**Divergent reactivity of indole-tethered ynones with Ag(I) and Au(I) catalysts: a combined synthetic and computational study**

|  |  |
| --- | --- |
| John T. R. Liddona James A. Rossi-AshtonaAimee K. ClarkeaJason M. Lynam\*aRichard J. K. Taylor\*aWilliam P. Unsworth\*aa University of York, Department of Chemistry, Heslington, York, YO10 5DD (UK).\* indicates the main/corresponding author.Jason.lynam@york.ac.uk;richard.taylor@york.ac.uk; william.unsworth@york.ac.ukClick here to insert a dedication. |  |
|  |

Received:
Accepted:
Published online:
DOI:

Abstract A combined synthetic and computational (DFT) study has been performed to account for the divergent reactivity of indole-tethered ynones when treated with Ag(I) and Au(I) catalysts. The two catalyst systems deliver spirocyclic indolenines and carbazoles respectively from the same precursors, with the reaction outcomes believed to be a result of differences in the rates of a key protodemetallation step. A ring opening/ring closing isomerisation process is proposed to enable the interconversion of spirocyclic and C-2 annulated indole intermediates, in contrast to the 1,2-migration mechanism tentatively proposed in previous studies.

**Key words** Ynones, indoles, spirocycles, carbazoles, silver, gold, catalysis

The selective synthesis of two or more products from common synthetic precursors is an efficient way to streamline the preparation of diverse organic compounds. Methods such as these are amongst their most useful when the reaction outcome is controlled by different catalysts; Bode and co-workers highlighted the value of such ‘catalyst selective synthesis’ in an excellent 2012 review,1 with several new methods having been reported since.2,3

Amongst these works is a recent contribution from our groups3a describing a divergent reaction system capable of selectively generating three distinct product scaffolds from indole-tethered ynones **1** (Scheme 1).4,5 Thus, it was found that ynones of the form **1** could be selectively converted into carbazoles (**5**) using Ph3PAuNTf2·½tol in CH2Cl2 at RT,6 into spirocyclic indolenines7 (**6**) upon treatment with AgOTf in CH2Cl2 at RT, and into quinolines (**7**) via a novel AlCl3-mediated rearrangement.8 We proposed that all three reactions are initiated by π-acid activation of the alkyne (which activates it towards dearomatising spirocyclisation)9,10 to form a vinyl metal intermediate of the form **2**, beforethis reactive intermediatediverges to one of the three products **5**–**7**, depending on the nature of the catalyst and the reaction conditions.



**Scheme 1** Catalyst selective synthesis of spirocycles, carbazoles and quinolines from indole-tethered ynones. [M] = Au(I)Ln, Ag(I)Ln or Al(III)Ln where L = ligand. tol = toluene, Tf = triflate.

This previous study was focused on demonstrating the synthetic utility of the catalyst-controlled divergent reactions, but little was done to explore the underlying reasons for the divergent reaction outcomes. Herein, we report progress to address this, concentrating on rationalising the difference in reactivity between the Ag(I)- and Au(I)-mediated processes, using a combination of synthetic results, *in situ* infrared (IR) spectroscopy and Density Functional Theory (DFT).

An interesting observation not explored in detail in our earlier studies is the difference in reaction times between the Ag(I)- and Au(I)-catalysed methods. The stark difference is exemplified by the published conditions used to promote the syntheses of carbazole **5a** and spirocycle **6a** from ynone **1a** (Scheme 2); while the spirocyclisation of **1a** to form **6a** wasshown to be complete in 1 hour following reaction with 1 mol% AgOTf in CH2Cl2, the synthesis of carbazole **5a** was reported to take 16 h, despite using a higher loading (5 mol%) of the Ph3PAuNTf2·½tol catalyst (Scheme 2).11 This observation was somewhat surprising, given that Au(I) catalysts of this type are typically thought to be superior π-acids compared to similar Ag(I) compounds, and that Au(I) catalysts have been shown to be more effective in a range of synthetic processes involving alkyne activation.12,13

This led us to consider that the initial alkyne activation is unlikely to be rate-determining in the Au(I) reaction (see later), but before undertaking any more detailed studies, it was decided to more accurately measure the rate of the conversion of ynone **1a** into carbazole **5a**. Previously, we used thin layer chromatography (TLC) to monitor reaction conversion, which appeared to be reliable for the formation of spirocycle **6a**, but co-elution of ynone **1a**with carbazole **5a**made the Au(I)-catalysed reaction series much more difficult to assess with confidence. Therefore, it was instead decided to monitor reaction conversion using *in situ* infrared spectroscopy using a ReactIRTM system,14 which was done by observing the decrease in intensity of the diagnostic alkyne stretch at 2202 cm-1 in the starting material **1a**. Interestingly, this experiment showed that the 16 h reaction time reported in our earlier work was needlessly long, with complete conversion into carbazole **5a** being observed in just 83 minutes using the published conditions. Thus, whilst the Au(I)-mediated reaction was still shown to be slower than analogous Ag(I)-mediated process to form **6a** (even with a higher catalyst loading), the rate difference is significantly less pronounced than was previously thought. Previous ReactIR studies had shown that the spirocyclisation to form **6a** with AgOTf is in fact complete within 30 min, 4b although to ensure full conversion was reached in the new examples in this paper, a 2 h reaction time was used as standard.



**Scheme 2** Divergent synthesis of carbazole **5a** and spirocycle **6a**.

New synthetic results confirm that the shorter reaction time for carbazole formation is general to other indole-tethered alkynes (Scheme 3). Thus, ynone starting materials **1b**–**e** (which had never been tested in this chemistry prior to this new study)15 were prepared by reacting Weinreb amide **8** with a selection of lithiated alkynes of the form **9**.4b Then, the resulting ynones **1b**–**e** were reacted with 5 mol% Ph3PAuNTf2·½tol in CH2Cl2 at RT, which furnished the expected carbazole products **5b**–**e** in high yields, with the measured reaction times (1–5 h) all being significantly shorter than those reported in our earlier paper.3a Especially pleasing was the efficient synthesis of carbazole **5e**, as an alkyl halide moiety was shown to be compatible with the chemistry for the first time; as a simple demonstration of the potential utility of this synthetic handle, carbazole **5e** was converted into tetracyclic product **10** upon treatment with sodium hydride in refluxing THF (Scheme 4). Pleasingly, the same ynones were also well tolerated in the divergent Ag(I)-catalysed series; thus, spirocycles **6b**–**e** were all prepared in high yields from ynones **1b**–**e** following reaction with 1 mol% AgOTf in CH2Cl2 for 2 h at RT. Note that isolated spirocycles of the form **6** do not react when treated with 5 mol% Ph3PAuNTf2·½tol in CH2Cl2 at RT, confirming that the carbazole products **5** are not formed simply via the rearrangement of spirocycles **6**.



**Scheme 3** Divergent synthesis of carbazoles **5b–e** and spirocycles **6b–e**.



**Scheme 4** Conversion of carbazole **5e** into tetracycle **10**

In order to rationalise the difference in behaviour between the silver and Au(I)-catalysed reactions, the C–C bond forming step was modelled using Density Functional Theory, using ynone **1a** as a representative system. The calculations demonstrated that the formation of **6a** from **1a** is under kinetic control (G298 = –93 kJ mol-1) when compared to the formation of **5a** (G298 = –228 kJ mol-1) (Scheme 5a). In the case of the Au(I)-catalysed reaction, the binding of ynone **1a** to the cationic fragment [Au(PPh3)]+ was envisaged, whereas the Ag(I)-catalysed process was modelled with the analogous group [Ag(PPh3)]+.16 Note, [Ag(PPh3)]+ was chosen for these modelling studies rather than AgOTf to significantly simplify the calculations; silver(I) complexes are kinetically labile, meaning that the precise nature of the active Ag(I) species is unclear for AgOTf, but the reaction of AgOTf with one equivalent of PPh3 results in the formation of known complex Ag(OTf)(PPh3). The validity of this system as a catalyst was confirmed experimentally by performing the reaction of **1a** with AgOTf with the addition of one equivalent of PPh3, which enabled spirocycle **6a** to be formed in quantitative yield with a 1 h reaction time. The same reaction was also monitored using ReactIR and was found to be complete in 25 minutes, and thus this catalyst system is similar to AgOTf alone (30 min, as measured by ReactIR).



**Scheme 5** DFT-calculated energies for (a) formation of compounds **5a** and **6a** from **1a** and (b) Ag(I)- and Au(I)-catalysed C–C bond formation from complex A. Energies are corrected zero-point energy-corrected electronic energies (top) and Gibbs energies at 298 K (bottom) in kJ mol-1 at the D3-PBE0/def2-TZVPP//BP86/SVP(P) level with COSMO solvent correction in CH2Cl2.

In both cases, the reference state for the calculations was taken as the *O*-bound alkyne complex **A** (Scheme 5b). The formation of the corresponding -alkyne complexes, **B**, occurs with only a small change in energy (+3 kJ mol-1) which is probably not relevant at this level of theory. The formation of slipped alkyne complexes **C** is proposed as the next step. Two transition states were found for C-C bond formation from **C**, with **tsCD** best viewed as nucleophilic attack by the 3-position of the indole ring at the carbocation in **C**. This gives the spirocyclic complexes **D**. The second transition state, **tsCE**, involved nucleophilic attack from the 2-position of the indole ring to give the carbazole precursor **E**. A subsequent keto-enol tautomerisation then gives **F**, which is the lowest energy state on this surface. Despite repeated attempts at different levels of theory, a transition state connecting complexes **D** and **E** (for both gold and silver) could not be located, which leads us to think that a 1,2-migration process probably does not operate. Such a 1,2-migration process has been proposed and calculated by DFT in a related Au(I)-catalysed cyclisation of *N*-propargyl tryptamines, in an important study by Gandon, Guinchard and co-workers,17 but it does not appear to be the case in our system.

In the case of the Au(I)-catalysed reactions, all of the states from **C** onwards on the reaction coordinate are lower in energy than the reference state and there is only a very small difference in energy between the two transition states **tsCD** and**tsCE**. Complex **DAu** is lower in energy than **EAu**, although the enolisation to form **FAu** provides a driving force to form the carbazole derivatives. The picture is somewhat different in the case of the silver complexes; here, the overall changes in energy (both E and G298) to form **DAg** and **FAg** are smaller. Furthermore, there is a much larger difference in energy between the two transition states **tsCD** and **tsCE**.

It is clear that in both cases, the formation of spirocycle **D** is a kinetically favoured process, *i.e.* proceeding through the lowest energy transition state **tsCD.** In the Au(I)-case it should be noted that the two transition states are quite close in energy and, at this level of theory could be viewed as being isoenergetic. The energetic span for the conversion of **DAg** to **EAg** is 60 kJ mol-1, whereas for **DAu** to **EAu** it is 74 kJ mol-1. It is not, therefore, the nature of these transition states which are solely dictating the outcome of the reaction. It is proposed that the nature of the product is dictated by the rates of protonation of the metal-carbon bonds in complexes **D** and **F**. In the case of the silver complexes, this must be more rapid than the subsequent isomerisation through **tsCE**, allowing for the kinetically controlled product to form. For the Au(I)-containing species, the reverse must be true and isomerisation from **D** to **F** must be faster than protonation, hence the thermodynamic product is observed.18, 19 Qualitatively, this may be related to the observation that the Ag(I)-catalysed reactions are faster than the Au(I) analogues (and suggests that protodemetallation may be rate limiting in the Au(I) systems). Of further interest, the isomerisation of **D** to **F** through ring-opened form **C** (via reversible ring opening/closing) differs to the more concerted 1,2-migration pathway that was tentatively proposed in our original study.3a,20,21

To conclude, in this study we have extended the scope of our Ag(I)/Au(I)-controlled divergent reaction system for the conversion of indole-tethered ynones into spirocycles and carbazoles, and established a new reaction protocol for the Au(I)-catalysed variant in which the reaction time is significantly reduced. The improved reaction conditions were successfully used to prepare a series of novel carbazoles and their spirocyclic analogues for the first time. DFT studies suggest that the difference in both the reaction rates and their outcomes is largely down to differences in the rate of protodemetallation, depending on the catalyst. Of further note, it appears that cyclisation of the indole (via C-2 or C-3) onto the activated alkyne is reversible, enabling the C-2 and C-3 adducts to interconvert via a ring opening/ring closing equilibrium. This mechanistic explanation differs to that proposed in our original study,3a and we hope that these new results will help to inform related synthetic studies involving both alkyne activation and indole dearomatisation.

The experimental section has no title; please leave this line here.

Except where stated, all reagents were purchased from commercial sources and used without further purification. Dichloromethane was obtained from an Innovative Technology Inc. PureSolv® solvent purification system. Anhydrous THF was obtained by distillation over sodium and benzophenone immediately before use. 1H NMR (400 MHz) and 13C NMR (100 MHz) spectra were recorded on a JEOL ECX400 or JEOL ECS400 spectrometer. All spectral data was acquired at 295 K. Chemical shifts (δ) are quoted in parts per million (ppm). The residual solvent peak, δH 7.26 and δC 77.0 for CDCl3. Coupling constants (*J*) are reported in Hertz (Hz) to the nearest 0.1 Hz. Signal assignment was achieved by analysis of DEPT, COSY, HMBC and HSQC experiments where required. Infrared (IR) spectra were recorded on a PerkinElmer UATR 2 Spectrometer as a thin film dispersed from either CH2Cl2 or CDCl3. Mass spectra (high-resolution) were obtained by the University of York Mass Spectrometry Service, using Electrospray Ionisation (ESI) on a Bruker Daltonics, Micro-tof spectrometer. Melting points (Mp) were determined using Gallenkamp apparatus and Mettler Toledo DSC822e. Thin layer chromatography was carried out on Merck silica gel 60F254 pre-coated aluminium foil sheets and were visualised using UV light (254 nm) and stained with basic aqueous potassium permanganate. Flash column chromatography was carried out using slurry packed Fluka silica gel (SiO2), 35–70 μm, 60 Å, under a light positive pressure, eluting with the specified solvent system. For synthetic procedures and spectroscopic data for compounds **8**, **1a**, **5a** and **6a** see reference 4b.

**Procedures**

**General procedure A: ynone synthesis.** To a stirred solution of a suitable terminal alkyne (6.89 mmol) in THF (10 mL) at −78 °C under argon was added n-BuLi (2.4 mL, 5.73 mmol, 2.4 M in hexanes) dropwise. The mixture was stirred for 30 min at −78 °C and then transferred via cannula to a −78 °C solution of a Weinreb amide (500 mg, 2.29 mmol) in THF (10 mL). Upon complete transfer of the lithiated alkyne, the mixture was warmed to RT and stirred for the specified amount of time. The reaction was quenched by the careful addition of sat. aq. NH4Cl (20 mL). The organics were separated and the aqueous layer was extracted with EtOAc (3 × 15 mL). The organics were combined, washed with brine (15 mL), dried over MgSO4, concentrated in vacuo and purified by column chromatography to afford the ynone product.

**General procedure B: carbazole synthesis.** To a solution of ynone (0.193 mmol) in CH2Cl2 (2 mL) was added Ph3PAu(NTf2)·½tol (7.5 mg, 9.64 µmol). The reaction mixture was stirred under air at RT for the specified amount of time until completion was observed by TLC. The reaction mixture was concentrated *in vacuo* and purified by column chromatography to afford the desired carbazole product.

**General procedure C: spirocycle synthesis.** To a solution of ynone (0.30 mmol) in CH2Cl2 (3 mL) was added AgOTf (1.5 mg, 6 µmol). The reaction mixture was stirred under air at RT for 2 h. The reaction mixture was concentrated *in vacuo* and purified by column chromatography to afford the desired spirocyclic product.

**4-Cyclopentyl-1-(1*H*-indol-3-yl)but-3-yn-2-one (1b)**

Synthesised using general procedure A with ethynylcyclopentane (0.80 mL, 6.89 mmol), THF (20 mL), 2-(1*H*-indol-3-yl)-*N*-methoxy-*N*-methylacetamide **8** (500 mg, 2.29 mmol) and *n*-BuLi (2.4 mL, 5.73 mmol, 2.4 M in hexanes) stirring at RT for 30 min. Purification by column chromatography (9:1 hexane:EtOAc, then 2:1 hexane:EtOAc) afforded the *title compound* **1b** as a pink solid (403 mg, 70%)

Mp 103–105 °C; Rf = 0.45 (hexane:EtOAc, 2:1).

IR (ATR): 3279, 2961, 2870, 2205, 1660, 1457, 1339, 1246, 1181, 739 cm-1.

1H NMR (400 MHz, CDCl3): δ = 1.48–1.59 (m, 4 H), 1.60–1.68 (m, 2 H), 1.82–1.91 (m, 2 H), 2.65–2.73 (m, 1 H), 3.98 (s, 2 H), 7.12–7.17 (m, 2 H), 7.19–7.24 (m, 1 H), 7.37 (d, J = 8.4 Hz, 1 H), 7.62 (d, J = 7.6 Hz, 1 H), 8.20 (br s, 1 H).

13C NMR (100 MHz, CDCl3): δ = 25.1, 29.9, 33.0, 42.0, 80.4, 100.0, 107.8, 111.2, 118.9, 119.6, 122.2, 123.5, 127.4, 136.1, 186.1.

HRMS (ESI): m/z [M + H]+ calcd for C17H18NO: 252.1382; found: 252.1383.

**4-(4-Fluorophenyl)-1-(1*H*-indol-3-yl)but-3-yn-2-one (1c)**

Synthesised using general procedure A with 1-ethynyl-4-fluorobenzene (0.80 mL, 6.89 mmol), THF (20 mL), 2-(1*H*-indol-3-yl)-*N*-methoxy-*N*-methylacetamide **8** (500 mg, 2.29 mmol) and *n*-BuLi (2.4 mL, 5.73 mmol, 2.4 M in hexanes) stirring at RT for 30 min. Purification by column chromatography (9:1 hexane:EtOAc, then 2:1 hexane:EtOAc) afforded the *title compound* **1c** as a yellow solid (381 mg, 60%)

Mp 126–128 °C; R*f* = 0.48 (hexane:EtOAc, 2:1).

IR (ATR): 3408, 2203, 1657, 1599, 1505, 1458, 1232, 1156, 1094, 837, 743 cm-1.

1H NMR (400 MHz, CDCl3): δ = 4.09 (s, 2 H), 6.98–7.04 (m, 2 H), 7.15–7.20 (m, 2 H), 7.22–7.27 (m, 2 H), 7.30–7.35 (m, 2 H), 7.41 (d, *J* = 8.4 Hz, 1 H), 7.68 (d, *J* = 7.6 Hz, 1 H), 8.22 (br s, 1 H).

13C NMR (100 MHz, CDCl3): δ = 41.9, 87.8, 91.0, 107.7, 111.3, 115.9 (d, 4*J*CF = 3.8 Hz), 116.0 (d, 2*J*CF = 22.0 Hz), 118.9, 119.9, 122.3, 123.7, 127.4, 135.4 (d, 3*J*CF = 8.5 Hz), 136.1, 163.9 (d, 1*J*CF = 3.8 Hz), 185.5.

HRMS (ESI): *m*/*z* [M + H]+ calcd for C18H13FNO: 278.0979; found: 278.0976.

**1-(1*H*-Indol-3-yl)-4-(3-methoxyphenyl)but-3-yn-2-one (1d)**

Synthesised using general procedure A with 1-ethynyl-3-methoxybenzene (0.86 mL, 6.89 mmol), THF (20 mL), 2-(1*H*-indol-3-yl)-*N*-methoxy-*N*-methylacetamide **8** (500 mg, 2.29 mmol) and *n*-BuLi (2.4 mL, 5.73 mmol, 2.4 M in hexanes) stirring at RT for 30 min. Purification by column chromatography (9:1 hexane:EtOAc, then 2:1 hexane:EtOAc) afforded the *title compound* **1d** as a brown solid (570 mg, 86%)

Mp 56–58 °C; R*f* = 0.48 (hexane:EtOAc, 2:1).

IR (ATR): 3408, 2192, 1660, 1575, 1457, 1224, 1094, 1039, 743 cm-1.

1H NMR (400 MHz, CDCl3): δ = 3.76 (s, 3 H), 4.10 (s, 3 H), 6.83–6.85 (m, 1 H), 6.95–7.00 (m, 2 H), 7.16–7.26 (m, 4 H), 7.40 (d, *J* = 8.4 Hz, 1 H), 7.69 (d, *J* = 8.4 Hz, 1 H), 8.25 (br s, 1 H).

13C NMR (100 MHz, CDCl3): δ = 41.9, 55.3, 87.6, 92.0, 107.6, 111.3, 117.3, 117.6, 118.9, 119.8, 120.8, 122.3, 123.7, 125.6, 127.4, 129.6, 136.1, 159.2, 185.6.

HRMS (ESI): *m*/*z* [M + H]+ calcd for C19H16NO2: 290.1175; found: 290.1176.

**7-Chloro-1-(1*H*-indol-3-yl)hept-3-yn-2-one (1e)**

Synthesised using general procedure A with 5-chloropent-1-yne (0.73 mL, 6.89 mmol), THF (20 mL), 2-(1*H*-indol-3-yl)-*N*-methoxy-*N*-methylacetamide **8** (500 mg, 2.29 mmol) and *n*-BuLi (2.4 mL, 5.73 mmol, 2.4 M in hexanes) stirring at RT for 30 min. Purification by column chromatography (9:1 hexane:EtOAc, then 2:1 hexane:EtOAc) afforded the *title compound* **1e** as a brown solid (375 mg, 63%)

Mp 43–45 °C; R*f* = 0.40 (hexane:EtOAc, 2:1).

IR (ATR): 3408, 2212, 1664, 1457, 1339, 1240, 1164, 1095, 1010, 743 cm-1.

1H NMR (400 MHz, CDCl3): δ = 1.83 (app. pentet, *J* = 6.9 Hz, 2 H), 2.46 (t, *J* = 6.9 Hz, 2 H), 3.38 (t, *J* = 6.9 Hz, 2 H), 3.97 (s, 2 H), 7.13–7.18 (m, 2 H), 7.20–7.25 (m, 1 H), 7.38 (d, *J* = 8.4 Hz, 1 H), 7.60 (d, *J* = 7.6 Hz, 1 H), 8.22 (br s, 1 H).

13C NMR (100 MHz, CDCl3): δ = 16.3, 30.1, 42.0, 43.0, 81.3, 93.2, 107.6, 111.3, 118.8, 119.8, 122.3, 123.6, 127.3, 136.1, 185.7.

HRMS (ESI): *m*/*z* [M + Na]+ calcd for C15H1435CINNaO: 282.0659; found: 282.0656.

**1-Cyclopentyl-9*H*-carbazol-3-ol (5b)**

Synthesised using general procedure B with 4-cyclopentyl-1-(1*H*-indol-3-yl)but-3-yn-2-one **1b** (48.5 mg, 0.193 mmol), Ph3PAu(NTf2)·½tol (7.5 mg, 4.82 µmol), CH2Cl2 (2 mL) at RT for 2.5 h. Purification by column chromatography (9:1 hexane:EtOAc, then 2:1 hexane:EtOAc) afforded the *title compound* **5b** as a brown solid (48.5 mg, 100%).

Mp 108–110 °C; R*f* = 0.45 (hexane:EtOAc, 2:1).

IR (ATR): 3433, 3232, 2950, 1583, 1423, 1390, 1314, 1176, 1150, 1112, 916, 850 cm-1.

1H NMR (400 MHz, CDCl3): δ = 1.72–1.84 (m, 4 H), 1.84–1.94 (m, 2 H), 2.13–2.23 (m, 2 H), 3.34 (pentet, *J* = 7.4 Hz, 1 H), 4.85 (s, 1 H), 6.91 (d, *J* = 3.0 Hz, 1 H), 7.17–7.22 (m, 1 H), 7.34 (d, *J* = 2.3 Hz, 1 H), 7.39–7.43 (m, 1 H), 7.43–7.44 (m, 1 H), 7.92 (br s, 1 H), 7.97 (d, *J* = 7.6 Hz, 1 H).

13C NMR (100 MHz, CDCl3): δ = 25.3, 32.7, 41.0, 103.0, 110.7, 111.8, 119.0, 120.4, 123.4, 123.6, 125.7, 129.1, 129.6, 133.3, 134.0, 140.0, 149.4.

HRMS (ESI): *m*/*z* [M + Na]+ calcd for C17H17NNaO: 274.1203; found: 274.1202.

**1-(4-Fluorophenyl)-9*H*-carbazol-3-ol (5c)**

Synthesised using general procedure B with 4-(4-fluorophenyl)-1-(1*H*-indol-3-yl)but-3-yn-2-one **1c** (53.5 mg, 0.193 mmol), Ph3PAu(NTf2)·½tol (7.5 mg, 9.64 µmol), CH2Cl2 (2 mL) at RT for 5 h 20 min. Purification by column chromatography (9:1 hexane:EtOAc, then 2:1 hexane:EtOAc) afforded the *title compound* **5c** as an orange solid (47 mg, 88%).

Mp 136–138 °C; R*f* = 0.39 (hexane:EtOAc, 2:1).

IR (ATR): 3462, 1607, 1514, 1494, 1317, 1221, 1156, 834 cm-1.

1H NMR (400 MHz, CDCl3): δ = 4.88 (s, 1 H), 6.97 (d, *J* = 2.3 Hz, 1 H), 7.20–7.26 (m, 3 H), 7.38–7.44 (m, 2 H), 7.50 (d, *J* = 2.3 Hz, 1 H), 7.59–7.65 (m, 2 H), 8.01 (d, *J* = 7.6 Hz, 1 H), 8.05 (br s, 1 H).

13C NMR (100 MHz, CDCl3): δ = 105.0, 110.8, 114.6, 116.1, 116.2 (d, 2*J*CF = 22 Hz), 119.3, 120.5, 123.2, 124. 6, 124.7, 126.2, 129.8, 129.9 (d, 3*J*CF = 7.8 Hz), 132.3, 134.5 (d, 4*J*CF = 3.0 Hz), 140.3, 149.5, 162.3 (d, 1*J*CF = 247 Hz).

HRMS (ESI): *m*/*z* [M + H]+ calcd for C18H13FNO: 278.0979; found: 279.0976.

**1-(3-Methoxyphenyl)-9*H*-carbazol-3-ol (5d)**

Synthesised using general procedure B with 1-(1*H*-indol-3-yl)-4-(3-methoxyphenyl)but-3-yn-2-one **1d** (55.8 mg, 0.193 mmol), Ph3PAu(NTf2)·½tol (7.5 mg, 9.64 µmol), CH2Cl2 (2 mL) at RT for 2.5 h. Purification by column chromatography (9:1 hexane:EtOAc, then 2:1 hexane:EtOAc) afforded the *title compound* **5d** as a brown solid (46.3 mg, 83%).

Mp 169–171 °C; R*f* = 0.38 (hexane:EtOAc, 2:1).

IR (ATR): 3369, 1596, 1484, 1456, 1408, 1318, 1243, 1171, 1036, 778 cm-1.

1H NMR (400 MHz, CDCl3): δ = 3.90 (s, 3 H), 4.85 (s, 1 H), 7.00 (dd, *J* = 8.3, 2.3 Hz, 1 H), 7.04 (d, *J* = 2.5 Hz, 1 H), 7.19–7.24 (m, 2 H), 7.26–7.29 (m, 1 H), 7.37–7.42 (m, 2 H), 7.47 (dd, *J* = 8.0, 8.0 Hz, 1 H), 7.51 (d, *J* = 2.3 Hz, 1 H), 8.02 (d, *J* = 7.6 Hz, 1 H), 8.19 (br s, 1 H).

13C NMR (100 MHz, CDCl3): δ = 55.4, 105.0, 110.8, 113.1, 114.0, 114.5, 119.1, 120.5, 120.6, 123.2, 124.5, 125.5, 126.1, 130.3, 132.2, 140.0, 140.3, 149.5, 160.2.

HRMS (ESI): *m*/*z* [M + H]+ calcd for C19H16NO2: 290.1176; found: 290.1176.

**1-(3-Chloropropyl)-9*H*-carbazol-3-ol (5e)**

Synthesised using general procedure B with 7-chloro-1-(1*H*-indol-3-yl)hept-3-yn-2-one **1e** (50 mg, 0.193 mmol), Ph3PAu(NTf2)·½tol (7.5 mg, 9.64 µmol), CH2Cl2 (2 mL) at RT for 1 h. Purification by column chromatography (9:1 hexane:EtOAc, then 2:1 hexane:EtOAc) afforded the *title compound* **5e** as an off-white solid (49.1 mg, 98%).

Mp 131–133 °C; R*f* = 0.41 (hexane:EtOAc, 2:1).

IR (ATR): 3388, 1627, 1599, 1502, 1456, 1438, 1314, 1232, 1172, 1149, 1112, 848, 749 cm-1.

1H NMR (400 MHz, CDCl3): δ = 2.24 (app. pentet, *J* = 6.9 Hz, 2 H), 3.06 (t, *J* = 6.9 Hz, 2 H), 3.61 (t, *J* = 6.9 Hz, 2 H), 4.68 (s, 1 H), 6.84 (d, *J* = 3.0 Hz, 1 H), 7.18–7.23 (m, 1 H), 7.38–7.40 (m, 1 H), 7.42 (dd, *J* = 6.9, 1.5 Hz, 1 H), 7.44–7.47 (m, 1 H), 7.98 (d, *J* = 7.6 Hz, 1 H), 8.04 (br s, 1 H).

13C NMR (100 MHz, CDCl3): δ = 27.8, 32.4, 44.6, 103.8, 110.9, 114.8, 119.1, 120.4, 123.3, 123.6, 124.0, 126.0, 133.6, 140.2, 149.4.

HRMS (ESI): *m*/*z* [M + Na]+ calcd for C15H1435ClNNaO: 282.0648; found: 282.0656.

**5,6-Dihydro-4*H*-pyrido[3,2,1-jk]carbazol-2-ol (10)**

To a microwave vial containing carbazole **5e** (21 mg, 0.81 mmol) in THF (3 mL) under argon was added NaH (3.2 mg, 0.81 mmol). The sealed microwave vial containing the reaction mixture was then heated to reflux for 20 h. The reaction was quenched by the addition of sat. aq. NH4Cl (5 mL). The organics were separated and the aqueous layer was extracted with EtOAc (3 × 10 mL). The organics were combined, washed with brine (10 mL), dried over MgSO4, concentrated *in vacuo* and purified by column chromatography (9:1 hexane:EtOAc, then 1:1 hexane:EtOAc) to afford the *title compound* **10** as a brown solid (15 mg, 83%).

Mp 142–144 °C; R*f* = 0.41 (hexane:EtOAc, 2:1).

IR (ATR): 3326, 2933, 1630, 1600, 1492, 1474, 1454, 1440, 1356, 1297, 1247, 1071, 946, 744 cm-1.

1H NMR (400 MHz, CDCl3): δ = 2.30 (app. pentet, *J* = 6.1 Hz, 2 H), 3.03 (t, *J* = 6.1 Hz, 2 H), 4.20 (t, *J* = 6.1 Hz, 2 H), 4.71(br s, 1 H), 6.79–6.81 (m, 1 H), 7.18 (dd, *J* = 7.6, 7.6 Hz, 1 H), 7.33 (d, *J* = 2.3 Hz, 1 H), 7.36 (d, *J* = 7.6 Hz, 1 H), 7.42–7.47 (m, 1 H), 8.01 (d, *J* = 7.6 Hz, 1 H).

13C NMR (100 MHz, CDCl3): δ = 22.5, 24.9, 40.8, 103.2, 108.2, 112.5, 117.0, 120.7, 120.9, 121.7, 122.3, 125.3, 132.9, 140.3, 149.1.

HRMS (ESI): *m*/*z* [M + Na]+ calcd for C15H14NO: 224.1072; found: 224.1070.

**1-Phenylspiro[cyclopent[5]ene-2,3'-indol]-4-one (6a)**

Synthesised using general procedure C with 4-phenyl-1-(1*H*-indol-3-yl)but-3-yn-2-one **1b** (155 mg, 0.60 mmol), AgOTf (1.5 mg, 6.0 µmol) and PPh3 (157 mg, 0.60 mmol) in CH2Cl2 (6 mL) at RT for 1 h. Purification by column chromatography (1:4 hexane:Et2O) afforded the *title compound* **6a** (150 mg, 100%), whose spectroscopic data were identical to those previously reported.4b

**1-Cyclopentylspiro[cyclopent[5]ene-2,3'-indol]-4-one (6b)**

Synthesised using general procedure C with 4-cyclopentyl-1-(1*H*-indol-3-yl)but-3-yn-2-one **1b** (75 mg, 0.30 mmol), AgOTf (1.5 mg, 6.0 µmol) in CH2Cl2 (3 mL) at RT for 2 h. Purification by column chromatography (1:4 hexane:Et2O) afforded the *title compound* **6b** as a yellow solid (75 mg, 100%).

Mp 89–91 °C; R*f* = 0.38 (100% Et2O).

IR (ATR): 2955, 2869, 1717, 1693, 1604, 1548, 1453, 1247, 1194, 760 cm-1.

1H NMR (400 MHz, CDCl3): δ = 1.28–1.48 (m, 5 H), 1.57–1.69 (m, 2 H), 1.70–1.79 (m, 2 H), 2.64 (d, *J* = 18.8 Hz, 1 H), 2.92 (d, *J* = 18.8 Hz, 1 H), 6.31 (s, 1 H), 7.23 (d, *J* = 7.3 Hz, 1 H), 7.31 (dd, *J* = 7.3, 7.3 Hz, 1 H), 7.43 (dd, *J* = 7.8, 7.3 Hz, 1 H), 7.71 (d, *J* = 7.8 Hz, 1 H), 8.01 (s, 1 H).

13C NMR (100 MHz, CDCl3): δ = 25.2, 33.9, 34.1, 40.12, 40.13, 40.5, 68.0, 121.6, 121.9, 127.1, 129.0, 129.4, 139.6, 155.7, 173.3, 185.2, 205.8.

HRMS (ESI): *m*/*z* [M + H]+ calcd for C17H18NO: 252.1386; found: 252.1383.

**2-(4-Fluorophenyl)spiro[cyclopent[2]ene-1,3'-indol]-4-one (6c)**

Synthesised using general procedure C with 4-(4-fluorophenyl)-1-(1*H*-indol-3-yl)but-3-yn-2-one **1c** (83 mg, 0.30 mmol), AgOTf (1.5 mg, 6.0 µmol) in CH2Cl2 (3 mL) at RT for 2 h. Purification by column chromatography (1:4 hexane:Et2O) afforded the *title compound* **6c** as a pink solid (80 mg, 96%).

Mp 122–124 °C; R*f* = 0.38 (100% Et2O).

IR (ATR): 3072, 1693, 1601, 1507, 1237, 1163, 1194, 908, 834, 759 cm-1.

1H NMR (400 MHz, CDCl3): δ = 2.67 (d, *J* = 18.7 Hz, 1 H), 3.04 (d, *J* = 18.7 Hz, 1 H), 6.79 (s, 1 H), 6.83–6.89 (m, 2 H), 6.93–6.99 (m, 2 H), 7.23 (d, *J* = 7.3 Hz, 1 H), 7.29 (dd, *J* = 7.3, 7.3 Hz, 1 H), 7.45 (dd, *J* = 7.8, 7.3 Hz, 1 H), 7.77 (d, *J* = 7.8 Hz, 1 H), 8.19 (s, 1 H).

13C NMR (100 MHz, CDCl3): δ = 42.3, 65.9, 116.1 (d, 2*J*CF = 22.0 Hz), 121.5, 122.2, 127.8, 128.5 (d, 4*J*CF = 3.0 Hz), 129.0 (d, 3*J*CF = 8.6 Hz), 129.2, 130.5, 140.6, 154.8, 164.3 (d, 1*J*CF = 254 Hz), 170.5, 173.9, 204.0.

HRMS (ESI): *m*/*z* [M + H]+ calcd for C18H13FNO: 278.0980; found: 278.0976.

**2-(3-Methoxyphenyl)spiro[cyclopent[2]ene-1,3'-indol]-4-one (6d)**

Synthesised using general procedure C with 1-(1*H*-indol-3-yl)-4-(3-methoxyphenyl)but-3-yn-2-one **1d** (87 mg, 0.30 mmol), AgOTf (1.5 mg, 6.0 µmol) in CH2Cl2 (3 mL) at RT for 2 h. Purification by column chromatography (1:4 hexane:Et2O) afforded the *title compound* **6d** as a yellow oil (87 mg, 100%).

R*f* = 0.35 (100% Et2O).

IR (ATR): 1720, 1693, 1572, 1547, 1455, 1288, 1252, 1205, 1038, 909, 843, 773 cm-1.

1H NMR (400 MHz, CDCl3): δ = 2.68 (d, *J* = 18.7 Hz, 1 H), 3.04 (d, *J* = 18.7 Hz, 1 H), 3.51 (s, 3 H), 6.31–6.34 (m, 1 H), 6.69 (d, *J* = 7.8 Hz, 1 H), 6.81–6.85 (m, 2 H), 7.11 (dd, *J* = 8.0, 7.8 Hz, 1 H), 7.24–7.32 (m, 2 H), 7.44 (dd, *J* = 7.8, 7.3 Hz, 1 H), 7.76 (d, *J* = 7.8 Hz, 1 H), 8.19 (s, 1 H).

13C NMR (100 MHz, CDCl3): δ = 42.2, 54.9, 65.9, 111.1, 117.7, 119.3, 121.6, 122.0, 127.7, 129.1, 129.8, 130.9, 133.5, 140.9, 154.9, 159.5, 171.8, 174.2, 204.3.

HRMS (ESI): *m*/*z* [M + H]+ calcd for C19H16NO2: 290.1174; found: 290.1176.

**2-(3-Chloropropyl)spiro[cyclopent[2]ene-1,3'-indol]-4-one (6e)**

Synthesised using general procedure C with 7-chloro-1-(1*H*-indol-3-yl)hept-3-yn-2-one **1e** (78 mg, 0.30 mmol), AgOTf (1.5 mg, 6.0 µmol) in CH2Cl2 (3 mL) at RT for 2 h. Purification by column chromatography (100% Et2O) afforded the *title compound* **1e** as a yellow oil (62.5 mg, 80%).

R*f* = 0.23 (100% Et2O).

IR (ATR): 2923,1718, 1693, 1612, 1550, 1456, 1250, 1193, 906, 756, 729 cm-1.

1H NMR (400 MHz, CDCl3): δ = 1.77–1.92 (m, 4 H), 2.67 (d, *J* = 18.9 Hz, 1 H), 2.94 (d, *J* = 18.9 Hz, 1 H), 3.33–3.45 (m, 2 H), 6.32 (s, 1 H), 7.22 (d, *J* = 7.5 Hz, 1 H), 7.33 (dd, *J* = 7.5, 7.5 Hz, 1 H), 7.45 (dd, *J* = 7.5, 7.5 Hz, 1 H), 7.72 (d, *J* = 7.5 Hz, 1 H), 7.97 (s, 1 H).

13C NMR (100 MHz, CDCl3): δ = 25.9, 29.9, 40.3, 43.4, 67.6, 121.5, 121.8, 127.5, 129.2, 131.3, 139.0, 155.5, 172.9, 178.1, 205.2.

HRMS (ESI): *m*/*z* [M + H]+ calcd for C15H1535ClNO: 260.0839; found: 260.0837.

Funding Information

This work was conducted using funding from EPSRC (EP/M018601/01, J. T. R. L. and EP/R013748/1, A. K. C.), the University of York (J. A. R.-A., A. K. C., W. P. U.), and the Leverhulme Trust (Early Career Fellowship, ECF-2015-13, W. P. U.)

Supporting Information

Details of the computational methods, energies, xyz coordinates and vibrational modes for calculated structures.

References

1. Mahatthananchai, J.; Dumas, A. M.; Bode, J. W. *Angew. Chem., Int. Ed*. **2012**, *51*, 10954.
2. For recent catalyst selective synthesis methods, see: (a) Dooley. J.D.; Chidipudi S. R.; Lam, H. W. *J. Am. Chem. Soc*. **2013**, *135*, 10829. (b) Cheng, Q-Q.; Yedoyan, J.; Arman, H.; Doyle, M. P. *J. Am. Chem. Soc*. **2016**, *138*, 44. (c) Zhan, G.; Shi, M-L.; He, Q.; Lin, W-J.; Ouyang, Q.; Du, W.; Chen, Y-C. *Angew. Chem., Int. Ed*. **2016**, *55*, 2147. (d) Liao, J-Y.; Ni, Q.; Zhao, Y. *Org. Lett*. **2017**, *19*, 4074; (e) Mishra, U. K.; Yadav, S.; Ramasastry, S. S. V. *J. Org. Chem*. **2017**, *82*, 6729. (f) Feng, J-J.; Zhang, J. *ACS Catal*. **2017**, *7*, 1533.
3. For examples from our groups, see: (a) Liddon, J. T. R.; James, M. J.; Clarke, A. K.; O’Brien, P.; Taylor, R. J. K.; Unsworth, W. P. *Chem. Eur. J*. **2016**, *22*, 8777. (b) James, M. J.; O’Brien, P.; Taylor, R. J. K.; Unsworth, W. P*. Angew. Chem., Int. Ed*. **2016**, *55*, 9671. (c) Clarke, A. K.; Taylor, R. J. K.; Unsworth, W. P. *Tetrahedron* **2018**, DOI: 10.1016/j.tet.2018.02.003
4. For related papers on the cyclisation of electron-rich aromatics onto tethered alkynes from our groups, see: (a) Unsworth, W. P.; Cuthbertson, J. D.; Taylor, R. J. K. *Org. Lett*. **2013**, *15*, 3306. (b) James, M. J.; Cuthbertson, J. D.; O’Brien, P.; Taylor, R. J. K.; Unsworth, W. P. *Angew. Chem., Int. Ed*. **2015**, *54*, 7640. (c) James, M. J.; Clubley, R. E.; Palate, K. Y.; Procter, T. J.; Wyton, A. C.; O’Brien, P.; Taylor, R. J. K.; Unsworth, W. P. Org. Lett. 2015, 17, 4372. (d) Clarke, A. K.; James, M. J.; O’Brien, P.; Taylor, R. J. K.; Unsworth, W. P. *Angew. Chem., Int. Ed*. **2016**, *55*, 13798. (e) James, M. J.; Grant, N. D.; O’Brien, P.; Taylor, R. J. K.; Unsworth, W. P. *Org. Lett*. **2016**, *18*, 6256. (f) Liddon, J. T. R.; Clarke, A. K.; Taylor, R. J. K.; Unsworth, W. P. *Org. Lett*. **2016**, *18*, 6328. (g) Clarke, A. K.; Liddon, J. T. R.; Cuthbertson, J. D.; Taylor, R. J. K.; Unsworth, W. P. *Org. Biomol. Chem*. **2017**, *15*, 233.
5. For important contributions from other groups, see: (a) Zhang, X.; Larock, R. C.; *J. Am. Chem. Soc*. **2005**, *127*, 12230. (b) Dohi, T.; Nakae, T.; Ishikado, Y.; Kato, D.; Kita, Y. *Org. Biomol. Chem*., **2011**, *9*, 6899 (c) Peshkov, V. A.; Pereshivko, O. P.; Van der Eycken, E. V. *Adv. Synth. Catal.* **2012**, *354*, 2841. (d) Schröder, F.; Erdmann, N.; Noël, T.; Luque, R.; Van der Eycken, E., *Adv. Synth. Catal.* **2015**, *357*, 3141. (e) Schröder, F.; Sharma, U.; Mertens, M.; Devred, F.; Debecker, D.; Luque, R.; Van der Eycken, E. *ACS Catal.* **2016**, *6*, 8156. (f) Magne, V.; Blanchard, F.; Marinetti, A.; Voituriez, A.; Guinchard, X. *Adv. Synth. Catal.* **2016**, *358*, 3355. (g) He, Y.; Li, Z.; Tian, G.; Song, L.; Van Meervelt, L.; Van der Eycken, E. V. *Chem. Commun*. **2017**, *53*, 6413. (h) Jha, M.; Dhiman, S.; Cameron, T. S.; Kumar, D.; Kumar, A. *Org. Lett.* **2017**, *19*, 2038. (i) He, Y.; Robeyns, K.; Van Meervelt, L.; Van der Eycken, E. V. *Angew. Chem. Int. Ed.* **2018**, *57*, 272. (j) Vacala, T. L.; Carlson, P. R.; Arreola-Hester, A.; Williams, C, G.; Makhoul, E. W. Vadola, P. A. *J. Org. Chem.* **2018**, *83*, 1493.
6. For related methods to prepare carbazoles, see: (a) Wang, L.; Li, G.; Liu, Y.; *Org. Lett*. **2011**, *13*, 3786. (b) Hashmi, A. S. K.; Yang, W.; Rominger, F. *Chem. Eur. J*. **2012**, *18*, 6576. (c) Qiu, Y.; Fu, C.; Zhang, X.; Ma, S. *Chem. Eur. J*. **2014**, *20*, 10314. (d) Suarez, A.; Suarez-Pantiga, S.; Nieto-Faza, O.; Sanz, R. *Org. Lett.* **2017**, *19*, 5074. (e) Tharra, P.; Baire, B. *Org. Lett.* **2018**, *20*, 1118.
7. James, M. J.; O’Brien, P.; Taylor, R. J. K.; Unsworth, W. P. *Chem. Eur. J*. **2016**, *22*, 2856.
8. A Brønsted acid catalysed variant of this quinoline-forming rearrangement was subsequently developed, see: Fedoseev, P.; Van der Eycken, E. *Chem. Commun.* **2017**, *53*, 7732.
9. For reviews on dearomatisation reactions, see: (a) Liang, X.-W.; Zheng, C.; You, S.-L. *Chem. Eur. J*. **2016**, *22*, 11918. (b) Roche, S. P.; Youte Tendoung, J.-J.; Tréguier, B. *Tetrahedron* **2015**, *71*, 3549. (c) Zhuo, C.-X.; Zhang, W.; You, S.-L. *Angew. Chem., Int. Ed*. **2012**, *51*, 12662. (d) Zhuo, C. X.; Zheng, C.; You, S.-L. *Acc. Chem. Res*. **2014**, *47*, 2558. (e) Zheng, C. You, S.-L. *Chem* **2016** *1*, 830.
10. For the synthesis and biological properties of spirocycles, see reference 7 and: (a) Rios, R. *Chem. Soc. Rev.* **2012**, *41*, 1060. (b) Franz, A. K.; Hanhan, N. V.; Ball-Jones, N. R. *ACS Catal.* **2013**, *3*, 540. (c) Zheng, Y.; Tice, C. M.; Singh, S. B. *Bioorg. Med. Chem. Lett*. **2014**, *24*, 3673. (d) Zheng, Y.-J.; Tice, C. M. *Expert Opin. Drug Discov*. **2016**, *11*, 831. (e) Chambers, S. J.; Coulthard, G.; Unsworth, W. P.; O’Brien, P.; Taylor, R. J. K. *Chem. Eur. J*. **2016**, *22*, 6496. (f) Müller, G.; Berkenbosch, T.; Benningshof, J. C. J.; Stumpfe, D.; Bajorath, J. *Chem. Eur. J*. **2017**, *23*, 703. (g) Adams, K.; Ball, A. K.; Birkett, J.; Brown, L.; Chappell, B.; Lo, P. K. T.; Patmore, N. J.; Rice, C. R.; Ryan, J.; Raubo, P.; Sweeney, J. S. *Nat. Chem.* **2017**, *9*, 369.
11. Mézailles, N.; Ricard, L.; Gagosz, F. *Org. Lett.* **2005**, *7*, 4133.
12. Gronnier, C.; Faudot dit Bel, P.; Henrion, G.; Kramer, S.; Gagosz, F. *Org. Lett.* **2014**, *16*, 2092.
13. For reviews on gold catalysis, see: (a) Fürstner, A. *Chem. Soc. Rev.* **2009**, *38*, 3208. (b) Jiménez-Núñez, E.; Echavarren, A. M. *Chem. Rev.* **2008**, *108*, 3326. (c) Li, Z.; Brower, C.; He, C. *Chem. Rev.* **2008**, *108*, 3351.
14. For the use of ReactIRTM to monitor similar reactions, see reference 4d and: Unsworth, W. P.; Kitsiou, C.; Taylor, R. J. K. *Org. Lett*. **2013**, *15*, 258
15. Ynones **1b**, **1d** and **1e** are novel compounds. Ynone **1c** has been used in a related study by Van der Eycken and co-workers (reference 8).
16. (a) For the structural characterisation of silver(I) phosphine complexes see: (a) Bardajı́, M.; Crespo, O.; Laguna, A.; Fische, A. K. *Inorg. Chim. Acta* **2000**, *304*, 7; (b) Lettko, L.; Wood, J. S.; Rausch, M. D*. Inorg. Chim. Acta* **2000**, *308*, 37.
17. Magné, V.; Marinettim A.; Gandon, V.; Voituriez, A.; Guinchard, X. *Adv. Synth. Catal.* **2017**, *359*, 4036.
18. Unfortunately, we were unable to directly observe a spirocyclic intermediate during the earlier described ReactIR studies on the Au(I) reaction system.
19. To corroborate this, we had hoped that adding 1 equivalent of propanoic acid to the typical Au(I) mediated reaction of **1a** would enable spirocycle **6a** to be produced, rather than carbazole **5a**,by facilitating protodemetallation, but carbazole **5a** was the only product isolated in this reaction.
20. For a similar stepwise rearrangement involving the overall 1,2-migration of aza-spiroindolenines, see: Wu, Q.-F.; Zheng, C.; Zhuo, C.-X.; You, S.-L. *Chem. Sci*. **2016**, *7*, 4453.
21. The protodemetallation step itself was not modelled. Because the nature of the base that is needed to facilitate the proton shuffle from the indolenine nitrogen to the carbon-metal bond is unclear, such calculations would fail to give meaningful results. Examination of the predicted structures of **D** revealed that there are no elemental intramolecular steps that could lead to protodemetallation, therefore the proton shuffle is likely to be intermolecular.

**Checklist (have these on hand for manuscript submission in ScholarOne):**

* cover letter, including a statement of the work’s significance
* full mailing address, telephone and fax numbers, and e-mail address of the corresponding author
* email address for each author
* original Word file
* original graphics files zipped into one zip file
* eye-catching graphical abstract as an individual file
* 5–8 key words
* separate Supporting Information file
* separate zipped Primary Data files including cover sheet (optional)

**Useful links:**

* [SYNTHESIS homepage](http://www.thieme.de/de/synthesis/journal-information-55920.htm)
* [SYNTHESIS information and tools for authors](http://www.thieme.de/de/synthesis/authors-55962.htm)
* [Graphical abstract samples](https://www.thieme.de/statics/dokumente/thieme/final/de/dokumente/zw_synthesis/CFZ-Sample-Graphical-Abstracts.pdf) (PDF file download)
* [What is “Primary Data”](http://www.thieme.de/de/synthesis/author-guidelines-58874.htm)?
* [ScholarOne](https://mc.manuscriptcentral.com/synthesis) (manuscript submission)