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Note

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Synthesis of 2-(3′-Indolyl)tetrahydrofurans by Oxidative Cycloetherification

Rachel M. Gillard and Jonathan Sperry*

School of Chemical Sciences, University of Auckland, 23 Symonds St., Auckland, New Zealand

j.sperry@auckland.ac.nz

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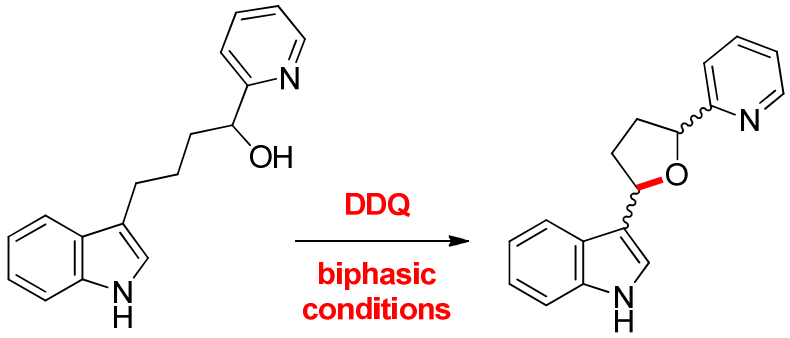
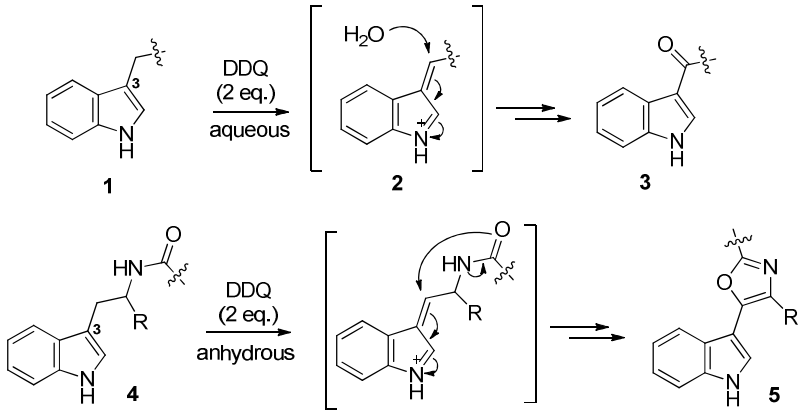
Abstract



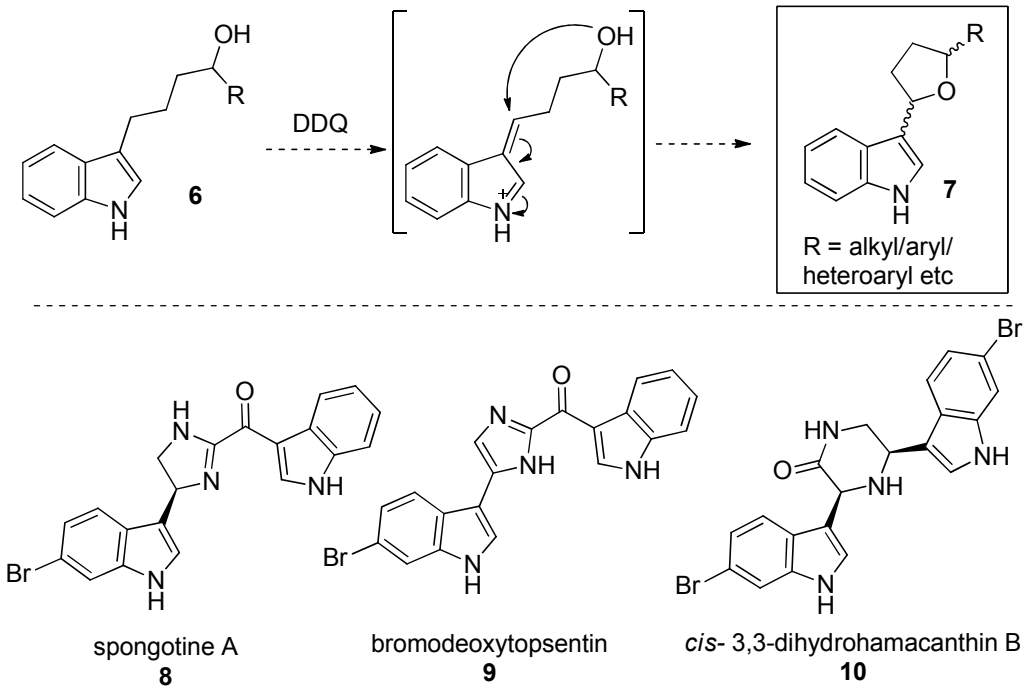
A series of 2-(3′-indolyl)tetrahydrofurans have been prepared by a DDQ-mediated oxidative cycloetherification process. Performing the reaction under biphasic conditions prevents reductive cleavage of the products by the spent oxidant ($DDQH_2$).

The Yonemitsu oxidation is the DDQ-mediated functionalization of alkyl groups at the C3 position of the indole nucleus (Scheme 1).[1] Subjecting a 3-alkylindole **1** to DDQ generates α,β-unsaturated iminium ion **2**, which under aqueous conditions undergoes attack at the β-position by water to give an intermediate alcohol that upon oxidation by a second equivalent of DDQ, affords ketone **3**.[2] A variant[1c] of this process involves exposing acylated tryptamines (**4**; R = H) and tryptophans (**4**; R = CO_2P) to DDQ under anhydrous conditions, with the resulting iminium ion undergoing intramolecular cyclization followed by aromatization to give 5-(3′-indolyl)oxazoles **5**,[3] a structural motif present in several natural products.[4]



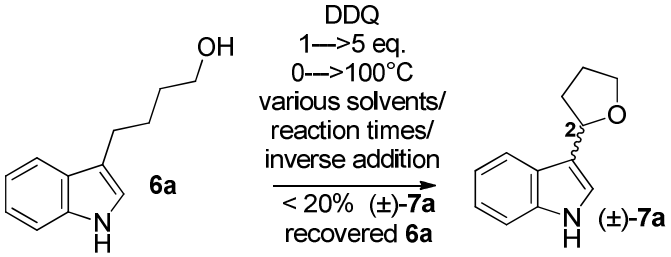
Scheme 1. Yonemitsu oxidation

In the course of our quest to discover small molecules that selectively inhibit the pyruvate kinase (PK) of MRSA,[5] we sought a synthetic route to cyclic ether analogues of the natural products **8-10**, selective inhibitors of this enzyme.[6] It was planned that a series of indole-3-butanols **6** would undergo a DDQ-mediated oxidative cycloetherification[7,8] to form 2-(3′-indolyl)tetrahydrofurans **7**,[9] a study that would provide the desired analogues but also represent a novel application of the Yonemitsu oxidation (Scheme 2).



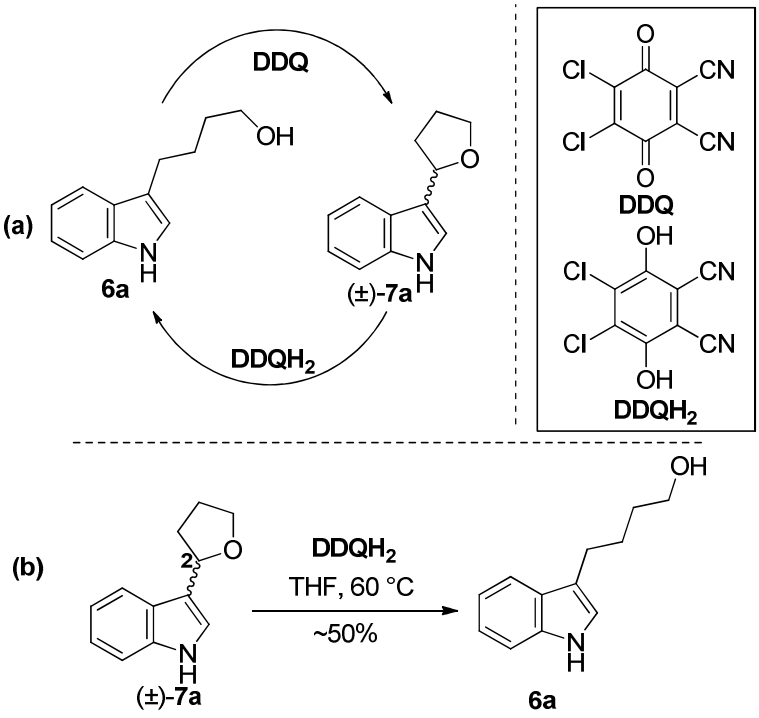
Scheme 2. Proposed route to 2-(3′-indolyl)tetrahydrofurans **7** as cyclic ether analogues of alkaloids **8-10**.

Initially, the synthesis of 2-(3′-indolyl)tetrahydrofuran (±)-**7a** by the oxidative cycloetherification of indole-3-butanol (**6a**)[10] was attempted. Encouraging early results showed that DDQ promoted the conversion of **6a** to (±)-**7a** under a variety of conditions, albeit in low yield. Although a detailed overview is not provided herein, an extensive optimisation study never uncovered conditions that gave (±)-**7a** in yields above 20% (Scheme 3). However, a recurring result throughout these studies was the consistently good recovery of the starting material **6a**.



Scheme 3. Unsatisfactory conversion of **6a** to (±)-**7a**

A possible explanation for the results outlined in Scheme 3 was that the C2–O bond in (±)-**7a** was being reductively cleaved by the spent oxidant ($DDQH_2$; Scheme 4A). Subjecting pure (±)-**7a** to $DDQH_2$ in THF gave **6a** in good yield at 60 °C (Scheme 4B), proving that the desired product does indeed undergo reductive cleavage. We are not aware of any reports detailing the use of hydroquinones to effect reductive cleavage of C_{sp3}-O bonds, a process that is more commonly performed using hydrogenolytic[11] or dissolving metal[12] conditions, with lithium tri-*tert*-butoxyaluminium hydride-Et_3B[13] and trialkylsilanes[14] also effective.

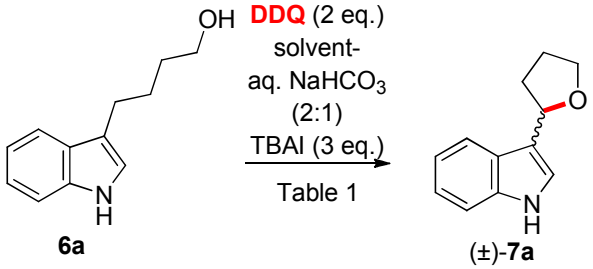


Scheme 4. (a) Interconversion of **6a** and (±)-**7a** in the presence of DDQ and $DDQH_2$; (b) Reductive cleavage of (±)-**7a** with $DDQH_2$.

With this knowledge at hand, an obvious strategy would be to remove the $DDQH_2$ as it is formed during the reaction. By conducting the reaction under biphasic conditions using a basic aqueous component, the $DDQH_2$ would enter the aqueous phase as it is formed and thus

the reductive cleavage of the product would be prevented. Table 1 outlines our efforts in this regard. Subjecting **6a** to DDQ in a biphasic solvent mixture of dichloromethane and saturated aqueous sodium bicarbonate in the presence of the phase transfer catalyst tetrabutylammonium iodide (TBAI) gave a 28% yield of the product (±)-**7a** (entry 1), which could be increased by raising the temperature to reflux (entry 2). A noticeable improvement in yield occurred upon changing the organic solvent to 1,2-dichloroethane (1,2-DCE) and heating at 60 °C (entry 3), which increased to 73% yield when heated to reflux (entry 4). Changing the solvent to toluene had a detrimental effect on the yield (entry 5), which was only marginally improved upon heating to reflux (entry 6).

Table 1. Oxidative cycloetherification of **6a** under biphasic conditions[a]



6a (±)-**7a**

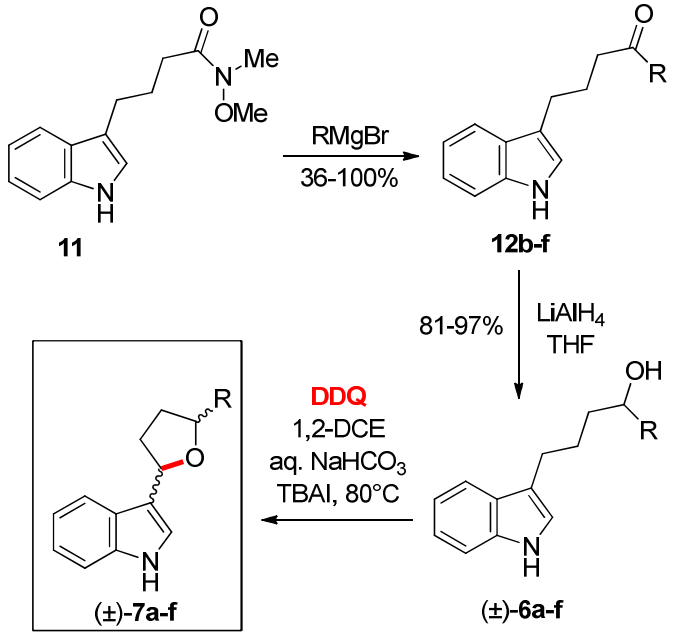
Entry	Organic solvent	Temp	Time (h)	Yield (%)
1	CH_2Cl_2	rt	24	28
2	CH_2Cl_2	reflux	24	41
3	1,2-DCE	60 °C	24	63
4	**1,2-DCE**	**reflux**	**3**	**73**
5	Toluene	80 °C	24	20
6	Toluene	reflux	2.5	34

[a] one equivalent of DDQ gave poor yields

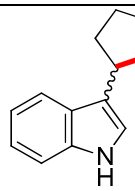
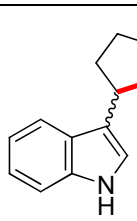
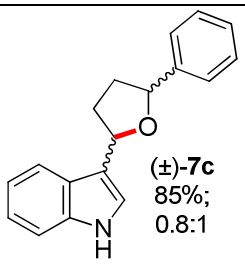
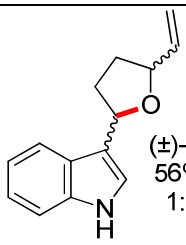
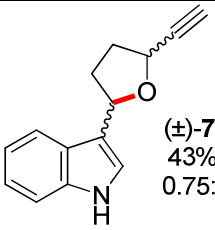
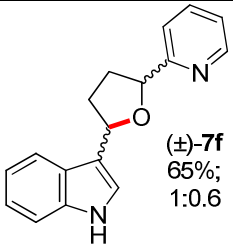
Next, the scope of the optimised oxidative etherification reaction was examined. The cyclisation precursors **6b-f** were readily prepared in racemic form by the addition of various

Grignard reagents to the Weinreb amide **11**[15] followed by reduction of the resulting ketones **12b-f** (Table 2). This methodology can be used to access 2-(3′-indolyl)tetrahydrofurans with a variety of substituents at the 5-position of the THF ring, including alkyl (entry 2), aryl (entry 3), alkenyl (entry 4), alkynyl (entry 5) and heteroaryl (entry 6). The products (±)**-7b-f** were all formed as an inseparable mixture of *cis* and *trans*-diastereomers.[16] In all of the examples shown in Table 2, substrate **6** was completely consumed and competing alcohol oxidation was not observed. The non-stereoselective nature of the cyclisation is likely contributing to the diastereomeric ratios observed in the THF products, which may also equilibrate under the reaction conditions.

Table 2. Synthesis of 2-(3′-indolyl)tetrahydrofurans (±)**-7a-f**



Entry	Product (yield; *cis:trans*)[a]	Entry	Product (yield; *cis:trans*)[a]

1	 (±)-**7a** 73%	**2**	 (±)-**7b** 55%; 1:0.4
3	 (±)-**7c** 85%; 0.8:1	**4**	 (±)-**7d** 56%; 1:1
5	 (±)-**7e** 43%; 0.75:1	**6**	 (±)-**7f** 65%; 1:0.6

[a] Diastereomeric ratio calculated by ^{1}H NMR.

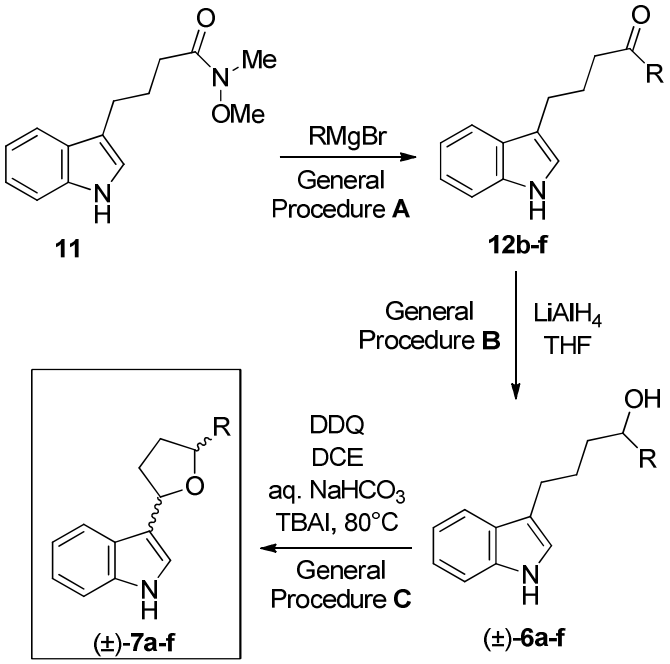
To conclude, a DDQ-mediated oxidative cycloetherification of indole-3-butanols to 2-(3′-indolyl)tetrahydrofurans has been developed. Reductive cleavage of the products by $DDQH_2$ can be avoided by performing the reaction under biphasic conditions. These results constitute a novel application of the Yonemitsu oxidation and the biphasic oxidation conditions reported herein should find utility in any DDQ-mediated synthetic transformation that is hindered by the spent oxidant.

Experimental section

General. All reactions were carried out in oven-dried glassware under a nitrogen atmosphere unless otherwise stated. Analytical thin layer chromatography was performed using 0.2 mm silica plates and compounds were visualized under 365 nm ultraviolet irradiation followed by staining with either alkaline permanganate or ethanolic vanillin solution. Infrared spectra

were obtained as thin films between sodium chloride plates. Absorption maxima are expressed in wavenumbers (cm^{-1}). Melting points were recorded on a melting point apparatus and are uncorrected. NMR spectra were recorded as indicated on an NMR spectrometer operating at 500, 400 and 300 MHz for ^{1}H nuclei and 125, 100 and 75 MHz for ^{13}C nuclei. Chemical shifts are reported in parts per million (ppm) relative to the tetramethylsilane peak recorded as δ 0.00 ppm in $CDCl_3$/ TMS solvent, or the residual acetone (δ 2.05 ppm), chloroform (δ 7.24 ppm), DMSO (δ 2.50 ppm) or methanol (δ 3.31 ppm) peaks. The ^{13}C NMR values were referenced to the residual acetone (δ 29.9 ppm) chloroform (δ 77.1 ppm), DMSO (δ 39.5 ppm) or methanol (δ 49.0 ppm) peaks. ^{13}C NMR values are reported as chemical shift δ and assignment. ^{1}H NMR shift values are reported as chemical shift δ, relative integral, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet), coupling constant (*J* in Hz) and assignment. Assignments are made with the aid of DEPT 90, DEPT 135, COSY, NOESY and HSQC experiments. High resolution mass spectra were obtained by electrospray ionization in positive ion mode at a nominal accelerating voltage of 70 eV on a microTOF mass spectrometer.

Synthesis of 2-(3′-indolyl)tetrahydrofurans 7a-f: General Procedures



General Procedure A – Grignard addition

To a solution of Weinreb amide **8** in THF at 0 °C was added the appropriate Grignard reagent and the resulting solution was stirred at the quoted temperature for the time stated. The reaction mixture was quenched with water (20 mL), extracted with ethyl acetate (3 x 25 mL) and the combined organic extracts dried (Na_2SO_4), filtered and concentrated *in vacuo*. The crude residue was purified via column chromatography eluting with the solvent(s) stated to give the ketone product.

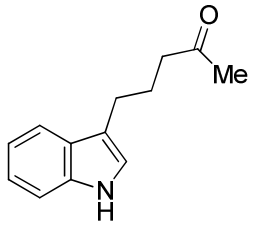
General Procedure B – $LiAlH_4$ reduction

To a solution of ketone in THF at 0 °C was added $LiAlH_4$ (1 M in THF) and the reaction was stirred at this temperature for the time stated. Ethyl acetate (1 mL) was slowly added followed by water (1 mL) and the reaction mixture was poured onto a saturated aqueous solution of Rochelle's salt (10 mL). The whole was extracted with ethyl acetate (3 x 10 mL) and the combined organic layers dried (Na_2SO_4), filtered and concentrated *in vacuo*. The crude residue was purified via column chromatography eluting with the solvent(s) stated to give the reduced product.

General Procedure C – Oxidative cycloetherification

To a mixture of cyclisation precursor, dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) and tetrabutylammonium iodide (TBAI) in a 2:1 mixture of 1,2-dichloroethane (1,2-DCE) and saturated aqueous sodium hydrogen carbonate solution was heated to 80 °C and stirred vigorously at this temperature for the time stated. The reaction mixture was poured onto a solution of saturated aqueous sodium hydrogen carbonate (20 mL) and ethyl acetate (30 mL) was added. The mixture was then washed with saturated aqueous sodium hydrogen carbonate (6 x 40 mL) and the organic layer dried (Na_2SO_4), filtered and concentrated *in vacuo*. The crude mixture was purified via column chromatography eluting with the solvent(s) stated to give the desired 2-(3′-indolyl)tetrahydrofuran as an inseparable mixture of *cis*- and *trans*-diastereomers in the case of **7b-f**.

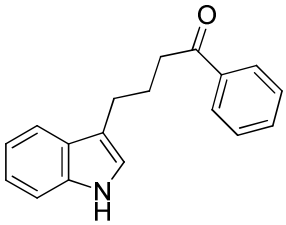
5-(Indol-3-yl)pentan-2-one (12b)



General procedure **A** was performed using Weinreb amide **11** (50 mg, 0.20 mmol) in THF (6 mL) and methylmagnesium bromide (3 M in ether, 0.34 mL) at 0 °C for 1 h. Workup and column chromatography eluting with hexanes-ethyl acetate (2:1) gave the *title compound* (41 mg, 0.203 mmol, 100%) as a colourless solid; mp 89–91 °C; ν_{max} (neat)/cm^{-1} 3323, 2972, 2869, 1703, 1620, 1457, 1433, 1404, 1353, 1255, 1243, 1221, 1164, 1104, 950, 777, 720; HRMS [ESI, (M + Na)$^+$] found 224.1046, [$C_{13}H_{15}NO$ + Na]$^+$ requires 224.1046; δ_H (400 MHz, $CDCl_3$) 7.96 (1 H, br s, NH), 7.61 (1 H, d, *J* 8.0, ArH), 7.36 (1 H, d, *J* 8.0, ArH), 7.19 (1 H, m, ArH), 7.12 (1 H, m, ArH), 6.98 (1 H, s, ArH), 2.79 (2 H, t, *J* 7.4, CH_2), 2.50 (2 H, t, *J* 7.4, CH_2), 2.11 (3 H, s, Me), 2.01 (2 H, m, CH_2); δ_C (100

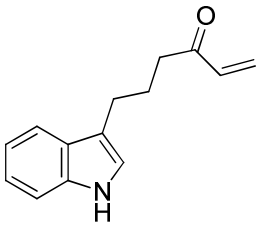
MHz, $CDCl_3$) 209.2 (C), 136.4 (C), 127.5 (C), 122.0 (CH), 121.4 (CH), 119.3 (CH), 118.9 (CH), 115.9 (C), 111.1 (CH), 43.3 (CH_2), 30.0 (Me), 24.4 (CH_2), 24.2 (CH_2).

4-(Indol-3-yl)-1-phenylbutan-1-one (12c)



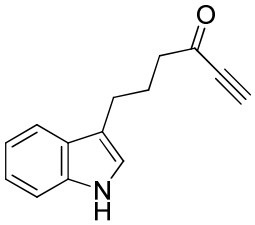
General procedure **A** was performed using Weinreb amide **11** (181 mg, 0.74 mmol) in THF (2.6 mL) and phenylmagnesium bromide solution [prepared from bromobenzene (1.01 mL, 1.51 mmol), magnesium powder (73 mg, 3.3 mmol) and iodine (25 mg, 0.2 mmol) in ether (6 mL)] at rt for 2 h. Workup and column chromatography eluting with hexanes-ethyl acetate (2:1) gave the *title compound* (89 mg, 0.034 mmol, 46%) as a colourless solid, mp 88–90 °C; ν_{max} (neat)/cm^{-1} 3324, 3060, 2874, 2839, 2159, 2030, 1676, 1619, 1596, 1578, 1455, 1447, 1323, 1261, 1198, 1099, 1060, 768, 746, 690, 654; HRMS [ESI, $(M + H)^+$] found 264.1390, $[C_{18}H_{17}NO + H]^+$ requires 264.1383; δ_H (400 MHz, $CDCl_3$) 7.96 (1 H, br s, NH), 7.92 (2 H, dd, *J* 8.4, 1.4, ArH), 7.63 (1 H, d, *J* 8.0, ArH), 7.54 (1 H, m, ArH), 7.43 (2 H, m, ArH), 7.36 (1 H, d, *J* 8.0, ArH), 7.20 (1 H, td, *J* 7.6, 1.2, ArH), 7.12 (1 H, m, ArH), 7.01 (1 H, s, ArH), 3.05 (2 H, t, *J* 7.4, CH_2), 2.89 (2 H, t, *J* 7.4, CH_2), 2.19 (2 H, m, CH_2); δ_C (100 MHz, $CDCl_3$) 200.5 (C=O), 137.1 (C), 136.4 (C), 132.9 (CH), 128.6 (2 x CH), 128.1 (2 x CH), 127.5 (C), 122.0 (CH), 121.5 (CH), 191.3 (CH), 119.0 (CH), 116.0 (C), 111.1 (CH), 38.1 (CH_2), 24.6 (2 x CH_2).

6-(Indol-3-yl)hex-1-en-3-one (12d)



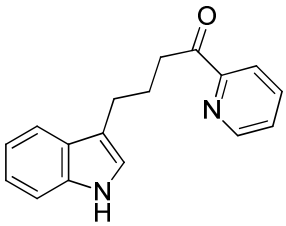
General procedure **A** was performed using Weinreb amide **11** (100 mg, 0.41 mmol) in THF (10 mL) and vinylmagnesium bromide (1 M in ether, 2.0 mL) at 0 °C for 1 h. Workup and column chromatography eluting with hexanes-ethyl acetate (4:1) gave the *title compound* (65 mg, 0.31 mmol, 75%) as a yellow oil; δ_H (400 MHz, $CDCl_3$) 7.96 (1 H, br s, NH), 7.61 (1 H, d, *J* 7.4, ArH), 7.36 (1 H, d, *J* 8.2, ArH) 7.19 (1 H, td, *J* 7.6, 1.5, ArH), 7.12 (1 H, td, *J* 7.5, 1.2, ArH), 6.99 (1 H, s, ArH), 6.34 (1 H, m, CH=CH_2), 6.18 (1 H, dd, *J* 14.1, 1.0, CH=CHCH), 5.79 (1 H, dd, *J* 14.1, 1.0, CH=CHCH), 2.82 (2 H, t, *J* 7.2, CH_2), 2.66 (2 H, t, *J* 7.2, CH_2), 2.07 (2 H, m, CH_2); Spectroscopic data is consistent with the literature.[15]

6-(Indol-3-yl)hex-1-yn-3-one (12e)



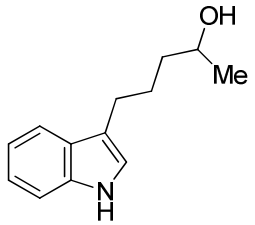
General procedure **A** was performed using Weinreb amide **11** (60 mg, 0.24 mmol) in THF (2 mL) and ethynylmagnesium bromide (0.5 M in ether, 2.5 mL) at 40 °C for 1 h. Workup and column chromatography eluting with hexanes-ethyl acetate (2:1) gave the *title compound* (50 mg, 0.24 mmol, 97%) as a yellow oil; δ_H (400 MHz, $CDCl_3$) 7.95 (1 H, br s, NH), 7.61 (1 H, d, *J* 6.9, ArH), 7.36 (1 H, d, *J* 7.3, ArH), 7.20 (1 H, td, *J* 7.6, 1.1, ArH), 7.12 (1 H, td, *J* 7.6, 1.1, ArH), 7.00 (1 H, s, ArH), 3.17 (1 H, s, CH), 2.82 (2 H, t, *J* 7.5, CH_2), 2.67 (2 H, t, *J* 7.5, CH_2), 2.11 (2 H, p, *J* 7.4, CH_2). Spectroscopic data is consistent with the literature.[15]

4-(Indol-3-yl)-1-(pyridin-2-yl)butan-1-one (12f)



General procedure **A** was performed using Weinreb amide **11** (123 mg, 0.5 mmol) in THF (1 mL) and 2-pyridylmagnesium bromide solution [prepared from 2-bromopyridine (237 mg, 1.5 mmol), magnesium powder (73 mg, 3.30 mmol) and iodine (25 mg, 0.2 mmol) in THF (6 mL)] at rt for 2 h. Workup and column chromatography eluting with hexanes-ethyl acetate (2:1) gave the *title compound* (47 mg, 0.18 mmol, 36%) as a yellow oil; ν_{max} (neat)/cm^{-1} 3335, 1687, 1580, 1567, 1447, 1367, 1326, 1275, 1203, 110, 1090, 992, 912, 778, 738, 726, 674; HRMS [ESI, $(M + Na)^+$] found 287.1165, $[C_{17}H_{16}N_2O + Na]^+$ requires 287.1155; δ_H (400 MHz, $CDCl_3$) 8.66 (1 H, m, ArH), 8.04 (1 H, m, ArH), 8.01 (1 H, br s, NH), 7.81 (1 H, td, *J* 1.8, 7.7, ArH), 7.64 (1 H, d, *J* 7.9, ArH), 7.44 (1 H, m, ArH), 7.34 (1 H, dt, *J* 8.0, 0.9, ArH), 7.18 (1 H, td, *J* 6.8, 1.1, ArH), 7.11 (1 H, td, *J* 7.5, 1.2, ArH), 7.02 (1 H, s, ArH), 3.33 (2 H, t, *J* 7.6, CH_2), 2.89 (2 H, t, *J* 7.6, CH_2), 2.19 (2 H, pen, *J* 7.6, CH_2); δ_C (100 MHz, $CDCl_3$) 202.1 (C), 153.6 (C), 148.9 (CH), 136.9 (CH), 136.4 (C), 127.6 (C), 127.0 (CH), 121.9 (CH), 121.8 (CH), 121.4 (CH), 119.14 (CH), 119.05 (CH), 116.2 (C), 111.0 (CH), 37.6 (CH_2), 24.8 (CH_2), 24.4 (CH_2).

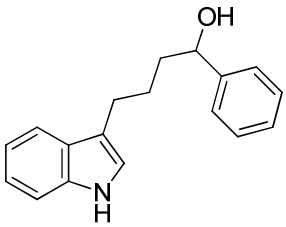
(±)-5-(Indol-3-yl)pentan-2-ol (6b)



General Procedure **B** was performed using **12b** (45 mg, 0.22 mmol) and $LiAlH_4$ (1 M in THF, 0.45 mL) in THF (1.2 mL) at 0 °C for 1 h. Workup and column chromatography eluting with ethyl acetate/hexanes (1:2) gave the *title compound* (44 mg, 0.22 mmol, 97%) as a colourless oil; ν_{max} (neat)/cm^{-1} 3525, 3211, 2966, 2924, 2871, 2838, 1456, 1441, 1367, 1335, 1241, 1216, 1128, 1099, 1078, 1006, 980, 931, 832, 792, 772; HRMS [ESI, $(M + Na)^+$] found 226.1196, $[C_{13}H_{17}NO + Na]^+$ requires 226.1202; δ_H (400 MHz, $CDCl_3$) 7.92 (1 H, br s, NH), 7.61 (1 H, d, *J* 8.0, ArH), 7.36 (1 H, d, *J* 8.4, ArH), 7.19 (1 H, m, ArH), 7.11 (1 H, m, ArH),

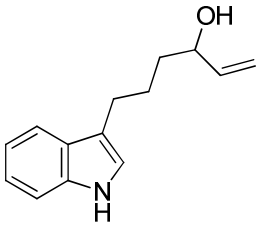
6.98 (1 H, s, ArH), 3.82 (1 H, m, CH), 2.77 (2 H, t, *J* 7.6, CH_2), 1.89–1.73 (2 H, m, CH_2), 1.60–1.53 (2 H, m, CH_2), 1.20 (3 H, d, *J* 6.1, Me); OH not observed; δ_C (100 MHz, $CDCl_3$) 136.4 (C=O), 127.6 (C), 121.9 (CH), 121.1 (CH), 119.2 (CH), 119.0 (CH), 116.7 (C), 111.1 (CH), 68.2 (CH), 39.2 (CH_2), 26.3 (CH_2), 25.1 (CH), 23.6 (Me).

(±)-4-(Indol-3-yl)-1-phenylbutan-1-ol (6c)



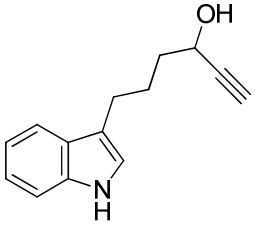
General Procedure **B** was performed using **12c** (80 mg, 0.30 mmol) and $LiAlH_4$ (1 M in THF, 0.61 mL) in THF (1.2 mL) at 0 °C for 1 h. Workup and column chromatography eluting with ethyl acetate/hexanes (1:4) gave the *title compound* (70 mg, 0.26 mmol, 87%) as a yellow oil; ν_{max} (neat)/cm^{-1} 3546, 3281, 3039, 2928, 2855, 1495, 1455, 1386, 1336, 1202, 1099, 1074, 1054, 1010, 933, 786, 763, 746; HRMS [ESI, $(M + Na)^+$] found 288.1360, $[C_{18}H_{19}NO + Na]^+$ requires 288.1359; δ_H (400 MHz, $CDCl_3$) 7.90 (1 H, br s, NH), 7.58 (1 H, d, *J* 7.3, ArH), 7.35–7.32 (5 H, m, ArH), 7.23 (1 H, t, *J* 4.3, ArH), 7.18 (1 H, td, *J* 7.4, 1.1, ArH), 7.10 (1 H, td, *J* 7.4, 1.1, ArH), 6.94 (1 H, s, ArH), 4.71 (1 H, t, *J* 6.3, CH), 2.79 (2 H, t, *J* 6.9, CH_2), 1.94–1.81 (3 H, m, CH_2), 1.76–1.69 (1 H, m, CH_2); OH not observed; δ_C (100 MHz, $CDCl_3$) 144.9 (C), 136.4 (C), 128.5 (2 x CH), 127.6 (CH), 126.0 (2 x CH), 121.9 (CH), 121.2 (CH), 119.1 (CH), 119.0 (CH), 116.5 (C), 111.0 (CH), 74.6 (CH), 38.9 (CH_2), 26.3 (CH_2), 25.0 (CH_2), 1 x (C) not observed.

(±)-6-(Indol-3-yl)hex-1-en-3-ol (6d)



General Procedure **B** was performed using **12d** (50 mg, 0.23 mmol) and $LiAlH_4$ (1 M in THF, 0.47 mL) in THF (1.5 mL) at 0 °C for 1 h. Workup and column chromatography eluting with ethyl acetate/hexanes (1:3) gave the *title compound* (46 mg, 0.21 mmol, 91%) as a brown oil; ν_{max} (neat)/cm^{-1} 3411, 3058, 2932, 2857, 1696, 1618, 1456, 1338, 1229, 1090, 989, 922, 667; HRMS [ESI, $(M + Na)^+$] found 238.1202, $[C_{14}H_{17}NO + Na]^+$ requires 238.1200; δ_H (400 MHz, $CDCl_3$) 7.92 (1 H, br s, NH), 7.61 (1 H, d, *J* 8.6, ArH), 7.35 (1 H, d, *J* 8.2, ArH), 7.19 (1 H, td, *J* 7.6, 1.1, ArH), 7.11 (1 H, td, *J* 7.6, 1.1, ArH), 6.98 (1 H, s, ArH), 5.87 (1 H, m, CH=CH_2), 5.22 (1 H, dt, *J* 13.8, 1.2, CH=CHCH), 5.10 (1 H, dt, *J* 13.8, 1.2, CH=CHCH), 4.14 (1 H, m, CH), 2.80 (2 H, td, *J* 7.5, 0.9, CH_2), 1.86–1.74 (2 H, m, CH_2), 1.68–1.62 (2 H, m, CH_2); OH not observed; δ_C (100 MHz, $CDCl_3$) 141.3 (CH), 136.4 (C), 127.6 (C), 121.9 (CH), 121.2 (CH), 119.1 (CH), 119.0 (CH), 116.6 (C), 114.7 (CH_2), 111.1 (CH), 73.2 (CH), 36.9 (CH_2), 25.9 (CH_2), 25.0 (CH_2).

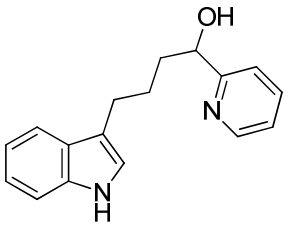
(±)-6-(Indol-3-yl)hex-1-yn-3-ol (6e)



General Procedure **B** was performed using **12e** (50 mg, 0.24 mmol) and $LiAlH_4$ (1 M in THF, 0.47 mL) in THF (1.5 mL) at 0 °C for 1 h. Workup and column chromatography eluting with ethyl acetate/hexanes (1:4) gave the *title compound* (41 mg, 0.19 mmol, 81%) as a brown oil; ν_{max} (neat)/cm^{-1} 3409, 3284, 3056, 2921, 2853, 2116, 2000, 1618, 1456, 1420, 1336, 1230, 1082, 1010, 892, 808; HRMS [ESI, $(M + Na)^+$] found 236.1040, $[C_{14}H_{15}NO + Na]^+$ requires 236.1046; δ_H (400 MHz, $CDCl_3$) 7.98 (1 H, br s, NH), 7.60 (1 H, d, *J* 7.9, ArH), 7.35 (1 H, d, *J* 8.0, ArH), 7.18 (1 H, t, *J* 7.4, ArH), 7.12 (1 H, t, *J* 7.4, ArH), 6.99 (1 H, s, ArH), 4.41 (1 H, s, CH), 2.82 (2 H, t, *J* 7.3, CH_2), 2.45 (1 H, d, *J* 2.2, CH), 1.93 – 1.80 (4 H, m, 2 x CH_2), OH

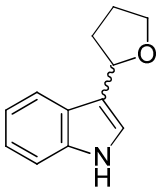
not observed; δ_C (100 MHz, $CDCl_3$) 136.4 (C), 127.5 (C), 121.9 (CH), 121.2 (CH), 119.2 (CH), 118.9 (CH), 116.3 (C), 111.1 (CH), 85.0 (C), 72.9 (CH), 62.3 (CH), 37.5 (CH_2), 25.5 (CH_2), 24.7 (CH_2).

(±)-4-(Indol-3-yl)-1-(pyridin-2-yl)butan-1-ol (6f)



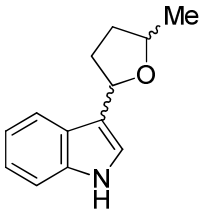
General Procedure **B** was performed using **12f** (45 mg, 0.17 mmol) and $LiAlH_4$ (1 M in THF, 0.34 mL) in THF (1.5 mL) at 0 °C for 20 min. Workup and column chromatography eluting with ethyl acetate/hexanes (1:2) gave the *title compound* (41 mg, 0.15 mmol, 91%) as a yellow oil; ν_{max} (neat)/cm^{-1} 3055, 2925, 2856, 1595, 1571, 1475, 1456, 1435, 1340, 1214, 1149, 1079, 1008, 908, 737; HRMS [ESI, $(M + Na)^+$] found 289.1314, $[C_{17}H_{18}N_2O + Na]^+$ requires 289.1311; δ_H (400 MHz, $CDCl_3$) 8.53 (1 H, d, *J* 4.8, ArH), 7.97 (1 H, br s, NH), 7.64 (1 H, td, *J* 7.7, 1.7, ArH), 7.57 (1 H, d, *J* 8.0, ArH), 7.32 (1 H, dd, *J* 8.0, 0.8, ArH), 7.22–7.15, (3 H, m, ArH), 7.09 (1 H, td, *J* 7.5, 1.2, ArH), 6.96 (1 H, s, ArH), 4.79 (1 H, q, *J* 3.8, CH), 2.80 (2 H, td, *J* 7.5, 1.7, CH_2), 1.96–1.79 (4 H, m, 2 x CH_2); OH not observed; δ_C (100 MHz, $CDCl_3$) 162.2 (C), 148.2 (CH), 136.7 (CH), 136.4 (C), 127.6 (C), 122.3 (CH), 121.8 (CH) 121.2 (CH), 120.4 (CH), 119.1 (CH), 119.0 (CH), 116.6 (C), 111.0 (CH), 72.7 (CH), 38.4 (CH_2), 25.7 (CH_2), 25.0 (CH_2).

(±)-2-(3′-Indolyl)tetrahydrofuran (7a)



General procedure **C** was performed using indole-3-butanol[10] (65 mg, 0.34 mmol), TBAI (381 mg, 1.03 mmol) and DDQ (140 mg, 0.62 mmol) in 1,2-DCE (4 mL) and saturated aqueous sodium hydrogen carbonate (2 mL) for 3 h. Workup and column chromatography eluting with hexanes/ethyl acetate (2:1) gave the *title compound* (47 mg, 0.25 mmol, 73%) as a colourless oil; ν_{max} (neat)/cm^{-1} 3340, 2966, 2861, 1663, 1619, 1553, 1461, 1424, 1376, 1351, 1338, 1249, 1221, 1085, 1033, 944, 921, 831; HRMS [ESI, (M + Na)$^+$] found 210.0894, [$C_{12}H_{13}NO$ + Na]$^+$ requires 210.0889; δ_H (400 MHz, $CDCl_3$) 8.07 (1 H, br s, NH), 7.69 (1 H, d, *J* 8.0, ArH), 7.34 (1 H, d, *J* 8.0, ArH), 7.20 (1 H, td, *J* 7.6, 0.9, ArH), 7.13 (2 H, m, ArH), 5.21 (1 H, m, CH), 4.14–4.08 (1 H, m, CH_2), 3.97–3.92 (1 H, m, CH_2), 2.37–2.31 (1 H, m, CH_2), 2.04–2.14 (3 H, m, CH_2); δ_C (100 MHz, $CDCl_3$) 136.9 (C), 126.1 (C), 122.2 (CH), 121.6 (CH), 119.64 (CH), 119.61 (CH), 117.6 (C), 111.4 (CH), 75.4 (CH), 68.1 (CH_2), 32.3 (CH_2), 26.3 (CH_2).

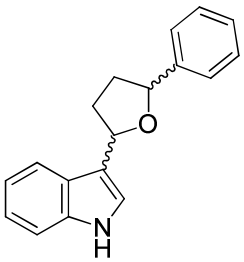
(±)-2-Methyl-5-(3′-indolyl)tetrahydrofuran (7b)



General procedure **C** was performed using **6b** (50 mg, 0.25 mmol), TBAI (273 mg, 0.74 mmol) and DDQ (140 mg, 0.62 mmol) in 1,2-DCE (4 mL) and saturated aqueous sodium hydrogen carbonate (2 mL) for 6 h. Workup and column chromatography eluting with hexanes/ethyl acetate (2:1) gave the *title compound* (27 mg, 0.14 mmol, 55%, *cis:trans* = 1:0.4) as a pink solid, mp 130 – 133 °C; ν_{max} (neat)/cm^{-1} 3252, 2968, 2924, 2869, 1666, 1618, 1552, 1490, 1458, 1458, 1431, 1373, 1333, 1249, 1226, 1143, 1099, 1064, 1009, 1000, 978, 920, 880, 868, 818, 776; HRMS [ESI, (M + Na)$^+$] found 224.1052, [$C_{13}H_{15}NO$ + Na]$^+$ requires 224.1046; δ_H (400 MHz, $CDCl_3$) 8.07 (2 H, br s, 2 x NH), 7.70 (2 H, t, *J* 7.2, 2 x ArH), 7.33 (2 H, d, *J* 7.2, 2 x ArH), 7.19 (2 H, td, *J* 7.6, 1.2, 2 x ArH), 7.14–7.10 (4 H, m, 4 x

ArH), 5.36 (1 H, t, *J* 7.2, CH, *cis*), 5.17 (1 H, t, *J* 7.2, CH-*trans*), 4.33 (1 H, m, CH-*cis*), 4.14 (1 H, m, CH-*trans*), 2.41–2.15 (6 H, m, 3 x CH_2), 1.73–1.66 (2 H, m, CH_2), 1.38 (3 H, d, *J* 6.0, Me-*trans*), 1.34 (3 H, d, *J* 6.0, Me-*trans*); δ_C (100 MHz, $CDCl_3$) 136.8 (2 x C), 125.9 (2 x C), 122.1 (2 x CH), 121.6 (CH), 121.3 (CH), 119.7 (CH), 119.6 (CH) 119.5 (2 x CH), 118.5 (2 x C), 111.2 (2 x CH), 75.51 (CH-*trans*), 75.49 (CH- *trans*), 75.0 (CH-*cis*), 74.7 (CH-*cis*), 34.4 (CH_2-*cis*), 33.4 (CH_2-*trans*), 33.3 (CH_2-*cis*), 32.6 (CH_2-*trans*), 21.6 (Me-*cis*), 21.5 (CH-*trans*).

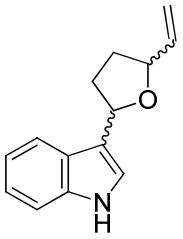
(±)-2-Phenyl-5-(3′-indolyl)tetrahydrofuran (7c)



General procedure **C** was performed using **6c** (50 mg, 0.19 mmol), TBAI (209 mg, 0.57 mmol) and DDQ (77 mg, 0.34 mmol) in 1,2-DCE (4 mL) and saturated aqueous sodium hydrogen carbonate (2 mL) for 2 h. Workup and column chromatography eluting with toluene gave the *title compound* (42 mg, 0.16 mmol, 85%, *cis:trans* = 0.8:1) as a colourless solid, mp 92 – 96 °C; ν_{max} (neat)/cm^{-1} 3260, 3057, 2928, 2872, 1488, 1455, 1325, 1255, 1232, 1214, 1103, 1019, 933, 869, 835, 761, 698; HRMS [ESI, $(M + Na)^+$] found 286.1213, $[C_{18}H_{17}NO + Na]^+$ requires 286.1202; δ_H (400 MHz, $CDCl_3$) 8.09 (2 H, br s, 2 x NH), 7.75 (2 H, t, *J* 8.1, 2 x ArH), 7.46 (4 H, t, *J* 8.4, 4 x ArH), 7.37–7.33 (6 H, m, 6 x ArH), 7.30–7.27 (2 H, m, 2 x ArH), 7.23–7.17 (4 H, m, 4 x ArH), 7.16–7.12 (2 H, m, 2 x ArH), 5.60 (1 H, t, *J* 7.2, CH-*trans*), 5.39 (1 H, t, *J* 7.2, CH-*cis*), 5.29 (1 H, t, *J* 7.2, CH-*trans*), 5.08 (1 H, t, *J* 7.2, CH-*cis*), 2.61–2.43 (4H, m, 2 x CH_2), 2.37–2.24 (2 H, m, CH_2), 2.12–2.02 (2 H, m, CH_2); δ_C (100 MHz, $CDCl_3$) 144.0 (C), 143.2 (C), 136.83 (C), 136.76 (C), 128.4 (2 x CH), 128.3 (2 x CH), 127.2 (CH), 127.1 (CH), 126.0 (2 x CH), 125.7 (2 x CH), 122.21 (CH), 122.19 (CH),

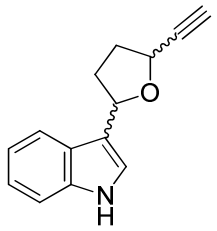
121.7 (CH), 121.3 (CH), 119.72 (CH), 119.70 (CH), 119.6 (2 x CH), 118.1 (C), 117.8 (C), 111.3 (2 x CH), 81.0 (CH), 80.5 (CH), 76.0 (2 x CH), 35.7 (CH_2), 34.7 (CH_2), 33.3 (CH_2), 32.4 (CH_2), 2 x (C) not observed.

(±)-2-Vinyl-5-(3′-indolyl)tetrahydrofuran (7d)



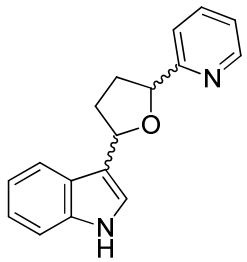
General procedure **C** was performed using **6d** (38 mg, 0.18 mmol), TBAI (196 mg, 0.53 mmol) and DDQ (72 mg, 0.32 mmol) in 1,2-DCE (4 mL) and saturated aqueous sodium hydrogen carbonate (2 mL) for 3 h. Workup and column chromatography eluting with toluene gave the *title compound* (21 mg, 0.099 mmol, 56%, *cis:trans* = 1:1) as a brown solid, mp 73 – 75 °C; ν_{max} (neat)/cm^{-1} 3261, 2934, 2875, 1547, 1457, 1428, 1336, 1233, 1108, 1020, 993, 931, 894, 866, 837, 662; HRMS [ESI, $(M + Na)^+$] found 236.1050, [$C_{14}H_{15}NO$ + $Na]^+$ requires 236.1046; δ_H (400 MHz, $CDCl_3$) 8.02 (2 H, br s, 2 x NH), 7.71–7.68 (2 H, m, 2 x ArH), 7.36 (2 H, d, *J* 8.2, 2 x ArH), 7.22–7.16 (4 H, m, 4 x ArH), 7.14–7.10 (2 H, m, 2 x ArH), 6.06–5.93 (2 H, m, 2 x $\underline{CH}$=CH_2), 5.40 (1 H, t, *J* 6.9, CH-*trans*), 5.35–5.30 (2 H, m, CH=$\underline{CH_2}$), 5.27 (1 H, t, *J* 6.9, CH-*cis*), 5.15–5.12 (2 H, m, CH=$\underline{CH_2}$), 4.68 (1 H, q, *J* 6.8, CH-*trans*), 4.49 (1 H, q, *J* 6.8, CH-*cis*), 2.44–2.13 (6 H, m, 3 x CH_2), 1.92–1.84 (2 H, m, CH_2); δ_C (100 MHz, $CDCl_3$) 139.6 (CH), 139.4 (CH), 125.92 (C), 125.89 (C), 122.18 (CH), 122.16 (CH), 121.5 (CH), 121.2 (CH), 119.7 (CH), 119.64 (CH), 119.60 (CH), 199.56 (CH), 118.3 (C), 118.2 (C), 115.4 (CH=$\underline{CH_2}$), 114.9 (CH=$\underline{CH_2}$), 111.2 (2 x CH), 80.3 (CH), 79.8 (CH), 75.7 (CH), 75.2 (CH), 32.9 (CH_2), 32.8 (CH_2), 32.3 (CH_2), 32.1 (CH_2). 2 x (C) not observed.

(±)-2-Ethynyl-5-(3′-indolyl)tetrahydrofuran (7e)



General procedure **C** was performed using **6e** (38 mg, 0.18 mmol), TBAI (197 mg, 0.53 mmol) and DDQ (73 mg, 0.32 mmol) in 1,2-DCE (4 mL) and saturated aqueous sodium hydrogen carbonate (2 mL) for 2 h. Workup and column chromatography eluting with hexanes-ethyl acetate (4:1) gave the *title compound* (16 mg, 0.076 mmol, 43%, *cis:trans* = 0.75:1) as a brown oil; ν_{max} (neat)/cm^{-1} 3412, 3289, 3059, 2928, 2871, 1619, 1555, 1457, 1425, 1336, 1234, 1022, 945, 907, 824; HRMS [ESI, $(M + H)^+$] found 212.1065, [$C_{14}H_{13}NO + H]^+$ requires 212.1070; δ_H (400 MHz, $CDCl_3$) 8.09 (2 H, br s, 2 x NH), 7.75 (1 H, d, *J* 6.9, ArH), 7.68 (1 H, d, *J* 6.9, ArH), 7.34 (2 H, m, 2 x ArH), 7.23–7.18 (2 H, m, 2 x ArH), 7.18–7.10 (4 H, m, 4 x ArH), 5.48 (1 H, t, *J* 7.0, (CH-*trans*), 5.28 (1 H, t, *J* 7.0, CH-*cis*), 4.91 (1 H, m, CH-*trans*), 4.77 (1 H, m, CH-*cis*), 2.52 (1 H, d, *J* 2.0, CH), 2.50 (1 H, d, *J* 2.0, CH), 2.49–2.33 (6 H, m, 3 x CH_2), 2.56–2.14 (2 H, m, 2 x CH_2); δ_C (100 MHz, $CDCl_3$) 136.8 (C), 136.7 (C), 125.8 (C), 125.7 (C), 122.3 (CH), 122.2 (CH), 122.1 (CH), 121.6 (CH), 119.7 (CH), 119.7 (CH), 119.6 (CH), 119.4 (CH), 117.1 (C), 116.8 (C), 111.29 (CH), 111.26 (CH), 84.4 (2 x C), 76.5 (CH), 75.2 (CH), 72.8 (CH), 72.6 (CH), 68.0 (CH), 67.8 (CH), 33.8 (CH_2), 32.5 (CH_2), 31.9 (CH_2), 29.7 (CH_2).

(±)-3′-(5-(Pyridin-2-yl)tetrahydrofuran-2-yl)indole (7f)



General procedure **C** was performed using **6f** (40 mg, 0.15 mmol), TBAI (166 mg, 0.45 mmol) and DDQ (61 mg, 0.27 mmol) in 1,2-DCE (4 mL) and saturated aqueous sodium hydrogen carbonate (2 mL) for 2 h. Workup and column chromatography eluting with hexanes/ethyl acetate (4:1) gave the *title compound* (26 mg, 0.098 mmol, 65%, *cis:trans* = 1:0.6) as a yellow oil; ν_{max} (neat)/cm^{-1} 3060, 2932, 1733, 1592, 1570, 1457, 1435, 1337, 1233, 1097, 1040, 1010, 949, 710 HRMS [ESI, (M + H)$^+$] found 265.1344, [$C_{17}H_{16}N_2O$ + H]$^+$ requires 265.1335; δ_H (400 MHz, $CDCl_3$) 8.78 (2 H, m, 2 x ArH), 8.22 (2 H, br s, 2 x ArH), 7.75 (2 H, d, *J* 7.1, 2 x ArH), 7.71 (1 H, td, *J* 6.1, 1.4, ArH), 7.63 (2 H, m, 2 x ArH), 7.57 (1 H, d, *J* 6.3, ArH), 7.37 (2 H, m, 2 x ArH), 7.24–7.12 (8 H, m, 8 x ArH), 5.58 (1 H, t *J* 5.7, CH-*cis*), 5.43 (1 H, t, *J* 5.7, CH-*trans*), 5.38 (1 H, t, *J* 5.7, CH-*cis*), 5.21 (1 H, t *J* 5.7, CH-*trans*), 2.71–2.62 (2 H, m, CH_2), 2.47–2.40 (2 H, m, CH_2), 2.33–2.20 (4 H, m, 2 x CH_2); δ_C (100 MHz, $CDCl_3$) 163.4 (C), 163.0 (C), 149.1 (CH), 148.8 (CH), 136.8 (C), 136.79 (C), 126.1 (C), 125.9 (C), 122.2 (2 x CH), 122.1 (2 x CH), 121.8 (CH), 121.5 (CH), 120.3 (CH), 120.0 (CH), 119.8 (CH), 119.7 (CH), 119.6 (CH), 117.7 (C), 117.68 (C), 111.3 (2 x CH), 81.5 (CH), 81.2 (CH), 76.5 (CH), 76.3 (CH), 33.8 (CH_2), 33.3 (CH_2), 33.0 (CH_2), 31.8 (CH_2), one CH not observed.

Supporting Information

^{1}H and ^{13}C NMR spectra for all novel compounds and NOESY spectra for **7b-f**. This material is available free of charge via the Internet at http://pubs.acs.org

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References

(1) (a) Oikawa, Y.; Yonemitsu, O. *J. Org. Chem*. **1977**, *42*, 1213–1216; (b) Oikawa, Y.; Yoshioka, T.; Mohri, K.; Yonemitsu, O. *Heterocycles* **1979**, *12*, 1457–1462; (c) Yoshioka, T.; Mohri, K.; Oikawa, Y.; Yonemitsu, O. *J. Chem. Res., Synop*. **1981**, 194–195; *J. Chem. Res., Miniprint* **1981**, 2252–2281.

(2) Yonemitsu oxidation of 3-alklylindoles under aqueous conditions: (a) Hagen, T. J.; Narayanan, K.; Names, J.; Cook, J. M. *J. Org. Chem*. **1989**, *54*, 2170–2178; (b) Ekebergh, A.; Börje, A.; Märtensson, J. *Org. Lett.* **2012**, *14*, 6274–6277.

(3) Yonemitsu oxidation of acylated tryptamine/tryptophan derivatives under anhydrous conditions: (a) Burgett, A. W. G.; Li, Q.; Wei, Q.; Harran, P. G. *Angew. Chem. Int. Ed*. **2003**, *42*, 4961–4966; (b) Sperry, J.; Moody, C. J. *Tetrahedron* **2010**, *66*, 6483–6495.

(4) (a) Joshi, B. S.; Taylor, W. I.; Bhate, D. S.; Karmarkar, S. S. *Tetrahedron* **1963**, *19*, 1437–1439; (b) Umehara, K.; Yoshida, K.; Okamoto, M.; Iwami, M.; Tanaka, H.; Kohsaka, M.; Imanaka, H. *J. Antibiot.* **1984**, *37*, 1153–1160; (c) Guella, G.; Mancini, I.; N'Diaye, I.; Pietra, F. *Helv. Chim. Acta* **1994**, *77*, 1999–2006; (d) N'Diaye, I.; Guella, G.; Mancini, I.; Pietra, F. *Tetrahedron Lett.* **1996**, *37*, 3049–3050; (e) Miyake, F.; Hashimoto, M.; Tonsiengsom, S.; Yakushijin, K.; Horne, D. A. *Tetrahedron* **2010**, *66*, 4888–4893; (f) Takahashi, S.; Matsunaga, T.; Hasegawa, C.; Saito, H.; Fujita, D.; Kiuchi, F.; Tsuda, Y.; *Chem. Pharm. Bull*. **1998**, *46*, 1527–1529; (g) Pettit, G. R.; Knight, J. C.; Herald, D. L.; Davenport, R.; Pettit, R. K.; Tucker, B. E.; Schmidt, J. M. *J. Nat. Prod*. **2002**, *65*, 1793–1797; (h) Lachia, M.; Moody, C. J. *Nat. Prod. Rep.* **2008**, *25*, 227–253; (i) Hanssen, K., Ø.; Schuler, B.; Williams, A. J.; Demissie, T. B.; Hansen, E.; Andersen, J. H.; Svenson, J.; Blinov, K.; Repisky, M.; Mohn, F.; Meyer, G.; Svendsen, J.-S.; Ruud, K.; Elyashberg, M.; Gross, L.; Jaspars, M.; Isaksson, J. *Angew. Chem. Int. Ed*. **2012**, *51*, 12238–12241.

(5) Zoraghi, R.; Campbell, S.; Kim, C.; Dullaghan, E. M.; Blair, L. M.; Gillard, R. M.; Reiner, N. E.; Sperry, J. *Bioorg. Med. Chem. Lett.* **2014**, *24*, 5059–5062.

(6) Zoraghi, R.; Worrall, L.; See, R. H.; Strangman, W.; Popplewell, W. L.; Gong, H.; Samaai, T.; Swayze, R. D.; Kaur, S.; Vuckovic, M.; Finlay, B. B.; Brunham, R. C.; McMaster, W. R.; Davies-Coleman, M. T.; Strynadka, N. C.; Andersen, R. J.; Reiner, N. E.. *J. Biol. Chem.* **2011***, 286*, 44716–44725.

(7) For examples of DDQ-mediated oxidative cycloetherifications, see: (a) Harwood, L. M.; Robertson, J. *Tetrahedron Lett.* **1987**, *28*, 5175–5176; (b) Oikawa, Y.; Horita, K.; Yonemitsu, O. *Heterocycles* **1985**, *23*, 553–556; (c) Pelter, A.; Ward, R. S.; Venkateswarlu, R.; Kamakshi, C. *Tetrahedron* **1991**, *47*, 1275–1284; (d) Jevric, M.; Taylor, D. K.; Greatrez, B. W.; Tiekink, E. R. T. *Tetrahedron* **2005**, *61*, 1885–1891; (e) Ramdayal, F. D.; Kiemkle, D. J.; LaLonde, R. T. *J. Org. Chem.* **1999**, *64*, 4607–4609; (f) LaLonde, R. T.; Ramdayal, F.; Sarko, A.; Yanai, K.; Zhang, M. *J. Med. Chem.* **2003**, *46*, 1180–1190; (g) Fang, B.; Xie, X.; Jing, P.; Zhao, C.; Li, H.; Ma, H.; She, X. *Tetrahedron* **2013**, *69*, 11025–11030; (h) Pearson, A. J.; Kole, S. L.; Yoon, J. *Organometallics* **1986**, *5*, 2075–2081.

(8) DDQ-mediated cycloetherification during the synthesis of several sarpagine alkaloids: (a) Yu, J.; Wearing, X. Z.; Cook, J. M. *Tetrahedron Lett.* **2004**, *45*, 3937–3940; (b) Zhou, H.; Han, D.; Liao, X.; Cook, J. M. *Tetrahedron Lett.* **2005**, *46*, 4219–4224; (c) Yin, W.; Ma, J.; Rivas, F. M.; Cook, J. M. *Org. Lett.* **2007**, *9*, 295–298; (d) Yu, J.; Liao, X.; Cook, J. M. *Org. Lett.* **2002**, *4*, 4681–4684; (e) Zhou, H.; Liao, X.; Yin, W.; Ma, J.; Cook, J. M. *J. Org. Chem.* **2006**, *71*, 251–259; (f) Yu, J.; Wearing, X. Z.; Cook, J. M. *J. Org. Chem.* **2005**, *70*, 3963–3979; (g) Yu, J.; Wang, T.; Wearing, X. Z.; Ma, J.; Cook, J. M. *J. Org. Chem.* **2003**, *68*, 5852–5859.

(9) The acid catalysed cyclization of 3-(alditoyl)indoles affords 3-(furanosyl)indoles: Cornia, M.; Casiraghi, G.; Zetta, L. *J. Org. Chem.* **1991**, *56*, 5466–5468.

(10) Blair, L. M.; Sperry, J. *Synlett* **2013**, *24*, 1931–1936.

(11) (a) Baker, R. H.; Cornell, K. H.; Cron, M. J. *J. Am. Chem. Soc.* **1948**, *70*, 1490–1492; (b) Nishikawa, T.; Koide, Y.; Kajii, S.; Wada, K.; Ishikawa, M.; Isobe, M. *Org. Biomol. Chem.* **2005**, *3*, 687–700; (c) Roy, S. C.; Rana, K. K.; Guin, C. *J. Org. Chem.* **2002**, *67*, 3242–3248.

(12) (a) Gillingham, D. G.; Kataoka, O.; Garber, S. B.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2004**, *126*, 12288–12290; (b) Abell, A. D.; Massy-Westropp, R. A. *Tetrahedron* **1985**, *41*, 2451–2464; (c) Venkateswariu, R.; Kamakshi, C.; Moinuddin, S. G. A.; Subhash, P. V.; Ward, R. S.; Pelter, A.; Hursthouse, M. B.; Light, M. E. *Tetrahedron* **1999**, *55*, 13087–13108

(13) Brown, H. C.; Krishnamurthy, S.; Coleman, R. A. *J. Am. Chem. Soc.* **1972**, *94*, 1750–1751.

(14) (a) Gevorgyan, V.; Liu, J. X.; Rubin, M.; Benson, S.; Yamamoto, Y. *Tetrahedron Lett.* **1999**, *40*, 8919–8922; (b) DeNinno, M. P.; Etienne, J. B.; Duplantier, K. C. *Tetrahedron Lett.* **1995**, *36*, 669–672; (c) Watanabe, S.; Sueyoshi, T.; Ichihara, M.; Uehara, C.; Iwamura, M. *Org. Lett.* **2001**, *3*, 255–257; (d) Qin, H.-L.; Lowe, J. T.; Panek, J. S. *J. Am. Chem. Soc.* **2007**, *129*, 38–39.

(15) Kim, C. M.; Cole, P. A. *J. Med. Chem.* **2001***, 44*, 2479–2485.

(16) The *cis*- or *trans*-diastereomer could be identified by relevant NOE correlations. See supporting information for full details.