictet-Spengler reaction was studied next by using various Bronsted and Lewis acids. The reaction of vinylogous carbonate **2a** with $BF_3{\cdot}OEt_2$ in CH_2Cl_2 at 0 °C gave pyranobenzofuran **1a** in good yield and moderate diastereoselectivity favouring *cis*-isomer (Table 1, entry 1). When TMSOTf was used as the Lewis acid for this transformation, the reaction time was reduced and the product was formed with improved yield with moderate selectivity (Table 1, entry 2). Lowering the reaction temperature led to prolonged reaction times but resulted in the formation of pyranobenzofuran in good yield with good diastereoselectivity (Table 1, entry 4-5). Increasing the amount of TMSOTf used at low temperature reduced the reaction time and pyranobenzofuran **1a** was formed in 83% yield and good diastereoselectivity (Table 1, entry 6). Milder Lewis acids like $FeCl_3$ (Table 1, entry 7) and Bronsted acid like (±)-binolphosphoric acid (BPA) (Table 1, entry 8) were found to be ineffective and only starting material was recovered even after prolonged reaction time. Based on these results it was clear that TMSOTf was catalyst of choice for further study.

Attention was next turned towards studying the scope of this intramolecular *oxa*-Picet-Spengler cyclization for the synthesis of *C*-fused heterocycles. Towards this end, synthesis of various benzofuran, indole and thiophene tethered vinylogous carbonates was undertaken. The requisite benzofuran and indole vinylogous carbonates **2b-u** were prepared *via* tandem Sonogashira coupling/nucleopalladation of *o*-iodophenols (**3a-b**) and *N*-protected *o*-iodoaniline (**3c-e**) with various terminal alkynes **4a-i** bearing vinylogous carbonate moiety (Table 2).

Table 2 Synthesis of hetrocycle tethered vinylogous carbonates **2**.



Entry	Alkyne **4**	Aryl halide **3**	Yield (%)[a] Step I	Yield (%)[a] Step II	Product **2**
1			89	70	
2			92	66	
3			92	60	
4			90	61	
5			85	65	
6			80	56	
7			85	68	
8			87	61	
9			82	56	
10			90	94	
11			89	91	
12			92	91	

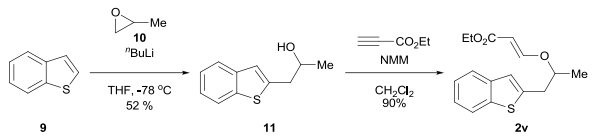


13	**4c**	**3d**	92	88	**2n**
14	**4d**	**3c**	90	74	**2o**
15	**4e**	**3c**	85	82	**2p**
16	**4f**	**3c**	80	85	**2q**
17	**4g**	**3c**	85	87	**2r**
18	**4c**	**3e**	92	56	**2s**
19	**4h**	**3c**	87	67	**2t**
20	**4i**	**3c**	82	60	**2u**
21	**4c**	**3f**	92	82	**6**
22	**4c**	**3g**	92	81	**7**
23	**4c**	**3h**	92	53	**8**

[a]Isolated yield.

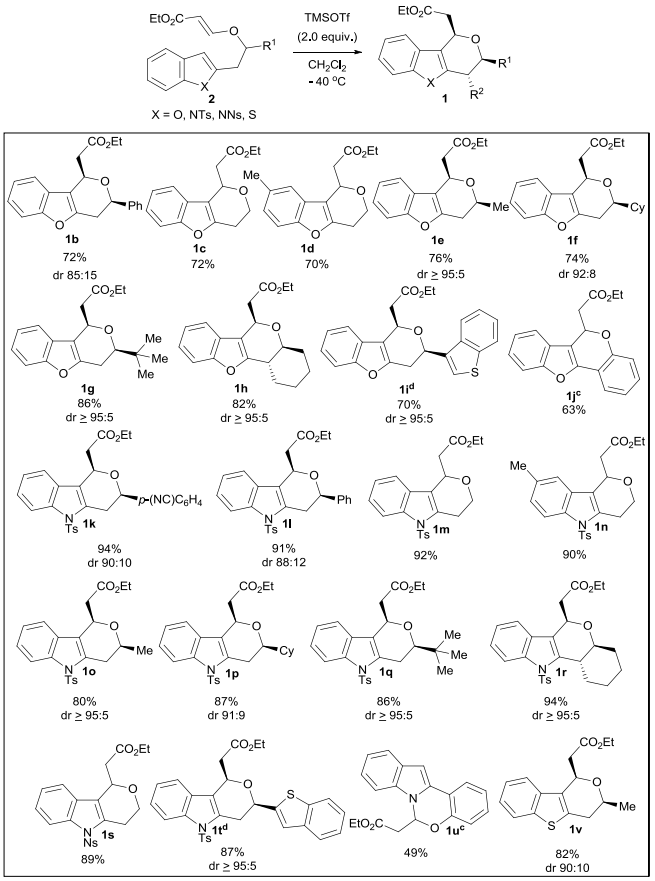
In general, reactions proceeded smoothly furnishing benzofuran and indole tethered vinylogous carbonates **2b-u** *via* the tandem Sonogashira coupling – nuclopalladation sequence (Table 2, entry 1-20). However, when carbamate protected *o*-iodoaniline (**3f**) (Table 2, entry 21) and *o*-iodoaniline (**3g**) (Table 2, entry 22) were used, only Sonogashira coupling products **6** and **7** were formed, respectively, in good yield and nucleopalladation reaction did not take place. Synthesis of thiophene-tethered vinylogous carbonate (Table 2, entry 23) proved to be unsuccessful using this route and only vinyl bis-sulfide **8** was obtained as the product.[11] To overcome this problem an alternative approach starting from benzothiophene (**9**) was explored (Scheme 3). Thus, opening of the propelene oxide (**10**) by anion generated from lithiation of benzothiophene (**9**) using *n*-BuLi furnished the alcohol **11**. Reaction of the alcohol **11** with ethyl propiolate in the presence of NMM gave the requisite vinylogous carbonate **2v** in good overall yield.

Scheme 3 Synthesis of benzothiophene-tethered vinylogous carbonate precursor **2v**.



Having the requisite vinylogous carbonates in hand, attention was turned towards studying the scope of the *oxa*-Pictet Spegler reaction. The results are summarized in Scheme 4.

Scheme 4 Synthesis of C-fused pyranoheterocycles.[a,b]

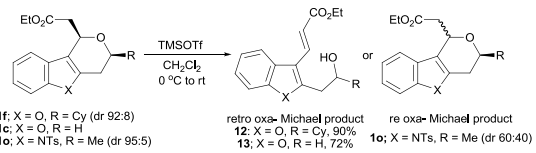


[a]Isolated yield. [b]In all the cases, dr was determined on the crude reaction mixtures by ^{1}H NMR. [c]Reaction performed at 0 °C. [d]4 equiv. of TMSOTf used at - 40 °C.

Vinylogous carbonates **2b-j** tethered to benzofurans as nucleophiles furnished the pyranobenzofurans **1b-j**, respectively, in good yields and excellent diastereoselectivty. When vinylogous carbonates **2k-u** bearing indole moiety were subjected to standard reaction conditions, the corresponding pyranoindoles **1k-u** were obtained in good yield and high diastereoselectivity. The reaction was found to work well with alkyl and aryl substitutions leading to the efficient formation of the pyranobenzofuran and pyranoindoles. In the cases where vinylogous carbonates were tethered on a ring (**2h** and **2r**), Lewis acid mediated intramolecular *oxa*-Pictet-Spengler reaction gave the corresponding pyranoheterocycles **1h** and **1r** in excellent yields as only detectable diastereomers. Pyranobenzothiophene **1v** could also be assembled in good yield and with excellent diastereoselectivity

suggesting that benzothiophene too participates in *oxa*-Pictet-Spengler reaction of vinylogous carbonates efficiently. Interestingly, when reaction was attempted with vinylogous carbonates **2i** and **2t** bearing benzothiophene moiety, *oxa*-Pictet-Spengler reaction lead to pyranobenzofuran **1i** and pyranoindole **1t**, respectively, in a highly chemoselective manner. In all these cases, the *cis*-isomer was found to be the major isomer whose structure was assigned based on NOE experiments. It was further unambiguously ascertained by single crystal X-ray diffraction analysis on the pyranoheterocycles **1a**, **1f** and **1k**.[12] In general, oxonium ion generation from phenol in intermolecular fashion is challenging. Vinylogous carbonates generated from phenol circumvent this problem, wherein oxonium ion is generated from preformed enol. Thus, vinylogous carbonate **2j** derived from phenol **5i** bearing benzofuran was subjected to treatment with TMSOTf, the tetrahydropyran ring formation was found to proceed efficiently furnishing the product **1j** in 66% yield. On the other hand, when *N*-tosyl indole was tethered as nucleophile, rather than the *oxa*-Pictet Spengler reaction, the aminal **1u** was obtained as the product *via* deprotection of *N*-tosyl group of indole moiety followed by Michael addition of nitrogen of indole to vinylogous carbonate moiety. All our efforts to optimize the reaction proved futile and only aminal **1u** was obtained as the only isolable product under the reaction conditions studied.

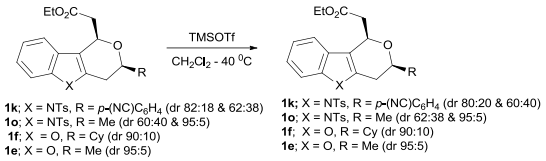
During this study, in one of the experiments, it was observed that when substrate vinylogous carbonates **2f** and **2c** were subjected to treatment with TMSOTf at 0 ºC and the reactions were slowly warmed up to room temperature, the alcohols **12** and **13** were obtained as the major products rather than the requisite pyranobenzofurans **1f** and **1c**. So we subjected the pyranobenzofurans **1f** and **1c** to treatment with TMSOTf (Scheme 5). The reactions indeed lead to the formation of the products **12** and **13**, respectively, which could be rationalized by retro-*oxa*-Michael reaction. On the other hand, when the pyranoindole **1o** (*cis:trans* = 95:5) was treated with TMSOTf, it lead to erosion of diastereoselectivity (*cis:trans* = 60:40). This suggested that the retro-*oxa*-Michael reaction in the case of **1o** might be reversible leading to erosion of diastereoselectivity.



Scheme 5 Retro-*oxa*-Michael reaction of pyranoheterocycles.

This observation prompted us to look at the mechanism of this reaction more closely in order to ascertain whether stereochemical outcome of the reaction is due to kinetic or thermodynamic control. To understand this, the pyranoindole **1k** and **1o** as well as pyranobenzofuran **1f** and **1e** with different starting diastereomeric ratios were re-subjected to reaction conditions in the presence of TMSOTf (Scheme 6). Interestingly, no change in the diastereomeric ratio was observed in all these cases. This experiment suggested that whereas retro-*oxa*-Michael reaction can happen at higher temperature, at least under the conditions employed to carry out the reaction (i.e. at lower temperature), this reaction is sufficiently slow and the stereochemical outcome is a result of kinetic control.

Scheme 6 Mechanistic investigation of *Oxa*-Pictet-Spengler reaction.



Formation of the *cis*-isomer as the major product can be rationalised based on the transition state model in which the substituent on the pyran ring occupies a *pseudo*equatorial orientation. During trapping of the oxonium ion by heteroaromatic ring, the incipient carbethoxymethylene group also prefers to occupy *pseudo*equatorial orientation (transition state structure **A** rather than the pseudoaxial orientation (transition state structure **B**) to avoid 1,3-diaxial interaction (Figure 2).

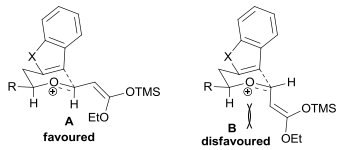
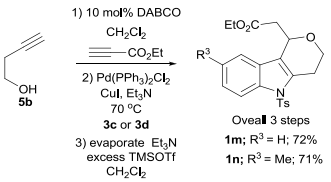


Figure 2 Plausible transition state structures to rationalise outcome of the *oxa*-Pictet-Spengler Cyclization

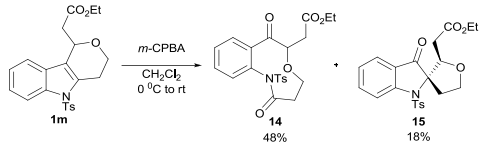
At this juncture, it was thought that doing the entire sequence starting from the homopropargyl alcohol **5** in a 'one pot' manner will be attractive as it will obviate the need of isolation of any intermediate. In order to check this, the alcohol **5b** was treated with ethyl propiolate in the presence of 10 mol% DABCO in CH2Cl2. After complete consumption of starting material, *N*-tosyl protected iodoaniline **3c** or **3d** were sequentially along with $Pd(PPh_3)_2Cl_2$, CuI and Et_3N and mixture was heated at 70 ºC for 5 hours. After evaporating Et_3N, excess of TMSOTf (3 equiv.) was added to the reaction mixture to furnish the *C*-fused pyranoindoles **1m** and **1n** in good yield (Scheme 7).

Scheme 7 One-pot/Sequential Synthesis of *C*-fused pyranoindoles



Finally, *C*-fused pyranoindoles were further functionalized using oxidative conditions. Thus, the pyranoindole **1m** on *m*-CPBA oxidation led to a mixture of ring enlarged 9-membered keto lactam **14** and spirooxindole **15** in good yield (Scheme 8).[13,14]

Scheme 8 Synthesis of keto lactam and spirooxindole using oxidative rearrangement.



Conclusions

In conclusion, we have developed a general strategy for the stereoselective synthesis of pyranoheterocycles. The products are formed in good yield and diastereoselectivity. The reaction sequence can be carried out in 'one pot' manner with comparable efficiency. The pyranoindoles were further functionalised under oxidative conditions to give access to 9-membered lactam and spirooxindole.

General experimental

Melting points are recorded using Sigma melting point apparatus in capillary tubes and are uncorrected. IR spectra were recorded on JASCO FT-IR 8300 and Nicolet 6700 spectrophotometer. ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra were recorded on Bruker Avance 400 spectrometer. ^{1}H (500 MHz) and ^{13}C (125 MHz) NMR spectra were recorded on Bruker Avance 500 spectrometer. The chemical shifts (δ ppm) and coupling constants (Hz) are reported in the standard fashion with reference to either internal tetramethylsilane or residual $CHCl_3$ (7.26 ppm for ^{1}H) or the central line (77.16 ppm) of $CDCl_3$ (for ^{13}C). In the ^{13}C NMR spectra, the nature of the carbons (C, CH, CH_2 or CH_3) was determined by recording the DEPT 135 experiment and is given in parentheses. High resolution mass measurements were carried out using Micromass Q-ToF (Waters) or maXis impact (Bruker) instrument using direct inlet mode. X-ray diffraction studies were carried out using Bruker Single Crystal Kappa Apex II. Analytical thin-layer chromatographies (TLC) were performed on glass plates (7.5 × 2.5 and 9 × 5.0 cm) coated with Merck or Acme's silica gel G containing 13% calcium sulfate as binder or on pre-coated 0.2 mm thick Merck 60 F245 silica plates and various combinations of ethyl acetate and hexanes were used as eluent. Visualization of spots was accomplished by either exposure to iodine vapour or $KMnO_4$ stain. All small-scale dry reactions were carried out using standard syringe septum technique. Dry dichloromethane and dry DMF were prepared by distilling over calcium hydride. Triethylamine was obtained by distillation over KOH and stored over KOH. $BF_3{\cdot}OEt_2$ was obtained from Aldrich. All the commercial reagents were used as such without further purification. The homopropargylic alcohols **5** were synthesized following literature protocol.[10]

General procedure for the preparation of vinylogous carbonates 4 from the alcohols 5

To a stirred solution of homopropargylic alcohol **5** (1 equiv.) in dry CH_2Cl_2, was added N-methylmorpholine (1 equiv.) and ethyl propiolate (1.1 equiv.) at r.t. and stirred for *ca.* 5 h (TLC). The reaction mixture was then concentrated under reduced pressure and residue was purified by silica gel column chromatography using EtOAc/petroleum ether as the eluent to yield the vinylogous carbonate **4**.

General procedure for the synthesis of heterocycles tethered to vinylogous carbonate 2.

A solution of $[PdCl_2(PPh_3)_2]$ (5 mol%), CuI (10 mol%), alkyne **4** (1.2 equiv.), *o*-iodo phenol (**3a-b**) or *N*- protected aniline (**3c-e**) (1.0 equiv.) and Et_3N (6 equiv.) in DMF was stirred at 70 °C for 5 h under N_2 or in a sealed reaction tube. Reaction was monitored by TLC. After completion of the reaction, saturated NH_4Cl solution was added and the mixture was extracted with ether. The combined organic layers were dried (anhyd. Na_2SO_4) and the solvent was evaporated. The residue was purified by silica gel column chromatography using EtOAc/petroleum ether as eluent to furnish requisite heteoannulated product **2**.

Typical procedure for the 'One pot' synthesis of *C*-fused pyranoindole 1.

A reaction tube with a magnetic stirring bar was charged with ethyl propiolate (1.0 mmol), 3-butyn-ol (1.0 mmol), DABCO (0.10 mmol) and CH_2Cl_2 (2.0 mL). The reaction mixture was stirred for 4 h at r.t. and then the solvent was evaporated under reduced pressure. *N*-protected amine (0.8 mmol), $[PdCl_2(PPh_3)_2]$ (5 mol%), CuI (10 mol%) and Et_3N (3 mL) were added and the reaction vessel was placed in an oil bath at 70 °C. The reaction mixture was stirred for *ca.* 5 h and then it was cooled to rt. Et_3N was evaporated under reduced pressure and dry CH_2Cl_2 (3.0 mL) was added to the reaction tube, which was followed by drop-wise addition of TMSOTf (3 equiv.) at rt. The reaction mixture was stirred at rt for *ca.* 4 h (TLC). The reaction mixture was then quenched with saturated aq. $NaHCO_3$ (10 mL), extracted with CH_2Cl_2 (2 × 10 mL) and combined organic layer was washed with brine and dried (anhyd. Na_2SO_4). Evaporation of the solvent and purification of the residue on a silica gel column using EtOAc/petroleum ether (1:4) as eluent furnished pyranoindoles **1m-n** in good yield.

(Note: In the cases where diastereomeric mixtures of products were obtained, the data for the major isomer is mentioned.)

Ethyl 2-((1*R,3*R**)-3-(4-cyanophenyl)-3,4-dihydro-1*H*-pyrano[4,3-*b*]benzofuran-1-yl)acetate (1a)**.

To a cold (- 40 °C) magnetically stirred solution of the vinylogous carbonate **2a** (56 mg, 0.16 mmol) in dry CH_2Cl_2 (3.0 mL) was added drop wise TMSOTf (56 µL, 0.31 mmol) and the reaction mixture stirred at the same temperature for *ca*. 12 h (TLC control). The reaction mixture was then quenched with saturated aq. $NaHCO_3$ (10 mL), extracted with CH_2Cl_2 (3 × 15 mL) and combined organic layer was washed with brine and dried (anhyd. Na_2SO_4). Evaporation of the solvent and purification of the residue on a silica gel column using EtOAc/petroleum ether (1:4) as eluent furnished pyranobenzofuran **1a** (46 mg, 82%) as a pale yellow solid. m.p.: 158-160 °C; Physical appearance: pale yellow solid; R_f: 0.5 (1:4, EtOAc/petroleum ether); IR (neat): 3060, 2980, 2926, 2862, 2228, 1734, 1636, 1620, 1451, 1392, 1293, 1178, 1092, 1045, 836, 750 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (d, *J* = 8.5 Hz, 1H), 7.57 (d, *J* = 8.0 Hz, 2H), 7.49 (d, *J* = 8.5 Hz, 2H), 7.42 (d, *J* = 8.0 Hz, 2H), 7.31-7.23 (m, 2H), 5.51 (dd, *J* = 10.5, 9.6 Hz, 1H), 4.93 (dd, *J* = 10.8, 3.4 Hz, 1H), 4.25-4.21 (m, 2H), 3.20 (dd, *J* = 15.2, 2.8 Hz, 1H), 3.11 (dt, *J* = 15.2, 2.4 Hz, 1H), 2.99-2.91 (m, 1H), 2.78 (ABX, *J* = 15.2, 9.6 Hz, 1H), 1.27 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 170.9 (C), 154.8 (C), 151.2 (C), 146.5 (C), 132.5 (2 × CH), 126.4 (2 × CH), 125.1 (C), 124.1 (C), 123.1 (CH), 119.0 (CH), 118.9 (C), 114.0 (CH), 111.7 (CH), 75.0 (CH), 71.4 (CH), 61.0 (CH_2), 40.4 (CH), 32.2 (CH_2), 14.4 (CH_3); LRMS (ESI, M+Na$^+$): m/z 384; HRMS (ESI, M+Na$^+$) m/z calcd. for $C_{22}H_{19}NO_4Na$ 384.1212, found 384.1217.

Ethyl 2-((1*R,3*R**)-3-phenyl-3,4-dihydro-1*H*-benzofuro[3,2-*c*]pyran-1-yl)acetate (1b).**

Reaction of the vinylogous carbonate **2b** (50 mg, 0.15 mmol) with TMSOTf (52 µL, 0.30 mmol) in dry CH_2Cl_2, (4.0 mL) at - 40 °C, as described for the pyranobenzofuran **1a** followed by purification on a silica gel column using EtOAc/petroleum ether (1:19) as eluent furnished pyranobenzofuran (34 mg, 72 %) as a viscous liquid. Physical appearance: viscous yellow liquid; R_f: 0.5 (1:19, EtOAc/petroleum ether); IR (neat): 3033, 2981, 2934, 2907, 2857, 2853, 1735, 1451, 1293, 1270, 1176, 1046, 747 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.46-7.43 (m, 3H), 7.36-7.34 (m, 3H), 7.30-7.20 (m, 3H), 5.48 (dd, *J* = 9.2, 2.8 Hz 1H), 4.85 (dd, *J* = 9.2, 4.2 Hz, 1H), 4.24-4.15 (m, 2H), 3.16 (ABX, *J* = 15.8, 3.2 Hz, 1H), 3.01-3.0 (m, 2H), 2.77 (ABX, *J* = 15.2, 9.2 Hz, 1H), 1.24 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, CDCl3, DEPT): δ 171.1 (C), 154.8 (C), 152.1 (C), 141.3 (C), 128.6 (2 × CH), 127.9 (CH), 125.8 (C), 125.4 (2 × CH), 123.8 (CH), 122.9 (CH), 119.0 (CH), 114.0 (C), 111.6 (2 × CH), 75.8 (CH), 71.2 (CH), 60.9 (CH_2), 40.5 (CH_2), 32.3 (CH_2), 14.4 (CH_3); LRMS (ESI, M+Na^+): m/z 359. HRMS (ESI, M+Na^+) m/z calcd. for $C_{21}H_{20}O_4Na$ 359.1259, found 359.1267.

(1*RS*)-Ethyl 2-(3,4-dihydro-1*H*-benzofuro[3,2-*c*]pyran-1-yl)acetate (1c).

Reaction of the vinylogous carbonate **2c** (52 mg, 0.19 mmol)) with TMSOTf (70 µL, 0.39 mmol) in dry CH_2Cl_2, (4.0 mL) at - 40 °C, as described for the pyranobenzofuran 1a followed by purification on a silica gel column using ethyl acetate-hexane (1:19) as eluent furnished benzofuran (36 mg, 70%) as a viscous liquid. Physical appearance: viscous liquid; R_f: 0.6 (1:19, EtOAc/petroleum ether); IR (neat): 3017, 2964, 2934, 1730, 1644, 1260, 1371, 1087, 797, 757 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.39 (d, *J* = 7.6 Hz, 1H), 7.30 (br d, *J* = 6.8 Hz, 1H), 7.20-7.19 (m, 2H), 5.28 (dd, *J* = 10.0 2.8 Hz, 1H), 4.18 (ABX, *J* = 14.8, 9.2 Hz, 1H), 4.17 (q, *J* = 7.2 Hz, 2H), 3.85 (dq, *J* = 8.4, 4.0 Hz, 1H), 2.98 (ABX, *J* = 15.6, 2.8 Hz, 1H), 2.95-2.85 (m, 1H), 2.75-2.60 (m, 1H), 2.64 (ABX, *J* = 15.6, 10.0 Hz, 1H), 1.22 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT): *δ* 171.9 (C), 154.3 (C), 151.7 (C) ,125.3 (C), 123.6 (2 × CH), 122.7 (2 × CH), 118.7 (CH), 113.6 (C), 111.3 (CH), 70.1 (CH), 62.7 (CH_2), 60.8 (CH_2), 39.9 (CH_2), 24.7 (CH_2), 14.2 (CH_3); LRMS (ESI, M+H^+): m/z 261; HRMS (ESI, M+H^+): m/z calcd. for $C_{15}H_{17}O_4$ 261.1127, found 261.1116.

(1*RS*)-Ethyl 2-(8-methyl-3,4-dihydro-1H-benzofuro[3,2-*c*]pyran-1-yl)acetate (1d).

Reaction of the vinylogous carbonate 2d (65 mg, 0.18 mmol) with TMSOTf (36 µL, 0.27 mmol) in dry CH_2Cl_2, (4.0 mL) at - 40 °C, as described for the pyranobenzofuran **1a** followed by purification on a silica gel column using EtOAc/petroleum ether (1:19) as eluent furnished pyranobenzofuran **1d** (33 mg, 70 %) as a viscous liquid; Physical appearance: viscous liquid; R_f: 0.5 (1:19, EtOAc/petroleum ether); IR (neat): 2926, 2856, 1731, 1621, 1488, 1466, 1376, 1248, 1168, 819, 757 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.33 (d, *J* = 8.8 Hz, 1H), 7.15 (s, 1H), 7.05 (d, *J* = 8.8 Hz, 1H), 5.35 (dd, *J* = 4.2, 2.4 Hz, 1H), 4.23 (q, *J* = 7.2 Hz, 2H), 3.90 (ABX, *J* = 8.4, 4.0 Hz, 1H), 3.05 (ABX, *J* = 15.2, 3.2 Hz, 1H), 2.98-2.94 (m, 1H), 2.77-2.75 (m, 1H), 2.70 (ABX, *J* = 15.4, 9.5 Hz, 1H), 2.42 (s, 3H), 1.30 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$, DEPT): δ 171.2 (C), 152.8 (C), 151.9 (C), 132.3 (C), 125.6 (C), 124.8 (CH), 118.8 (CH), 113.5 (C), 112.0 (CH), 70.3 (CH), 62.8 (CH_2), 61.0 (CH_2), 40.0 (CH_2), 24.9 (CH_2), 14.4 (CH_3); LRMS (ESI, M+Na^+): m/z 297; HRMS (ESI, M+Na^+): m/z calcd. for $C_{16}H_{18}O_4Na$ 297.1103, found 297.1111.

Ethyl 2-((1*R,3*S**,)-3-methyl-3,4-dihydro-1*H*-benzofuro[3,2-*c*]pyran-1-yl)acetate (1e)**

Reaction of the vinylogous carbonate **2e** (100 mg, 0.36 mmol) with (134 µL, 0.73 mmol) in dry CH_2Cl_2, (4.0 mL) at - 40 °C as described for the pyranobenzofuran **1a** followed by purification on a silica gel column using EtOAc/petroleum ether (1:19) as eluent furnished the pyranobenzofuran **1e** (76 mg, 76%) as a oily pale liquid. Physical appearance: oily pale liquid; R_f: 0.5 (1:19, EtOAc/petroleum ether); IR (neat): 2978, 2965, 1737, 1637, 1452, 1294, 1177, 1044, 835, 746 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.60 (d, *J* = 8.0 Hz, 1H), 7.39 (d, *J* = 8.0 Hz, 2H), 7.28-7.20 (m, 2H), 5.34 (dd, *J* = 9.0, 3.0 Hz, 1H), 4.26 (q, *J* = 7.0 Hz, 2H), 3.98-3.92 (m,1H), 3.14 (ABX, *J* = 15.0, 3.0 Hz, 1H), 2.75-2.72 (m,1H), 2.69 (ABX, *J* = 15.0, 10.0 Hz, 1H), 1.44 (d, *J* = 6.0 Hz, 3H), 1.31 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$, DEPT): δ 171.2 (C), 154.6 (C), 152.4 (C), 125.4 (CH), 123.5 (CH), 122.7 (CH), 118.9 (CH), 113.8 (C), 111.5 (CH), 70.8 (CH), 70.6 (CH), 60.8 (CH_2), 40.3 (CH_2), 32.1 (CH_2), 21.6 (CH_3), 14.3 (CH_3); LRMS (ESI, M+Na^+): m/z 297; HRMS (ESI, M+Na^+): m/z calcd. for $C_{16}H_{18}NaO_4$ 297.1097, found 297.1092.

Ethyl 2-((1*R,3*R**)-3-cyclohexyl-3,4-dihydro-1*H*-benzofuro[3,2-*c*]pyran-1-yl)acetate (1f).**

Reaction of the vinylogous carbonate **2f** (55 mg, 0.16 mmol) with TMSOTf (56 µL, 0.40 mmol) in dry CH_2Cl_2, (4.0 mL), as described for the pyranobenzofuran **1a** followed by purification on a silica gel column using EtOAc/petroleum ether (1:9) as eluent furnished the pyranobenzofuran **1f** (40 mg, 74 %) as a viscous liquid. Physical appearance: viscous liquid; R_f: 0.6 (1:9, EtOAc/petroleum ether); IR (neat): 2927, 2853, 1738, 1738, 1639, 1598, 1463, 1452, 1371, 1294, 1245, 1226, 1175, 1092, 1020 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.44 (d, *J* = 8.0 Hz, 1H), 7.36 (d, *J* = 7.0 Hz, 1H), 7.24-7.18 (m, 2H), 5.23 (dq, *J* = 10.5, 3 Hz, 1H), 4.27-4.20 (m, 2H), 3.47 (dd, *J* = 14.0, 7.0 Hz, 2H), 3.19 (dt, *J* = 17.5 Hz, 1H), 2.73 (dd, *J* = 7, 2.5 Hz, 2H), 2.62 (ABX, *J* = 15.0, 10 Hz, 1H), 2.06 (brd, *J* = 13.0 Hz, 1H), 1.76-1.54 (m, 6H), 1.30 (t, *J* = 7.0 Hz, 3H), 1.25-1.02 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$, DEPT): δ 171.3 (C), 154.7 (C), 153.1 (C), 125.5 (C), 123.5 (CH), 122.7 (CH), 118.9 (CH), 114.1 (C), 114.5 (CH), 79.1 (CH), 70.9 (CH), 60.8 (CH_2), 42.7 (CH), 40.4 (CH) 29.3 (CH_2), 28.6 (CH_2), 28.2 (CH_2), 26.7 (CH_2), 26.2 (CH_2), 26.0 (CH_2), 14.4 (CH_3); LRMS (ESI, M+H^+): m/z 343; HRMS (ESI, M+H^+): m/z calcd. for $C_{21}H_{27}O_4$ 343.1909, found 343.1906.

Ethyl 2-((1*R,3*R**)-3-tert-butyl-3,4-dihydro-1*H*-benzofuro[3,2-*c*]pyran-1-yl)acetate (1g).**

Reaction of the vinylogous carbonate **2g** (63 mg, 0.17 mmol) with (61µL, 0.34 mmol) in dry CH_2Cl_2, (3.0 mL) at - 40 °C as described for the pyranobenzofuran **1a** followed by purification on a silica gel column using EtOAc/petroleum ether (1:19) as eluent furnished the tetrahydro benzofuran **1g** (38 mg, 70%) as a oily liquid; Physical appearance: oily liquid, R_f: 0.6 (1:19, EtOAc/petroleum ether); IR (neat): 2957, 2870, 1738, 1637, 1452, 1397, 1177, 1095, 1054, 745 cm^{-1}; **^1H** NMR (500 MHz, $CDCl_3$): δ 7.47 (d, *J* = 8.0 Hz, 1H), 7.38 (d, *J* = 8.0 Hz, 2H), 7.28-7.21 (m, 2H), 5.25 (dd, *J* = 10.0, 3.0 Hz, 1H), 4.40-4.20 (m, 2H), 3.44 (dd, *J* = 10.0, 3.0 Hz, 1H), 3.14 (dd, *J* = 15.0, 3.0 Hz, 1H), 2.81 (ddd, *J* = 16.0, 11.0, 3.0 Hz, 1H), 2.67 (dt, *J* = 16.0, 3.0 Hz, 1H), 2.64 (ABX, *J* = 15.0, 10.0 Hz, 1H), 1.31 (t, *J* = 7.0 Hz, 3H). 1.01 (s, 9H). **^{13}C** NMR (125 MHz, $CDCl_3$, DEPT): δ 171.3 (C), 154.7 (C), 153.3 (C), 125.4 (C), 123.4 (CH), 122.7 (CH), 118.9 (CH), 114.0 (C), 111.4 (CH), 81.9 (CH), 71.0 (CH), 60.7 (CH_2), 40.4 (CH_2), 34.2 (C), 25.7 (CH_2), 25.3 (3 × CH_3), 14.4 (CH_3); LRMS

(ESI, M+Na$^+$): m/z 339; HRMS (ESI, M+Na$^+$): m/z calcd. for $C_{19}H_{24}NaO_4$ 339.1567, found 339.1572.

Ethyl 2-((4a*S,6*R**,11b*S**)-2,3,4,4a,6,11b-hexahydro-1*H*-benzofuro[3,2-*c*]chromen-6-yl)acetate (1h)**.

Reaction of the vinylogous carbonate **2h** (50mg, 0.16 mmol) with TMSOTf (57 µL, 0.32 mmol) in dry CH_2Cl_2, (4.0 mL) at - 40 °C, as described for the pyranobenzofuran **1a** followed by purification on a silica gel column using EtOAc/petroleum ether (1:19) as eluent furnished pyranobenzofuran **1h** (41 mg, 82%) as a viscous liquid. Physical appearance: viscous liquid; R_f: 0.5 (1:19, EtOAc/petroleum ether); IR (neat): 2979, 2933, 2859, 1629, 1476, 1452, 1350, 1297, 1092, 873, 747 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.45 (d, *J* = 8.0 Hz, 1H), 7.36 (d, *J* = 8.0 Hz, 1H), 7.25-7.15 (m, 2H), 5.39 (dt, *J* = 9.0, 3.5 Hz, 1H), 4.22 (q, *J* = 7.0 Hz, 2H), 3.37 (ABXY, *J* = 9.5, 4.4, 1.5 Hz, 1H), 3.09 (ABX, *J* = 15.3, 3.0 Hz, 1H), 2.75-2.70 (m, 1H), 2.68 (ABX, *J* = 15.5, 9.5 Hz, 1H), 2.41 (dt, *J* = 11, 3 Hz, 1H), 2.06 (ABX, *J* = 12.0, 2.5 Hz, 1H), 1.90-1.81 (m, 2H), 1.60-1.55 (m, 1H), 1.41-1.26 (m, 4H), 1.27 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$, DEPT): δ 171.2 (C), 155.2 (C), 154.7 (C), 125.7 (C), 123.4 (CH), 122.7 (CH), 118.9 (CH), 113.1 (C), 111.6 (CH), 79.7 (CH), 70.9 (CH), 60.8 (CH_2), 41.3 (CH), 40.4 (CH_2), 31.6 (CH_2), 26.6 (CH_2), 25.3 (CH_2), 25.0 (CH_2), 14.3 (CH_3); LRMS (ESI, M+H$^+$): m/z 315; HRMS (ESI, M+H$^+$): m/z calcd. for $C_{19}H_{23}O_4$ 315.1596, found 315.1607.

Ethyl 2-((1*R,3*R**)-3-(benzo[b]thiophen-2-yl)-3,4-dihydro-1*H*-benzofuro[3,2-*c*]pyran-1-yl)acetate (1i)**.

Reaction of the vinylogous carbonate **2i** (64 mg, 0.16 mmol) with (236 µL, 0.64 mmol) in dry CH_2Cl_2, (3.0 mL) at - 40 °C as described for the pyranobenzofuran **1a** followed by purification on a silica gel column using EtOAc/petroleum ether (20:80) as eluent furnished the pyranobenzofuran**1i** (48 mg, 75%) as a oily liquid; Physical appearance: oily liquid. R_f: 0.3 (1:4, EtOAc/petroleum ether); IR (neat): 3052, 2924, 2857, 1732, 1451, 1293, 1177, 1045 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.84 (d, *J* = 8.0 Hz, 1H), 7.76 (d, *J* = 8.0 Hz, 2H), 7.50 (d, *J* = 8.0 Hz, 2H), 7.76 (d, *J* = 8.0 Hz, 2H), 7.42 (d, *J* = 8.0 Hz, 2H), 7.35-7.25 (m, 5H), 5.57 (dd, *J* = 10.0, 3.0 Hz, 1H), 5.18 (dd, *J* = 10.0, 4.0 Hz, 1H), 4.28-4.25 (m, 2H), 3.27 (dd, *J* = 10.0, 2.0 Hz, 1H), 3.24 (dd, *J* = 4.0, 2.0 Hz, 1H), 3.19 (dd, *J* = 15.0, 3.0 Hz, 1H), 2.80 (dd, *J* = 16.0, 10.0 Hz, 1H), 1.32 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$, DEPT): δ 170.9 (C), 151.2 (C), 145.1 (C), 139.7 (C), 139.5 (2 × CH), 125.2 (CH), 124.4 (CH), 123.9 (CH), 123.3 (CH), 123.1 (CH), 122.5 (CH), 120.3 (CH), 119.1 (CH), 114.0 (C), 114.6 (C), 111.7 (CH), 72.8 (CH), 71.6 (CH), 61.0 (CH_2), 40.3 (CH_2), 25.7 (CH_2), 14.4 (CH_3); LRMS (ESI, M+Na$^+$): m/z 415; HRMS (ESI, M+Na$^+$): m/z calcd. for $C_{23}H_{20}NaO_4S$ 415.0975, found 415.0902.

(6*RS*)-Ethyl 2-(6*H*-benzofuro[3,2-*c*]chromen-6-yl)acetate (1j).

Reaction of the vinylogous carbonate **2j** (50 mg, 0.16 mmol) with TMSOTf (57 µL, 0.32 mmol) in dry CH_2Cl_2, (5.0 mL) at 0 ^{0}C and the reaction mixture stirred at the same temperature for *ca* 16 h (TLC control). The work up as described for the pyranobenzofuran **1a** followed by purification on a silica gel column using EtOAc/petroleum ether (1:19) as eluent furnished benzofuran fused pyran **1j** (31 mg, 63%) as a viscous liquid; Pysical appearance: viscous liquid; R_f: 0.5 (1:19, EtOAc/petroleum ether) IR (neat): 2923, 2855, 1738, 1609, 1462, 1275, 1158, 725 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.57 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.53 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.45 (d, *J* = 8.0 Hz, 1H), 7.30-7.20 (m, 3H), 7.01 (td, *J* = 7.0 Hz, 1H), 6.93 (d, *J* = 8.0 Hz, 1H), 6.27 (d, *J* = 8.5, 5.0 Hz, 1H), 4.20-4.15 (m, 2H), 3.62 (ABX, *J* = 15.5, 8.0 Hz, 1H), 2.93 (ABX, *J* = 15.5, 5 Hz, 1H), 1.24 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$, DEPT): δ 170.1 (C), 155.9 (C), 152.8 (C), 130.3 (CH), 130.2 (C), 125.4 (C), 124.7 (CH), 123.6 (CH), 121.8 (CH), 120.9 (CH), 119.1 (CH), 117.0 (CH), 115.7 (C), 111.8 (CH), 110.6 (C), 73.0 (CH), 61.1 (CH_2), 41.5 (CH_2), 14.3 (CH_3); LRMS (ESI, M+H+): m/z 309; HRMS (ESI, M+H$^+$): m/z calcd. for $C_{19}H_{17}O_4$ 309.1127, found 309.1138.

Ethyl 2-((1*R,3*R**)-3-(4-cyanophenyl)-5-tosyl-1,3,4,5-tetrahydropyrano[4,3-*b*]indol-1-yl)acetate (1k)**.

Reaction of the vinylogous carbonate **2k** (90 mg, 0.18 mmol) with TMSOTf (63 µL, 0.35 mmol) in dry CH_2Cl_2, (4.0 mL) at - 40 °C, as described for the pyranobenzofuran **1a** followed by purification on a silica gel column using EtOAc/petroleum ether (1:4) as eluent furnished the pyranoindole **1k** (85 mg, 94%) as a white solid. Physical appearance: white solid; R_f: 0.5 (1:4, EtOAc/petroleum ether); m.p.: 148-150 ^{o}C (recrystallization CH_3CN); IR (neat): 2979, 2955, 2923, 1735, 1610, 1597, 1451, 1396, 1371, 1187, 1173, 1152, 1091, 1081, 702, 693 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.18 (d, *J* = 8.5 Hz, 1H), 7.69 (d, *J* = 8.5 Hz, 2H), 7.65 (d, *J* = 8.5 Hz, 2H), 7.58 (d, *J* = 8.5 Hz, 2H), 7.37-7.26 (m, 3H), 7.21 (d, *J* = 8.5 Hz, 2H), 5.48 (dq, *J* = 9.5, 2.5 Hz, 1H), 4.20-4.14 (m, 2H), 4.78 (dd, *J* = 10, 3 Hz, 1H), 3.60 (dt, *J* = 17.0, 2.5 Hz, 1H), 3.19 (dd, *J* = 15, 2.5 Hz, 1H), 2.98 (AB dd, *J* = 17.0, 3.0 Hz, 1H), 2.64 (ABX, *J* = 15.0, 9.5 Hz, 1H), 2.35 (s, 3H), 1.23 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$, DEPT): δ 170.8 (C), 146.5 (C), 145.3 (C), 136.5 (C), 135.7 (C), 132.9 (C), 132.4 (2 × CH), 132.4 (C), 130.1 (3 × CH), 126.5 (2 × CH), 124.8 (CH), 123.9 (CH), 118.9 (CH), 118.9 (C), 118.6 (C), 114.9 (CH), 111.7 (C), 74.7 (CH), 71.4 (CH), 60.9 (CH_2), 40.7 (CH_2), 33.1 (CH_2), 21.7 (CH_3), 14.4 (CH_3); LRMS (ESI, M+Na$^+$): m/z 537; HRMS (ESI, M+Na$^+$): m/z calcd. for $C_{29}H_{26}N_2O_5NaS$ 537.1460, found 537.1468.

Ethyl 2-((1*R,3*R**)-3-phenyl-5-tosyl-1,3,4,5-tetrahydropyrano[4,3-*b*]indol-1-yl)acetate (1l)**.

Reaction of the vinylogous carbonate **2l** (83 mg, 0.17 mmol) with TMSOTf (61 µL, 0.34 mmol) in dry CH_2Cl_2, (4.0 mL) at - 40 °C as described for the pyranobenzofuran **1a** followed by purification on a silica gel column using EtOAc/petroleum ether (1:4) as eluent furnished the pyranoindole **1l** (76 mg, 91%) as a viscous liquid. Physical appearance: viscous liquid; R_f: 0.5 (1:19, EtOAc/petroleum ether); IR (neat): 2978, 2955, 2924, 2853, 1736, 1598, 1451, 1371, 1186, 1151, 1091, 1451, 1372, 1290, 1245, 1226, 1174, 1152, 1092, 1020, 984 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): d 7.60 (d, *J* = 7.6 Hz,1H), 7.41 (d, *J* = 7.6 Hz, 2H), 7.35-7.30 (m, 2H), 7.26 (t, *J* = 7.6 Hz, 3H), 7.20 (d, *J* = 7.6 Hz, 1H), 7.14 (d, *J* = 8.0 Hz, 1H), 5.42 (d, *J* = 9.2 Hz 1H), 4.67 (d, *J* = 8.8 Hz, 1H), 4.15-4.10 (m, 2H), 3.51 (d, *J* =17.2 Hz, 1H), 3.12 (ABX, *J* = 14.4, 2.0 Hz, 1H), 3.01 (ABX, *J* = 17.2, 10.8 Hz, 1H), 2.28 (s, 3H), 1.16 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT): d 170.9 (C), 145.1 (C),141.3 (C), 136.5 (C), 135.8 (C), 133.8 (C), 130.1 (C), 130.1 (2 × CH), 128.6 (C), 128.5 (2 × CH), 127.8 (CH), 126.5 (2 × CH), 125.6 (2 × CH), 124.5 (CH), 123.7 (CH), 118.8 (CH), 114.8 (CH), 75.5 (CH), 71.3 (CH), 60.8 (CH_2), 40.8 (CH_2), 33.2 (CH_2), 21.7 (CH_3), 14.3 (CH_3). LRMS (ESI, M+H$^+$): m/z 490; HRMS (ESI, M+H$^+$) m/z calcd. for $C_{28}H_{28}NO_5S$ 490.1688, found 490.1689.

(1*RS*)-Ethyl 2-(5-tosyl-1,3,4,5-tetrahydropyrano[4,3-*b*]indol-1-yl)acetate (1m).

To a cold (- 40 °C) solution of the vinylogous carbonate **2m** (100 mg, 0.24 mmol) in dry CH_2Cl_2 (3.0 mL) was added TMSOTf (83 µL, 0.48 mmol) and the resulting mixture was slowly warmed up to rt. The work up as described for the pyranobenzofuran **1a** followed by purification on a silica

gel column using EtOAc/petroleum ether (1:9) as eluent furnished the pyranoindole **1m** (49 mg, 92%) as a yellow solid; Physical appearance: yellow solid; R_f: 0.5 (1:9, EtOAc/petroleum ether); m.p.: 109-111 °C; IR (neat): 2970, 2934, 2870, 1736, 1599, 1173, 1152, 975, 815, 747, 705, 676 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.17 (d, *J* = 8.0 Hz, 1H), 7.64 (d, *J* = 8.4 Hz, 2H), 7.30-7.27 (m, 2H), 7.24-7.21 (m, 1H), 7.20 (d, *J* = 8.4 Hz, 2Hf), 5.33 (dd, *J* = 10.0, 2.5 Hz, 1H), 4.20 (q, *J* = 7.2 Hz, 2H), 4.15-4.10 (m, 1H), 3.85-3.80 (m, 1H), 3.15-3.0 (m, 1H), 2.99 (ABX, *J* = 15.6, 2.5 Hz, 1H), 2.63 (ABX, *J* = 15.6, 10.0 Hz, 1H), 2.34 (s, 3H), 1.27 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 171.0 (C), 145.1 (C), 136.2 (C), 135.9 (C), 133.5 (C), 130.1 (2 × CH), 127.0 (C), 126.6 (2 × CH), 124.5 (CH), 123.7 (CH), 118.6 (CH), 118.4 (C), 114.7 (CH), 70.0 (CH), 62.0 (CH_2), 60.9 (CH_2), 39.9 (CH_2), 25.83 (CH_2), 21.7 (CH_3), 14.3 (CH_3); LRMS (ESI, $M+H^+$): m/z 414; HRMS (ESI, $M+H^+$): m/z calcd. for $C_{22}H_{24}NO_5S$ 414.1375, found 414.1383.

(1*RS*)-Ethyl 2-(8-methyl-5-tosyl-1,3,4,5-tetrahydropyrano[4,3-*b*]indol-1-yl)acetate (1n).

To a cold (- 40 °C) solution of the vinylogous carbonate **1n** (72 mg, 0.17 mmol) in dry CH_2Cl_2 (3.0 mL) was added TMSOTf (59 µL, 0.34 mmol) and the resulting mixture was slowly warmed up to rt. The work up as described for the pyranobenzofuran **1a** followed by purification on a silica gel column using EtOAc/petroleum ether (1:9) as eluent furnished the pyranoindole **1n** (62 mg, 90%) as a yellow solid; Physical appearance: yellow solid; R_f: 0.5 (1:9, EtOAc/petroleum ether); m.p.: 148-150 °C; IR (neat): 2924, 2860, 1736, 1599, 1463, 1371, 1309, 1280, 1169, 1092, 977, 917, 810, 733, 703, 670, 473 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 8.03 (d, *J* = 8.5 Hz, 1H), 7.64 (d, *J* = 8.5 Hz, 2H), 7.19 (d, *J* = 8.5 Hz, 1H), 7.19 (d, *J* = 8.5 Hz), 7.11 (d, *J* = 8.5 Hz, 1H), 7.08 (brs, IH), 5.3- 5.28 (m, 2H), 4.21 (q, *J* = 7.0 Hz, 2H), 4.12 (dt, *J* = 11.5, 5.5 Hz, 1H), 3.82 (dt, *J* = 11.5, 4.5 Hz, 1H), 3.15-3.00 (m, 2H), 2.99 (ABX, *J* = 15.5, 3.0 Hz, 1H), 2.62 (ABX, *J* = 15.5, 10.0 Hz, 1H), 2.40 (s, 3H), 2.34 (s, 3H), 1.27 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$, DEPT): δ 171.1 (C), 144.9 (C), 135.8 (C), 134.3 (C), 133.4 (C), 133.3 (C), 130.0 (2 × CH), 127.2 (C), 126.5 (2 × CH), 125.7 (CH), 118.6 (CH), 118.2 (C), 114.4 (CH), 70.0 (CH), 62.0 (CH_2), 60.9 (CH_2), 39.9 (CH_2), 25.8 (CH_2), 21.6 (CH_3), 21.4 (CH_3), 14.3 (CH_3); LRMS (ESI, $M+H^+$): m/z 428; HRMS (ESI, $M+H^+$): m/z calcd. for $C_{23}H_{26}NO_5S$ 428.1532, found 428.1541.

Ethyl 2-((1*R,3*S**)-3-methyl-5-tosyl-1,3,4,5-tetrahydropyrano[4,3-*b*]indol-1-yl)acetate (1o).**

Reaction of the vinylogous carbonate **2o** (72 mg, 0.17 mmol) with (62 µL, 0.34 mmol) in dry CH_2Cl_2 (3.0 mL) at - 40 °C as described for the pyranobenzofuran **1a** followed by purification on a silica gel column using EtOAc/petroleum ether (1:19) as eluent furnished the pyranoindole **1o** (58 mg, 80%) as a white amorphous solid. Physical appearance: white amorphous solid. R_f: 0.5 (1:19, EtOAc/petroleum ether); IR (neat): 2977, 1737, 1598, 1451, 1373, 1290, 1175, 1091, 984, 811, 747 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 8.16 (d, *J* = 8.0 Hz, 1H), 7.66 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 1H), 7.28-7.25 (m, 2H), 7.20 (d, *J* = 8.0 Hz, 2H), 5.20 (dd, *J* = 2.5, 10.0 Hz, 1H), 4.18 (q, *J* = 7.0 Hz, 2H), 3.80-3.75 (m,1H), 3.19 (dt, *J* = 17.0, 2.5 Hz, 1H), 3.10 (ABX, *J* = 15.0, 3.0 Hz, 1H), 2.79 (ddd, *J* = 17.0, 10.5, 2.5 Hz, 1H), 2.52 (ABX, *J* = 15.0, 10.0 Hz, 1H), 2.34 (s, 3H), 1.40 (d, *J* = 6.0 Hz, 3H), 1.24 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$, DEPT): δ 171.1 (C), 145.0 (C), 136.4 (C), 135.8 (C), 134.1 (C), 130.0 (2 × CH), 126.9 (C), 126.5 (2 × CH), 124.2 (CH), 123.6 (CH), 118.8 (CH), 118.6 (C), 114.7 (CH), 70.8 (CH), 70.5 (CH), 60.8 (CH_2), 40.6 (CH_2), 33.0 (CH_2), 21.6 (CH_3), 21.4 (CH_3), 14.3 (CH_3); LRMS (ESI, $M+Na^+$): m/z 450; HRMS (ESI, $M+Na^+$): m/z calcd. for $C_{23}H_{25}NNaO_5S$ 450.1346, found 450.1347.

Ethyl 2-((1*R,3*R**)-3-cyclohexyl-5-tosyl-1,3,4,5-tetrahydropyrano[4,3-*b*]indol-1-yl)acetate (1p).**

Reaction of the vinylogous carbonate **2p** (60 mg, 0.12 mmol) with (43 µL, 0.24 mmol) in dry CH_2Cl_2 (4.0 mL) at - 40 °C as described for the pyranobenzofuran **1a** followed by purification on a silica gel column using EtOAc/petroleum ether (1:19) as eluent furnished the pyranoindole **1p** (52 mg, 87%) as a white solid. Physical appearance: white solid; R_f: 0.4 (1:19, EtOAc/petroleum ether); m.p.: 62-64 °C; IR (neat): 2926, 2853, 1737, 1598, 1475, 1451, 1245, 1226, 1174, 1152, 1020, 984, 928, 813, 703, 679, 659, 575 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 8.16 (d, *J* = 8.0 Hz, 1H), 7.65 (d, *J* = 8.5 Hz, 2H), 7.30-7.25 (m, 2H), 7.22-7.19 (m, 3H), 5.20 (dq, *J* = 2.5, 10.0 Hz, 1H), 4.22-4.16 (m, 2H), 3.31 (ddd, *J* = 10.5, 7.5, 3 Hz, 1H), 3.19 (dt, *J* = 17.0, 2.5 Hz, 1H), 3.11 (ABX, *J* = 15.0, 3.0 Hz, 1H), 2.81 (ABX, *J* = 17.0, 10.5 Hz, 1H), 2.48 (ABX, *J* = 15.0, 10.0 Hz, 1H), 2.34 (s, 3H), 2.04 (d, *J* = 12.5 Hz, 1H), 1.83-1.75 (m, 3H), 1.58-1.55 (m, 1H), 1.31-1.25 (m, 7H), 1.1-1.0 (m. 2H); ^{13}C NMR (125 MHz, $CDCl_3$, DEPT): δ 171.1 (C), 145.0 (C), 136.5 (C), 135.9 (C), 134.7 (C), 130.0 (2 × CH), 126.9 (C), 126.5 (2 × CH), 124.2 (CH), 123.6 (CH), 119.0 (C), 118.8 (CH), 114.8 (CH), 78.7 (CH), 71.1 (CH), 60.8 (CH_2), 42.6 (CH_2), 40.7 (CH), 29.2 (CH_2), 29.13 (CH_2), 28.8 (CH_2), 26.7 (CH_2), 26.2 (CH_2), 26.0 (CH_2), 21.7 (CH_3), 14.4 (CH_3); LRMS (ESI, $M+H^+$): m/z 496; HRMS (ESI, $M+H^+$): m/z calcd. for $C_{28}H_{34}NO_5S$ 496.2158, found 496.2158.

Ethyl 2-((1*R,3*R**)-3-tert-butyl-5-tosyl-1,3,4,5-tetrahydropyrano[4,3-*b*]indol-1-yl)acetate (1q).**

Reaction of the vinylogous carbonate **2q** (63 mg, 0.13 mmol) with (50 µL, 0.26 mmol) in dry CH_2Cl_2 (3.0 mL) at - 40 °C as described for the pyranobenzofuran **1a** followed by purification on a silica gel column using EtOAc/petroleum ether (1:19) as eluent furnished the pyranoindole **1q** (54 mg, 86%) as a white solid. Physical appearance: white solid; R_f: 0.5 (1:19, EtOAc/petroleum ether); m.p.: 74-76 °C; IR (neat): 2957, 1737, 1598, 1451, 1372, 1291, 1092, 1019, 983, 925, 812, 750, 669 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 8.16 (d, *J* = 8.0 Hz, 1H), 7.66 (d, *J* = 8.0 Hz, 2H), 7.30-7.20 (m, 5H), 7.20 (d, *J* = 8.0 Hz, 2H), 5.20 (dd, *J* = 10.0, 3.0 Hz, 1H), 4.22-4.12 (m, 2H), 3.24 (dd, *J* = 10.0, 3.0 Hz, 1H), 3.10 (dd, *J* = 15.0, 3.0 Hz, 1H), 3.08-3.07 (m, 1H), 2.85 (ddd, *J* = 17.0, 10.0, 3.0 Hz, 1H), 2.49 (ABX, *J* = 15.0, 10.0 Hz, 1H), 2.34 (s, 3H), 1.27 (d, *J* = 7.0 Hz, 3H). 1.0 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$, DEPT): δ 171.1 (C), 145.0 (C), 136.5 (C), 135.9 (C), 134.9 (C), 130.0 (2 × CH), 126.9 (C), 126.5 (2 × CH), 124.1 (CH), 123.6 (CH), 118.9 (CH), 118.7 (C), 114.8 (CH), 81.6 (CH), 71.2 (CH), 60.7 (CH_2), 40.7 (CH_2), 34.2 (C), 26.2 (CH_2), 25.8 (CH_3), 21.7 (CH_3), 14.4 (CH_3); LRMS (ESI, $M+Na^+$): m/z 492; HRMS (ESI, $M+Na^+$): m/z calcd. for $C_{28}H_{34}NO_5S$ 492.1815, found 492.1816.

Ethyl 2-((4a*S,6*R**,11b*R**)-11-tosyl-1,2,3,4,4a,6,11,11b-octahydrochromeno[4,3-*b*]indol-6-yl)acetate (1r).**

Reaction of the vinylogous carbonate **2r** (37 mg, 0.08 mmol) TMSOTf with (29 µL, 0.16 mmol) in dry CH_2Cl_2 (3.0 mL) at - 40 °C as described for the pyranobenzofuran **1a** followed by purification on a silica gel column using EtOAc/petroleum ether (1:19) as eluent furnished the pyranoindole **1r** (34 mg, 94%) as a white solid. Physical appearance: white solid; R_f: 0.5 (1:19, EtOAc/petroleum ether) ;m.p.: 144-146 °C; IR (neat): 2981, 2933, 2860, 1623, 1598, 1475, 1452, 1297, 1371, 1092, 941, 873, 749 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.14 (d, *J* = 8.0 Hz, 1H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.35-7.30 (m, 1H), 5.36 (dt, *J* = 8.0, 2.4 Hz, 1H), 4.30.4.25 (m, 2H), 3.29 (dt, *J* = 12.0, 3.2 Hz, 1H), 2.38

(ABX, *J* = 15.6, 10.0 Hz, 1H), 2.36 (s, 3H), 3.08- 3 (m, 1H), 2.98 (ABX, *J* = 15.6, 2.0 Hz, 1H), 2.15-2.20 (m, 1H), 2.03-1.90 (m, 1H), 1.82-1.57 (m, 4H), 1.37 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 170.7 (C), 144.6 (C), 140.1 (C), 139.0 (C), 133.0 (C), 129.1 (CH), 128.9 (CH), 126.8 (2 × CH), 124.9 (2 × CH), 124.6 (C), 124.6 (CH), 118.7 (CH), 117.3 (CH), 81.2 (CH), 71.5 (CH), 60.9 (CH_2), 43.7 (CH_2), 40.4 (CH) 32.0 (CH_2), 31.3 (CH_2), 26.0 (CH_2), 25.5 (CH_2), 21.6 (CH_2), 14.3 (CH_3); LRMS (ESI, M+Na$^+$): m/z 490; HRMS (ESI, M+Na$^+$): m/z calcd. for $C_{26}H_{29}NO_5NaS$ 490.1664, found 490.1667.

(1*RS*)-Ethyl 2-(5-(2-nitrophenylsulfonyl)-1,3,4,5-tetrahydropyrano[4,3-*b*]indol-1-yl)acetate (1s).

To a cold (- 40 °C) solution of the vinylogous carbonate **2s** (53 mg, 0.12 mmol) in dry CH_2Cl_2 (3.0 mL) was added TMSOTf (43 µL, 0.24 mmol) and the resulting mixture was slowly warmed up to rt. The work up as described for the pyranobenzofuran **1a** followed by purification on a silica gel column using EtOAc/petroleum ether (1:4) as eluent furnished the pyranoindole **1s** (48 mg, 89%) as a yellow liquid. Physical appearance: yellow liquid; R_f: 0.3 (1:4, EtOAc/petroleum ether); IR (neat): 2978, 2926, 2857, 1735, 1599, 1580, 1267, 1176, 1152, 981,851 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 (d, *J* = 8.0 Hz, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.66 (t, *J* = 7.6 Hz, 2H), 7.54 (t, *J* = 7.6 Hz, 1H), 7.38-7.36 (m, 1H), 7.25-7.20 (m, 3H), 5.36 (brd, *J* = 9.6 Hz, 1H), 4.18 (q, *J* = 7.2 Hz, 2H), 4.15-4.10 (m, 1H), 3.85-3.80 (m, 1H), 3.03 (ABX, *J* = 15.6, 2.4 Hz, 1H), 3.0-2.95 (m, 1H), 2.75 (ABX, *J* = 15.6, 9.6 Hz, 1H), 1.24 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 170.8 (C), 147.7 (C), 136.3 (C), 134.8 (C), 134.6 (CH), 133.3 (CH), 132.9 (C), 128.8 (CH), 126.7 (C), 125.4 (CH), 124.9 (CH), 124.3 (CH), 118.9 (CH), 118.5 (C), 114.5 (CH), 69.8 (CH), 62.1 (CH_2), 61.0 (CH_2), 39.7 (CH_2), 25.6 (CH_2), 14.3 (CH_3); LRMS (ESI, M+H$^+$): m/z 445; HRMS (ESI, M+H$^+$): m/z calcd. for $C_{21}H_{21}N_2O_7S$ 445.1069, found 445.1078.

Ethyl 2-((1*R,3*R**)-3-(benzo[b]thiophen-2-yl)-5-tosyl-1,3,4,5-tetrahydropyrano[4,3-*b*]indol-1-yl)acetate (1t)**.

Reaction of the vinylogous carbonate **2t** (87 mg, 0.17 mmol) with (128 µL, 0.68 mmol) in dry CH_2Cl_2 (4.0 mL) at - 40 °C as described for the pyranobenzofuran **1a** followed by purification on a silica gel column using EtOAc/petroleum ether (20:80) as eluent furnished the pyranoindole **1t** (69 mg, 79%) as a pale yellow viscous liquid. Physical appearance: pale yellow viscous liquid; R_f: 0.4 (1:4, EtOAc/petroleum ether); IR (neat): 3053, 2981, 2923, 2852, 1732, 1597, 1451, 1371, 1174, 1092, 910, 747, 575 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.22 (d, *J* = 8.0 Hz, 1H), 7.84 (d, *J* = 7.0 Hz, 1H), 7.77 (d, *J* = 7.0 Hz, 1H), 7.69 (d, *J* = 8.0 Hz, 2H), 7.38-7.30 (m, 6H), 7.27 (t, *J* = 8.0 Hz, 1H), 7.21 (d, *J* = 8.0 Hz, 2H), 5.54 (dd, *J* = 10.0, 3.0, Hz, 1H), 5.04 (dd, *J* = 17.0, 10.0, 3.0, Hz, 1H), 4.26-4.20 (m, 2H), 3.76 (dt, *J* = 17.0, 3.0 Hz, 1H), 3.33 (ddd, *J* = 10.0, 3.0 Hz, 1H), 3.19 (ABX, *J* = 15.0, 3.0 Hz, 1H), 2.65 (ABX, *J* = 15.0, 10.0 Hz, 1H), 2.35 (s, 3H), 1.28 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$, DEPT): δ 170.8 (C), 145.3 (C), 145.1 (C), 139.5 (C), 139.6 (C), 136.6 (C), 135.7 (C), 132.8 (C), 130.1 (2 × CH), 126.7 (C), 126.6 (2 × CH), 124.7 (CH), 124.7 (CH), 124.7 (CH), 123.8 (CH), 123.7 (CH), 122.5 (CH), 120.2 (CH), 118.9 (CH), 118.6 (C), 114.8 (CH), 72.6 (CH), 71.7 (CH), 60.9 (CH_2), 40.6 (CH_2), 32.7 (CH_2), 21.7 (CH_3), 14.4 (CH_3); LRMS (ESI, M+Na$^+$): m/z 568; HRMS (ESI, M+Na$^+$): m/z calcd. for $C_{28}H_{34}NO_5S$ 568.1217, found 568.1223.

(6*RS*)-ethyl 2-(6H-benzo[5,6][1,3]oxazino[3,4-*a*]indol-6-yl)acetate (1u)

To a cold (0 °C) solution of the vinylogous carbonate **2u** (55 mg, 0.12 mmol) in dry CH_2Cl_2 (4.0 mL) was added TMSOTf (44 µL, 0.24 mmol) and the reaction mixture stirred at the same temperature for *ca* 8h (TLC control). The workup as described for the pyranobenzofuran **1a** followed by purification on a silica gel column using EtOAc/petroleum ether (1:19) as eluent furnished the aminol derivative **1u** (18 mg, 49%) as a low melting white solid. Physical appearance: low melting white solid; R_f: 0.5 (1:19, EtOAc/petroleum ether); IR (neat): 2932, 1734, 1737, 1584, 1469, 1413, 1302, 1222, 1179, 1161, 1034, 786, 739 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.72 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.66 (d, *J* = 8.0 Hz, 1H), 7.39 (d, *J* = 8.0 Hz, 1H), 7.30-7.20 (m, 2H), 7.20-7.10 (m, 2H), 7.08 (d, *J* = 8.0 Hz, 1H), 6.87 (dd, *J* = 8.5, 4.5 Hz, 1H), 6.86 (brs, IH), 4.20-4.15 (m, 2H), 2.94 (ABX, *J* = 15.0, 8.5 Hz, 1H), 2.73 (ABX, *J* = 15.0, 4.5 Hz, 1H), 1.22 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$, DEPT): δ 168.9 (C), 148.1 (C), 134.1 (C), 130.1 (C), 129.6 (CH), 129.3 (C), 124.1 (CH), 123.4 (CH), 122.7 (CH), 121.1 (CH), 120.9 (CH), 118.5 (CH), 118.0 (C), 109.0 (CH), 97.3 (CH), 80.5 (CH), 61.3 (CH_2), 39.6 (CH_2), 14.2 (CH_3); LRMS (ESI, M+H$^+$): m/z 308; HRMS (ESI, M+H$^+$): m/z calcd. for $C_{19}H_{18}NO_3$ 308.1287, found 308.1302.

Ethyl (3-methyl-3,4-dihydro-1*H*-[1]benzothieno[3,2-*c*]pyran-1-yl)acetate (1v).

Reaction of the vinylogous carbonate **2v** (52 mg, 0.18 mmol) with TMSOTf (63 µL, 0.36 mmol) in dry CH_2Cl_2 (3.0 mL), as described for the pyranobenzofuran **1a** followed by purification on a silica gel column using EtOAc/petroleum ether (1:19) as eluent furnished the benzothieno pyran **1v** ((44 mg, 83%) as a viscous liquid. Physical appearance: viscous liquid; R_f: 0.5 (1:19, EtOAc/petroleum ether); IR (neat): 3060, 2978, 2931, 2900, 1733, 1282, 1178, 1028, 752 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72 (d, *J* = 7.2 Hz, 1H), 7.47 (d, *J* = 7.6 Hz, 1H), 7.27-7.20 (m, 2H), 5.38 (dq, *J* = 9.2, 2.6 Hz, 1H), 4.67 (qd, *J* = 7.2, 2.8 Hz, 2H), 3.75 (sextet, *J* = 7.2 Hz, 1H), 3.16 (ABX, *J* = 15.4, 2.6 Hz, 1H), 2.71-2.69 (m, 2H), 2.54 (ABX, *J* = 15.4, 9.4 Hz, 1H), 1.30 (d, *J* = 6.0, Hz 1H), 1.20 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 171.5 (C), 138.9 (C), 136.4 (C), 136.3 (C), 129.2 (C), 124.3 (CH), 123.8 (CH), 122.9 (CH), 121.2 (CH), 72.4 (CH), 70.2 (CH), 60.7 (CH_2), 41.1 (CH_2), 33.9 (CH_2), 21.3 (CH_3), 14.4 (CH_3); LRMS (ESI, M+Na$^+$): m/z 313; HRMS (ESI, M+Na$^+$) m/z calcd. for $C_{16}H_{18}O_3NaS$ 313.0874, found 313.0882.

Oxidative rearrangement of 1m:

A solution of **1m** (137 mg, 0.33 mmol) in CH_2Cl_2 (5 mL) was cooled to −10 °C before adding *m*CPBA (114 mg, 0.66 mmol) in one portion. The reaction was stirred for 8 h while slowly warming to room temperature. The reaction mixture was then quenched with saturated aq. $NaHCO_3$ (10 mL), extracted with CH_2Cl_2 (3 × 15 mL) and combined organic layer was washed with brine and dried (anhyd. Na_2SO_4). Evaporation of the solvent and purification of the residue on a silica gel column using EtOAc/petroleum ether (20:80) as eluent furnished **15** (18 mg, 17%) as a viscous liquid further elution EtOAc/petroleum ether (30:70) as eluent **14** (67 mg, 48 %) as a white solid.

Ethyl 2-((2*R,2'*S**)-3'-oxo-1'-tosyl-4,5-dihydro-2*H*-spiro[furan-3,2'-indoline]-2-yl)acetate (15).**

Physical appearance: viscous liquid; R_f: 0.4 (20:80, EtOAc/petroleum ether); IR (neat): 2982, 2959, 2924, 2851, 1720, 1606, 1464, 1357, 1302, 1211, 1087, 1024, 950, 814, 756 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 (d, *J* = 8.4 Hz, 2H), 7.78 (d, *J* = 8.4 Hz, 1H), 7.71 (d, *J* = 8.4 Hz, 1H), 7.78 (td, *J* = 7.6, 1.2 Hz, 1H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.16 (t, *J* = 7.6 Hz, 1H), 5.09 (dd, *J* = 9.6, 4.0 Hz 1H), 4.33-4.29 (m, 2H), 4.01-3.97 (m, 2H), 2.90-2.85 (m, 1H), 2.51 (ABX, *J* = 16, 9.2 Hz, 1H), 2.40 (s, 3H), 2.38-2.29 (m, 1H), 2.10 (ABX, *J* = 15.6, 4.0 Hz, 1H), 1.14 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR

(100 MHz, $CDCl_3$, DEPT): δ 198.4 (C), 170.2 (C), 152.6 (C), 145.1 (C), 137.6 (CH), 137.4 (C), 130.3 (2 × CH), 127.1 (2 × CH), 124.7 (CH), 123.9 (CH), 122.3 (C), 115.1 (CH), 79.6 (CH), 78.7 (C), 67.8 (CH_2), 60.9 (CH_2), 35.2 (CH_2), 34.9 (CH_2), 21.7 (CH_3), 14.2 (CH_3); LRMS (ESI, M+H^+): m/z 430; HRMS (ESI, M+H^+) m/z calcd. for $C_{22}H_{24}NO_6S$ 430.1324, found 430.133

(6*RS*)-Ethyl 2-(2,7-dioxo-1-tosyl-1,2,3,4,6,7-hexahydrobenzo[*f*][1,5]oxazonin-6-yl)acetate (14)

Physical appearance: white solid; R_f: 0.3 (30:70, EtOAc/petroleum ether); IR (neat): 2982, 2930, 1732, 1705, 1597, 1480, 1449, 1366, 1273, 1211, 1173, 1090, 1030, 913, 815, 671 cm^{-1}; m.p.: 170-171 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 7.87 (δ, *J* = 8.4 Hz, 2H), 7.62-7.56 (m, 1H), 7.33 (d, *J* = 8.4Hz, 1H), 7.17 (dd, *J* = 6.8, 0.8 Hz, 1H), 4.47 (dd, *J* = 6.4, 4.0 Hz 1H), 4.13 (q, *J* = 7.2 Hz, 2H), 4.02 (t, *J* = 4.0 Hz, 3H), 3.96 (t, *J* = 12.0 Hz, 3H), 2.88 (ABX, *J* = 16.4, 4.0 Hz, 1H), 2.77 (ABX, *J* = 17.2, 6.4 Hz, 1H), 2.77-2.70 (m, 1H), 2.44 (s, 3H), 2.37 (ABX, *J* = 14.0, 6.8 Hz, 1H), 2.17 (ABX, *J* = 13.0, 2.8 Hz, 1H), 1.24 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 203.6 (C), 172.0 (C), 170.3 (C), 145.7 (C), 142.0 (C), 134.9 (CH), 132.5 (2 × CH), 132.0 (2 × CH), 131.1 (CH), 130.1 (CH), 129.7 (3 × CH), 129.5 (2 × CH), 82.5 (CH), 70.9 (CH_2), 61.0 (CH_2), 39.7 (CH_2), 37.6 (CH_2), 21.8 (CH_3), 14.2 (CH_3); LRMS (ESI, M+Na^+): m/z 468; HRMS (ESI, M+Na^+) m/z calcd. for $C_{22}H_{23}NO_7NaS$ 468.1087, found 468.1087.

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Notes and references

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