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Rh(II)-catalyzed intramolecular annulation of *N*-sulfonyl 1,2,3-triazoles with indole derivatives: A new method for synthesis pyranoindoles

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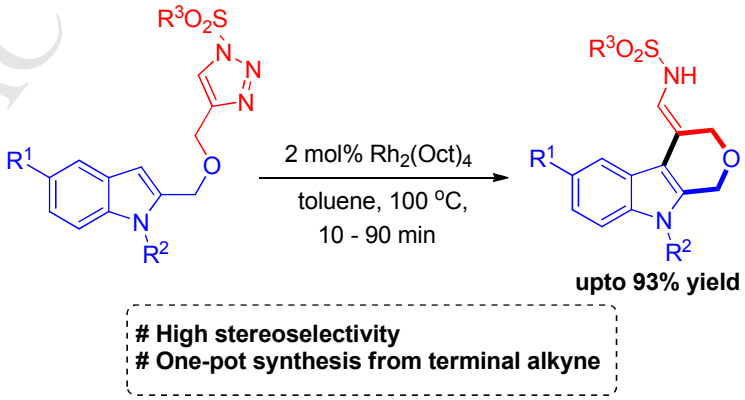
Abstract: A direct and highly stereoselective approach for the synthesis of *Z*-alkenyl-pyranoindoles had been developed by utilizing Rh(II)-catalyzed intramolecular cyclization of *N*-sulfonyl-1,2,3-triazoles with indole derivatives. A variety of pyranoindoles were obtained in 44 - 93% yields. Moreover, a more convenient synthesis of pyranoindoles starting from terminal alkyne was realized via a Cu-Rh sequentially catalyzed one-pot cascade reaction.



Keywords*:* sulfonyl triazoles, *α*-imino Rh(II) carbenes, Rh(II)-catalyzed, pyranoindoles, alkyne.

1. Introduction

Pyranoindole is an important structural motif, molecules comprising the pyranoindole framework are known to exhibit interesting biological activities. Etodolac[1] and pemedolac[2] bearing tetrahydropyrano[3,4-*b*]indole skeleton are anti-inflammatory and analgesic agents whereas some others are potent inhibitors of hepatitis C virus (HCV) NS5B polymerase[3] (Fig 1).

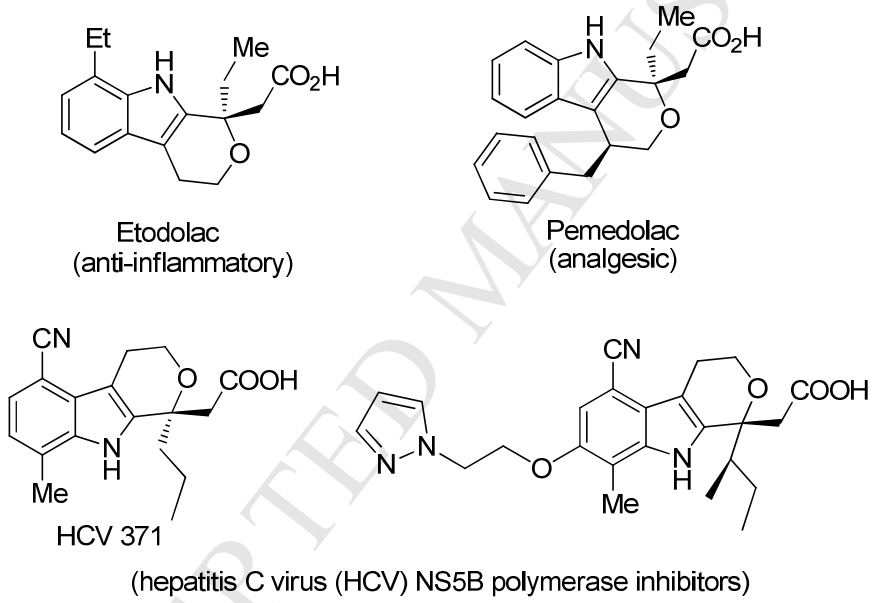
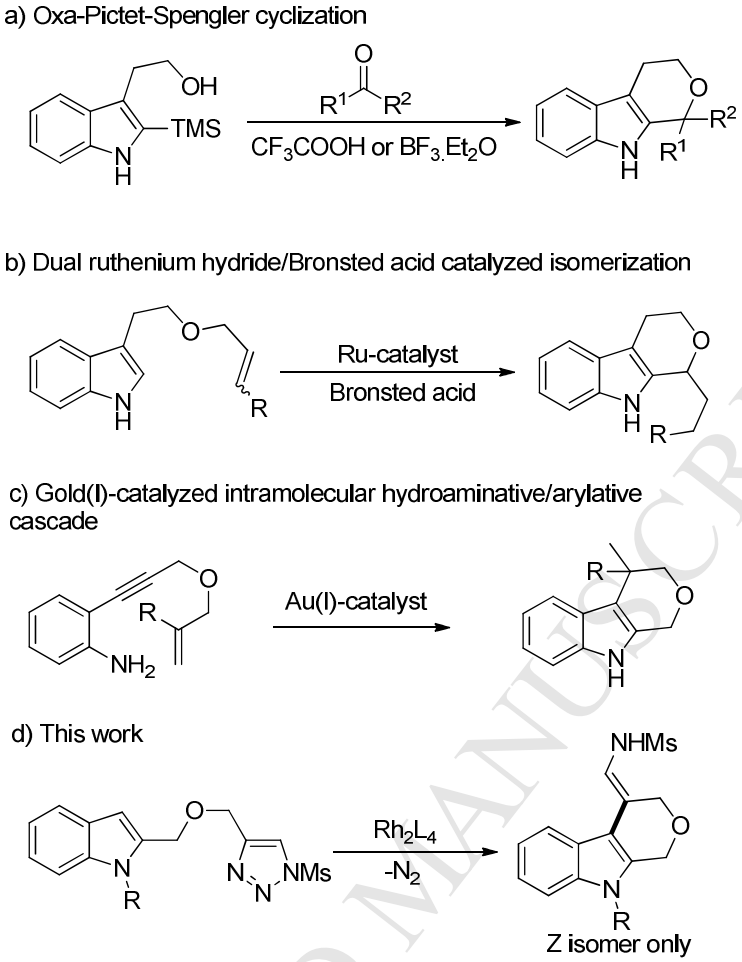


Fig. 1. Bioactive compounds bearing pyranoindole skeleton.

Due to their interesting pharmacological properties, pyranoindoles have received considerable attention and multiple synthetic routes towards this class of compounds have been developed.[4] Zhang and coworkers[5] demonstrated a silicon-directed oxa-Pictet-Spengler cyclizations of 2-(2-trimethylsilanyl-1*H*-indol-3-yl)-ethanols with various ketones and aldehydes for the synthesis of tetrahydro-pyrano-[3,4-*b*]indoles (eqn. a, Scheme 1). Likewise, Gharpure and Prasath explored oxa-Pictet–Spengler type reaction of vinylogous carbonates for stereoselective synthesis of pyranoindoles.[6]

Nielsen and co-workers had also demonstrated a ruthenium hydride/Brønsted acid-catalyzed tandem sequence towards the synthesis of pyranoindoles (eqn. b, Scheme 1).[7] In another interesting example, Porco Jr. group realized a Friedel-Crafts alkylation approach for the synthesis of pyrano-[3,4-*b*]indoles containing an uncommon C3-C4 substitution pattern.[8] Very recently, Asensio and co-workers reported an efficient synthesis of pyranoindoles *via* gold(I)-catalyzed intramolecular hydroaminative/arylative cascade (eqn. c, Scheme 1).[9] Recently, generation of *α*-imino Rh(II) carbenes from readily accessible *N*-sulfonyl-1,2,3-triazole and their reactions have enjoyed a great deal of popularity among the synthetic chemistry community.[10] The *N*-sulfonyl-1,2,3-triazole derived Rh(II) carbenes have been widely employed for the synthesis of *N*-heterocycles,[11] stereoselective cycloadditions,[12] C-H bond insertion,[11o,11p,13] X-H bond insertion (X = heteroatoms),[14] and other transformations[15]. In continuation of our effort on synthesis of biologically relevant heterocycles utilizing *N*-sulfonyl-1,2,3 triazoles,[16] herein we report Rh(II)-catalyzed intramolecular annulation of *N*-sulfonyl-1,2,3-triazoles towards highly stereoselective synthesis of pyranoindoles (eqn. d, Scheme 1).



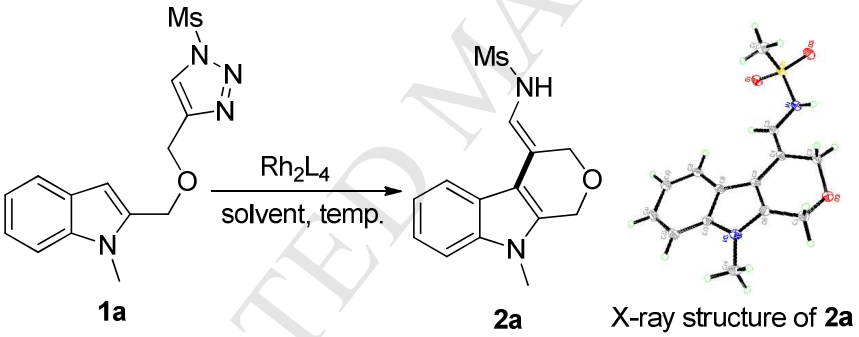
Scheme 1. Synthesis of pyranoindoles

2. Results and discussion

We began our initial investigation of Rh(II)-catalyzed intramolecular annulation, by taking indolyl triazole, **1a** (2-(((1-(methylsulfonyl)-1*H*-1,2,3-triazol-4-yl)methoxy)methyl)-1*H*-indole) as model substrate. The reaction of 0.1 M solution of **1a** in dichloromethane in the presence of 2 mol% [$Rh_2(Oct)_4$] at 30 ^oC resulted the exclusive *Z*-isomer **2a** in 30% isolated yield, which was unambiguously confirmed by single crystal X-ray diffraction analysis[17] (Table 1, entry 1). The model reaction in dichloroethane under similar conditions didn't show significant improvement (Table1, entry 2). However, when it was carried out in toluene at 30 ^oC, the isolated yield of desired **2a** was improved to 51%. Since sulfonyl triazole **1a** is only partially soluble in toluene at 30 ^oC, the reaction

temperature was raised to 100 ^{o}C under which product **2a** was produced in optimum yield (93%) in 10 minutes (Table 1, entry 6). Inspired by the result, we optimized the catalyst loading, lowering the catalyst loading to 1 mol% [$Rh_2(Oct)_4$] led to decrease in the isolated yield (68%) (Table 1, entry 7) whereas, an increase of catalyst loading to 3 mol%, didn't improve yield appreciably (Table 1, entry 8). Then we have tested a number of rhodium(II) catalysts such as, [$Rh_2(OPiv)_4$], [Rh_2(*S*-PTTL)$_4$], [Rh_2(*S*-NTTL)$_4$], [Rh_2(*S*-NTV)$_4$], [Rh_2(*S*-BNP)$_4$] and [$Rh_2(OAc)_4$] (Table 1, entries 9-14) for the model reaction in toluene at 100 ^{o}C. [$Rh_2(OPiv)_4$], [Rh_2(*S*-NTTL)$_4$] and [Rh_2(*S*-NTV)$_4$] also furnished the desired pyranoindole derivative **2a** in very good yield whereas [Rh_2(*S*-PTTL)$_4$], [$Rh_2(OAc)_4$] and [Rh_2(*S*-BNP)$_4$] were found to be comparatively less effective.

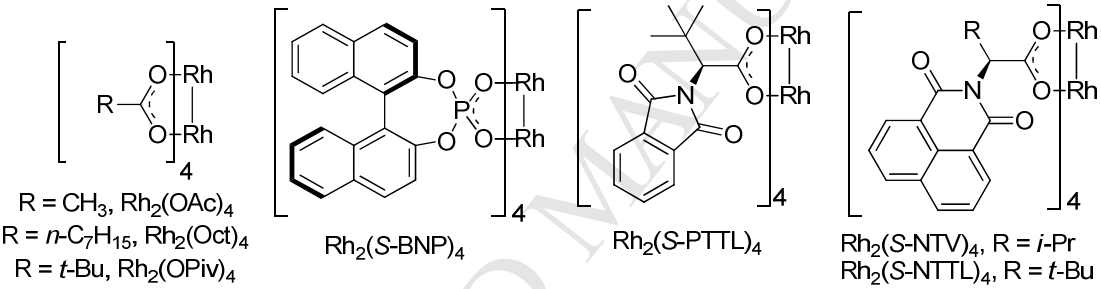
Table 1 Screening of reaction conditions[a]



Entry	Catalyst	Solvent	Temp.(^{o}C)	Yield[b] (%)
1	$Rh_2(Oct)_4$	DCM	30	30
2	$Rh_2(Oct)_4$	DCE	30	37
3	$Rh_2(Oct)_4$	Toluene	30	51
4	$Rh_2(Oct)_4$	Toluene	60	68
5	$Rh_2(Oct)_4$	Toluene	80	78
6	***$Rh_2(Oct)_4$***	***Toluene***	***100***	***93***
7[c]	$Rh_2(Oct)_4$	Toluene	100	68

8[d]	$Rh_2(Oct)_4$	Toluene	100	91
9	$Rh_2(OPiv)_4$	Toluene	100	91
10	Rh_2(*S*-PTTL)$_4$	Toluene	100	46
11	Rh_2(*S*-NTTL)$_4$	Toluene	100	88
12	Rh_2(*S*-NTV)$_4$	Toluene	100	81
13	$Rh_2(OAc)_4$	Toluene	100	54
14	Rh_2(*S*-BNP)$_4$	Toluene	100	14

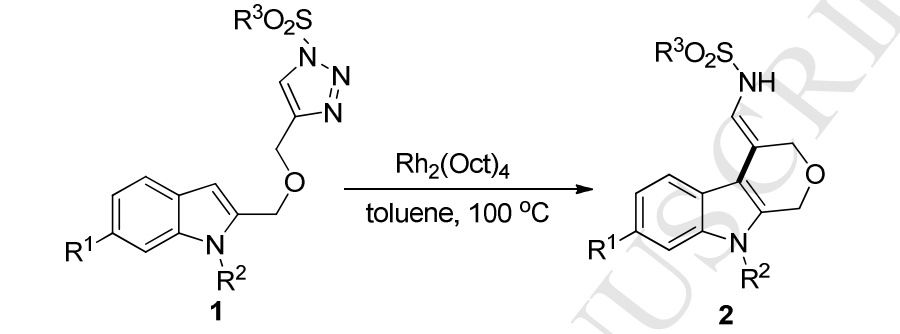
[a]Reaction conditions: 0.2 mmol of **1a** catalyzed by 2 mol% Rh_2L_4 catalyst in 2 ml solvent for 10-30 min. [b]Isolated yield. [c]With 1 mol% $Rh_2(Oct)_4$. [d]With 3 mol% $Rh_2(Oct)_4$.

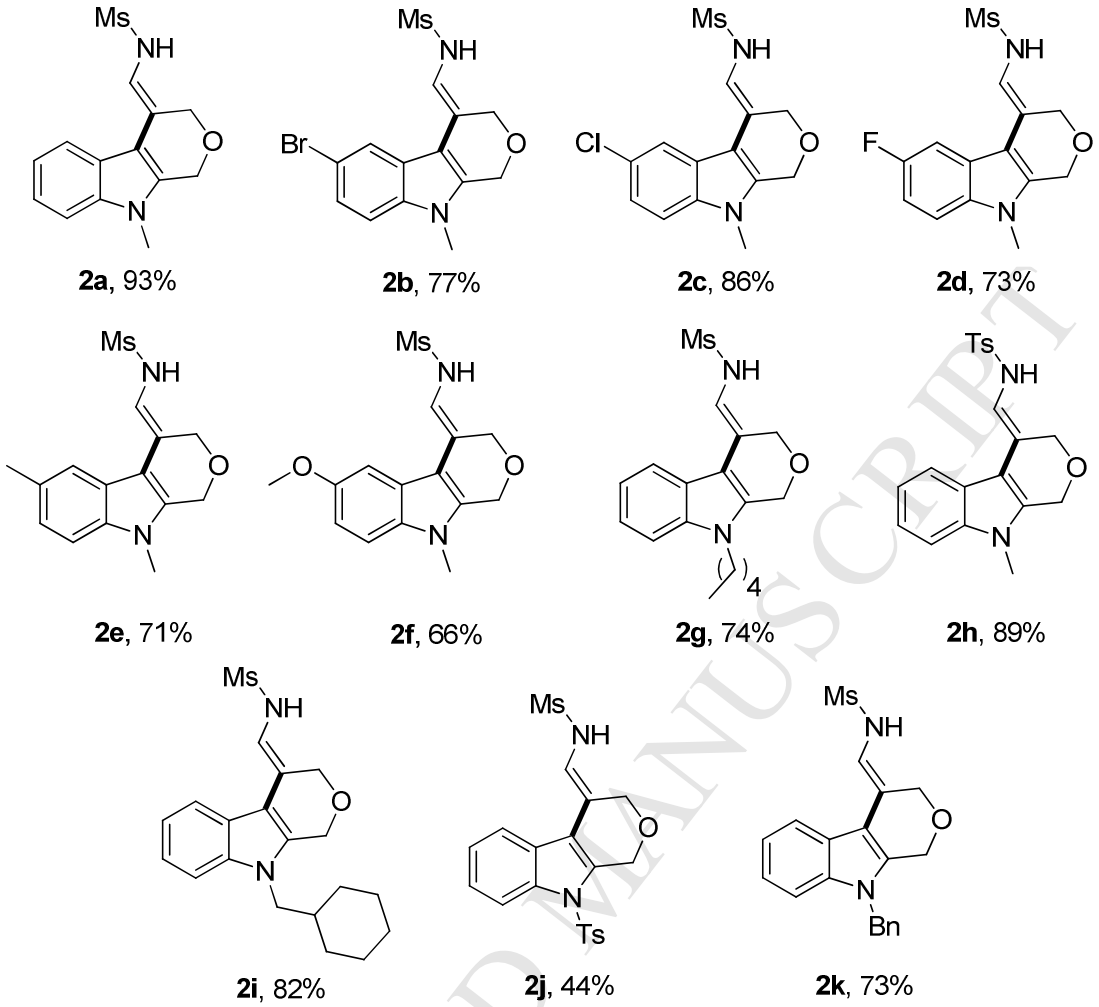


On the basis of the optimal reaction conditions (0.1 M solution of triazole in toluene in the presence of 2.0 mol% [$Rh_2(Oct)_4$] at 100 °C), we next explored the substrate scope as well as the functional group compatibility of our methodology (Table 2). Electron-withdrawing substituents (R^1 = Br, Cl, F) at the indole ring didn't influence the yield of the reactions significantly (Table 2, entries **2b**-**2d**), in all the cases the desired pyranoindole derivatives were achieved in good yields. While electron-donating substituents (R^1 = Me and OMe) at the indole ring led to comparatively lower yields of the desired pyranoindoles (Table 2, entries **2e** and **2f**). The intramolecular annulation of tosyl azide derived sulfonyl triazole **1h** furnished the desired pyranoindole derivative in good yield (Table 2, entry **2h**). However, from the mechanism we speculate that the electronic nature of protecting groups of indole could have significant effect on the yield of products. Indolyl triazoles with

electron-donating protecting groups (R^2 = *n*-pentyl, methylcyclohexane and benzyl) gave the desired products in good yields (Table 2, entries **2g**, **2i** and **2k**). As expected, protection of indole NH with electron-withdrawing group such as tosyl led to sluggish reaction rate and lower yield (44% isolated yield, Table 2, entry **2j**).

Table 2 Reaction scope[a, b]





2a, 93% **2b**, 77% **2c**, 86% **2d**, 73%

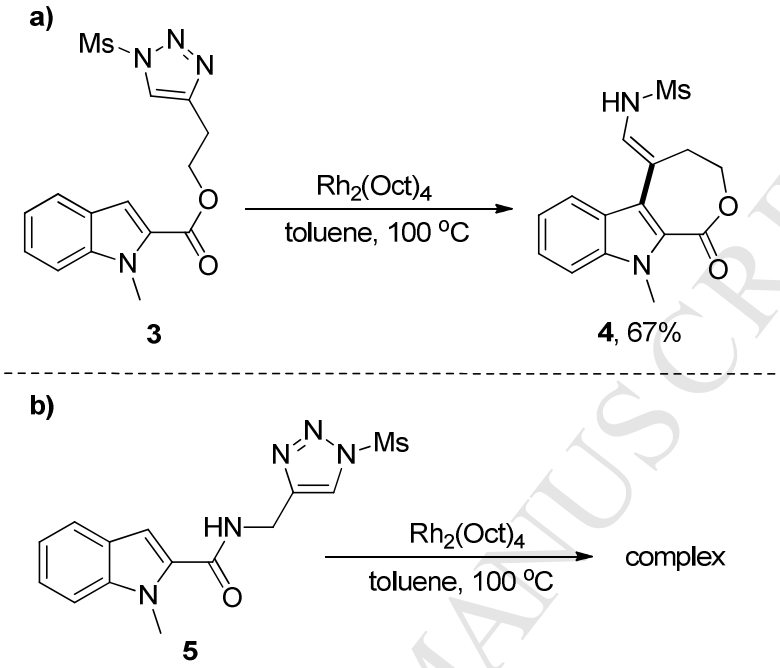
2e, 71% **2f**, 66% **2g**, 74% **2h**, 89%

2i, 82% **2j**, 44% **2k**, 73%

[a]Reaction conditions: 0.2 mmol of **1**, 2 mol% [$Rh_2(Oct)_4$] catalyst in 2 ml toluene at 100 [o]C for 10-90 min. [b]Isolated yield.

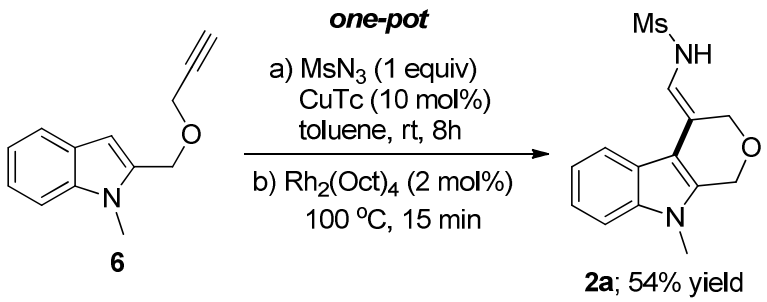
Indole fused seven membered rings are interesting structural motif found in biologically active compounds and natural products.[18] We also tried to explore our protocol for the synthesis of indole fused seven membered rings. The reactions of sulfonyl triazole **3** proceed smoothly to furnish the desired oxepinoindole **4** in 67% isolated yield, under our optimized reaction conditions (Scheme 2a). In order to extend the substrate scope of the method further, we tried to synthesize biologically relevant pyridoindole derivatives. Unfortunately, the reaction of sulfonyl triazole **5**

under our optimized reaction conditions failed to give the desired pyridoindole derivative leading to a complex mixture of undesired products (Scheme 2b).



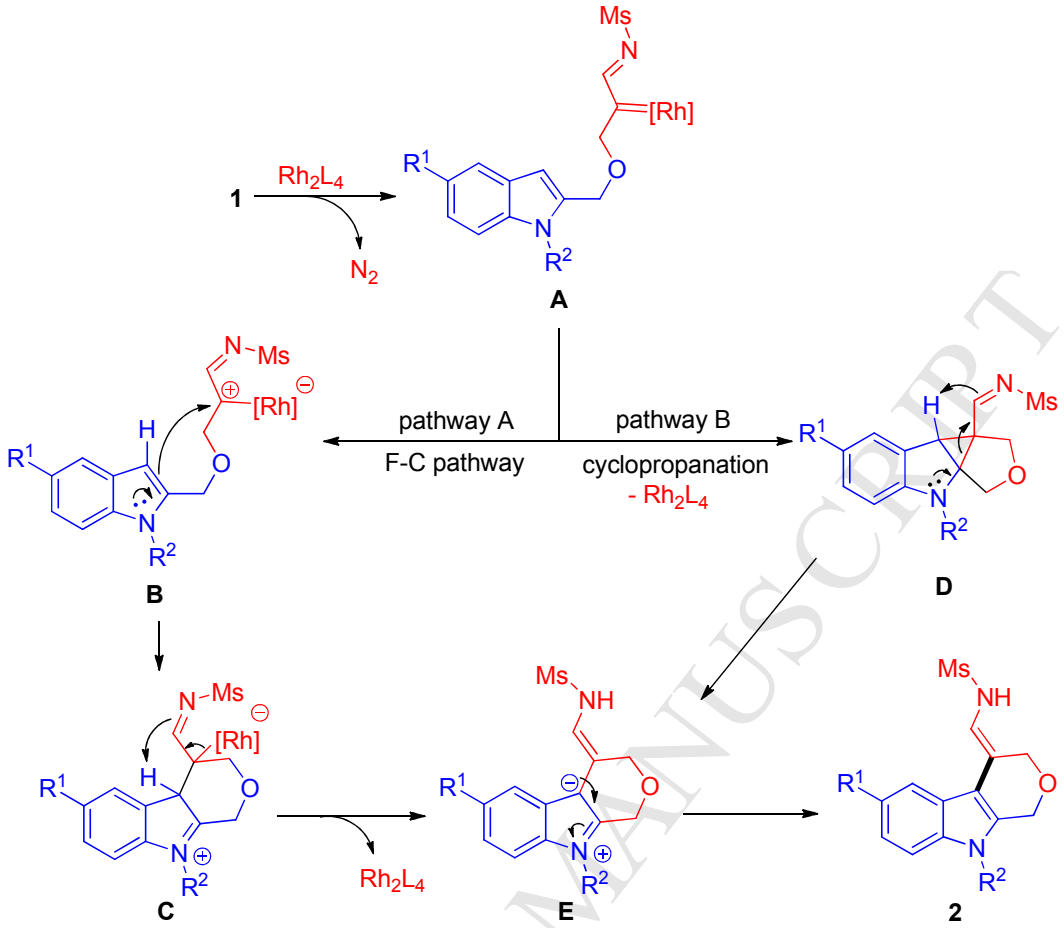
Scheme 2. Attempted synthesis of indole lactone and pyridoindole.

Based on our previous observations,[16] we envisioned that the pyranoindole derivatives could be synthesized in one-pot starting from terminal alkynes *via* Cu-Rh sequential catalysis. For that purpose, we carried out the reaction of terminal alkyne **6** with mesyl azide in the presence of CuTc (10 mol%) in toluene at room temperature. The terminal alkyne **6** was completely converted to *N*-sulfonyl-1,2,3-triazole within 8 h as evident from TLC analysis. Then, the reaction mixture was added 2 mol% of $Rh_2(Oct)_4$ and stirred at 100 ^oC under nitrogen atmosphere for additional 15 min to achieve the desired product **2a** in 54% isolated yield (Scheme 3).



Scheme 3. One-pot, sequential Cu-Rh catalyzed synthesis of pyranoindole.

A proposed mechanism of Rh(II)-catalyzed intramolecular annulation of *N*-sulfonyl-1,2,3-triazoles with indole derivatives towards highly stereoselective synthesis of pyranoindoles is outlined in Scheme 4. The *N*-sulfonyl-triazole **1** on treatment with dirhodium catalyst furnishes a highly reactive rhodium(II)-azavinyl carbene **A**. The intermediate **A** on intramolecular Friedel-Crafts alkylation results the intermediate **C**, which on subsequent loss of the rhodium-catalyst and intermolecular proton transfer from 3-position of indole ring to the nitrogen atom in enamine generates the desired product **2** (pathway A, Scheme 4). Alternatively, intramolecular cyclopropanation of the indole C(2)-C(3) bond gives the intermediate **D** (pathway B, Scheme 4).[19] The intermediate **D** on ring expansion and intermolecular proton transfer from 3-position of indole ring to the enamine nitrogen atom furnishes the desired product **2**.



Scheme 4. Proposed mechanism for the synthesis of pyranoindoles

3. Conclusion

In summary, an efficient rhodium(II)-catalyzed intramolecular annulation approach towards the synthesis of pyranoindole derivatives had been demonstrated by exploring the carbene transfer and subsequent cyclization of *N*-sulfonyl-1,2,3 triazole derived Rh(II) carbenoids. A variety of pyranoindole derivatives were obtained in moderate to excellent yields with high stereoselectivity. Moreover, a one-pot approach for the synthesis of pyranoindole derivative was also realized starting from terminal alkyne *via* sequential Cu-Rh catalysis. Further applications of this chemistry and more detailed mechanistic investigations are underway in our laboratory.

4. Experimental

4.1 General procedure for synthesis of triazoles 1

The *N*-sulfonyl-1,2,3-triazoles were synthesized from alkynes, according to a modified version of the literature procedure.[20] To a schlenk tube charged with copper(I) thiophene-2-carboxylate (CuTC, 0.1 mmol), the alkyne (1 mmol) and sulfonyl azide (1.1 mmol) solution in toluene were added and stirred at room temperature. After completion (monitored by TLC), the reaction mixture was diluted with ethyl acetate and passes through a small pad of silica. The filtrate was concentrated and purified by column chromatography to afford the *N*-sulfonyl-1,2,3-triazoles **1**.

4.2 General procedure for synthesis of pyranoindoles 2

To an oven dried schlenk tube equipped with magnetic stir bar, *N*-sulfonyl triazole **1** (0.2 mmol) and $Rh_2(Oct)_4$ (0.004 mmol) was added under N_2 followed by addition freshly distilled toluene (2.0 mL). The reaction was stirred at 100 °C under N_2 atmosphere and monitored with TLC analysis. After completion, the reaction mixture was directly purified by flash column chromatography with ethyl acetate and petroleum ether as eluents to afford **2**.

*4.2.1. N-((9-Methyl-2,3-dihydro-1H-carbazol-4(9H)-ylidene)methyl)methanesulf-onamide (**2a**).* White solid (54.5 mg, 93% yield); m.p. 147-152 ^{o}C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.19 (d, *J* = 8.1 Hz, 1H), 7.66 (d, *J* = 7.7 Hz, 1H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.19 (t, *J* = 7.0 Hz, 1H), 7.13 (t, *J* = 7.0 Hz, 1H), 6.48 (d, *J* = 7.9 Hz, 1H), 4.90 (s, 2H), 4.46 (s, 2H), 3.61 (s, 3H), 3.08 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 137.49, 136.00, 123.46, 121.75, 120.43, 119.83, 117.75, 112.41, 110.29, 105.45, 64.17, 62.55, 40.72, 29.90; IR (KBr plate, cm^{-1}) ν_{max} 519.57, 740.51, 971.00, 1086.85,

1135.54, 1154.58, 1325.01, 1473.87, 1507.63, 1541.60, 1652.88, 3446.59; HRMS (ESI-TOF) m/z $[M+H]^+$, Calcd for $C_{14}H_{17}O_3N_2S$ 293.0954. Found: 293.0954.

*4.2.2. N-((6-Bromo-9-methyl-2,3-dihydro-carbazol-4(9H)-ylidene)methyl)methane-sulfonamide (**2b**).* White solid (57 mg, 77% yield); m.p. 174-179 ^oC; ^1H NMR (400 MHz, DMSO-d_6) δ 9.22 (d, *J* = 8.3 Hz, 1H), 7.77 (s, 1H), 7.47 (d, *J* = 8.4 Hz, 1H), 7.30 (d, *J* = 8.7 Hz, 1H), 6.43 (d, *J* = 8.4 Hz, 1H), 4.90 (s, 2H), 4.45 (s, 2H), 3.62 (s, 3H), 3.11 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 137.48, 136.26, 124.99, 124.17, 121.83, 116.66, 113.09, 113.02, 112.37, 105.28, 64.13, 62.47, 40.95, 30.14; IR (KBr plate, cm^{-1}) ν_{max} 511.02, 764.22, 788.19, 973.36, 1090.82, 1150.38, 1324.79, 1473.06, 1541.57, 3243.46, 3446.60; HRMS (ESI-TOF) m/z $[M+H]^+$, Calcd for $C_{14}H_{16}O_3N_2BrS$ 371.0060. Found: 371.0059.

*4.2.3. N-((6-Chloro-9-methyl-2,3-dihydro-1H-carbazol-4(9H)-ylidene)methyl)-methanesulfonamide (**2c**).* White solid (56 mg, 86% yield); m.p. 198-202 ^oC; ^1H NMR (400 MHz, DMSO-d_6) δ 9.21 (d, *J* = 8.3 Hz, 1H), 7.65 (s, 1H), 7.51 (d, *J* = 8.7 Hz, 1H), 7.19 (d, *J* = 8.3 Hz, 1H), 6.44 (d, *J* = 8.3 Hz, 1H), 4.89 (s, 2H), 4.45 (s, 2H), 3.62 (s, 3H), 3.12 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 137.64, 136.02, 125.04, 124.30, 121.57, 118.93, 116.71, 113.05, 111.87, 105.37, 64.13, 62.49, 40.93, 30.15; IR (KBr plate, cm^{-1}) ν_{max} 516.15, 771.80, 796.49, 974.25, 1094.00, 1142.37, 1313.65, 1408.01, 1473.09, 1507.55, 1541.77, 1652.96, 3246.62; HRMS (ESI-TOF) m/z $[M+H]^+$, Calcd for $C_{14}H_{16}O_3N_2ClS$ 327.0565. Found: 327.0565.

*4.2.4. N-((6-Fluoro-9-methylpyrano[3,4-b]indol-4(1H,3H,9H)-ylidene)methyl)methan-esulfonamide (**2d**).* White solid (45.5 mg, 73% yield); m.p. 194-197 ^oC; ^1H NMR (400 MHz, DMSO-d_6) δ 9.17 (s, 1H), 7.49 (dd, *J* = 8.8, 4.5 Hz, 1H), 7.43 (d, *J* = 10.1 Hz, 1H), 7.03 (t, *J* = 9.1 Hz, 1H), 6.40 (s, 1H), 4.89 (s, 2H), 4.45 (s, 2H), 3.62 (s, 3H), 3.11 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 158.03, 137.87, 134.20, 123.38, 117.33, 112.67, 111.31, 109.46, 105.65, 105.01, 64.18, 62.55, 40.78, 30.17; IR (KBr

plate, cm^{-1}) ν_{max} 519.07, 775.28, 790.73, 844.75, 898.33, 926.53, 980.45, 1084.63, 1146.36, 1316.31, 1403.47, 1488.84, 1542.87, 1622.15, 3269.29; HRMS (ESI-TOF) m/z $[M+H]^+$, Calcd for $C_{14}H_{16}O_3N_2FS$ 311.0860. Found: 311.0857.

*4.2.5. N-((6,9-Dimethyl-2,3-dihydro-1H-carbazol-4-ylidene)methyl)methane-sulfonamide (**2e**).* White solid (45.6 mg, 71% yield); m.p. 168-172 ^oC; ^1H NMR (400 MHz, DMSO-d_6) δ 9.12 (d, *J* = 8.5 Hz, 1H), 7.42 (s, 1H), 7.35 (d, *J* = 8.3 Hz, 1H), 7.01 (d, *J* = 8.2 Hz, 1H), 6.44 (d, *J* = 8.5 Hz, 1H), 4.88 (s, 2H), 4.45 (s, 2H), 3.58 (s, 3H), 3.08 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 136.10, 135.96, 129.07, 123.72, 123.20, 119.62, 118.45, 112.09, 109.98, 104.93, 64.22, 62.58, 40.71, 29.91, 21.78; IR (KBr plate, cm^{-1}) ν_{max} 517.49, 766.08, 797.86, 971.87, 1091.63, 1140.76, 1315.74, 1408.90, 1490.44, 1542.28, 3267.00; HRMS (ESI-TOF) m/z $[M+H]^+$, Calcd for $C_{15}H_{19}O_3N_2S$ 307.1111. Found: 307.1108.

*4.2.6. N-((6-methoxy-9-methylpyrano[3,4-b]indol-4-ylidene)methyl) methanesulfonamide (**2f**)* White solid, 42.5 mg, 66% yield. m.p. 155-156 ^oC; ^1H NMR (400 MHz, DMSO) δ 9.13 (d, *J* = 8.5 Hz, 1H), 7.39 (d, *J* = 8.9 Hz, 1H), 7.08 (d, *J* = 1.6 Hz, 1H), 6.86 (dd, *J* = 8.8, 1.7 Hz, 1H), 6.39 (d, *J* = 8.5 Hz, 1H), 4.88 (s, 2H), 4.45 (s, 2H), 3.80 (s, 3H), 3.59 (s, 3H), 3.08 (s, 3H); ^{13}C NMR (101 MHz, DMSO) δ 154.55, 136.71, 132.80, 123.81, 118.41, 112.02, 110.91, 110.36, 105.01, 103.18, 64.23, 62.62, 56.00, 40.69, 30.02; IR (KBr plate, cm^{-1}) ν_{max} 798.56, 973.21, 1090.40, 1159.65, 1235.83, 1317.78, 1491.14, 1616.95, 3158.56; HRMS (ESI-TOF) m/z $[M+H]^+$, Calcd for $C_{15}H_{19}O_4N_2S$ 323.1057. Found: 323.1060.

*4.2.7. N-((9-Pentylpyrano[3,4-b]indol-4(1H,3H,9H)-ylidene)methyl)methane-sulfonamide (**2g**).* White solid (51.7 mg,74% yield); m.p. 145-149 ^oC; ^1H NMR (400 MHz, DMSO-d_6) δ 9.17 (d, *J* = 8.6 Hz, 1H), 7.65 (d, *J* = 7.7 Hz, 1H), 7.48 (d, *J* = 8.0 Hz, 1H), 7.15 (dt, *J* = 14.7, 7.1 Hz, 2H), 6.49 (d, *J* = 8.5 Hz, 1H), 4.89 (s, 2H), 4.47 (s, 2H), 4.04 (t, *J* = 6.9 Hz, 2H), 3.08 (s, 3H), 1.69 – 1.45 (m, 2H), 1.37 – 1.11 (m,

4H), 0.83 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 136.84, 135.58, 123.56, 121.78, 120.39, 119.94, 117.80, 112.46, 110.53, 105.54, 64.28, 62.63, 43.25, 40.73, 29.84, 28.85, 22.29, 14.32; IR (KBr plate, cm^{-1}) ν_{max} 418.91, 742.08, 801.67, 1093.27, 1144.74, 1323.08, 1419.49, 1457.54, 1473.89, 1507.51, 1540.68, 1558.31, 1636.08, 2927.88, 3241.10, 3446.21; HRMS (ESI-TOF) m/z $[M+H]^+$, Calcd for $C_{18}H_{25}O_3N_2S$ 349.1580. Found: 349.1575.

*4.2.8. 4-methyl-N-((9-methylpyrano[3,4-b]indol-4(1H,3H,9H)-ylidene)methyl)-benzenesulfonamide (**2h**)* White solid, 65.5 mg, 89% yield. m.p. 91-94 ^{o}C; ^{1}H NMR (400 MHz, DMSO) δ 9.67 (d, *J* = 8.9 Hz, 1H), 7.76 (d, *J* = 6.9 Hz, 2H), 7.59 – 7.27 (m, 3H), 7.17 (dd, *J* = 17.8, 7.9 Hz, 2H), 6.38 (d, *J* = 8.7 Hz, 1H), 5.77 (s, 1H), 4.84 (s, 2H), 4.33 (s, 2H), 3.58 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (101 MHz, DMSO) δ 143.54, 138.11, 137.44, 136.21, 130.28, 126.72, 123.31, 121.76, 120.63, 119.38, 118.69, 111.68, 110.40, 105.15, 63.98, 62.45, 55.39, 29.89; IR (KBr plate, cm^{-1}) ν_{max} 550.91, 1050.42, 1085.33, 1138.44, 1159.58, 1326.95, 1474.06, 2973.13, 3420.69; HRMS (ESI-TOF) m/z $[M+H]^+$, Calcd for $C_{20}H_{21}O_3N_2S$ 369.1265. Found: 369.1267.

*4.2.9. N-((9-(Cyclohexylmethyl)pyrano[3,4-b]indol-4(1H,3H,9H)-ylidene)methyl)-methane-sulfonamide (**2i**).* White solid (61.5 mg, 82% yield); m.p. 94-97 ^{o}C; ^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.62 (d, *J* = 7.8 Hz, 1H), 7.25 (d, *J* = 8.1 Hz, 1H), 7.13 (t, *J* = 7.4 Hz, 1H), 7.07 (t, *J* = 7.3 Hz, 1H), 6.48 (d, *J* = 8.3 Hz, 1H), 6.26 (d, *J* = 8.2 Hz, 1H), 4.78 (s, 2H), 4.44 (s, 2H), 3.67 (d, *J* = 7.4 Hz, 2H), 2.97 (s, 3H), 1.75 – 1.65 (m, 2H), 1.60 – 1.48 (m, 4H), 1.08 (s, 3H), 0.96 – 0.77 (m, 2H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 137.27, 135.82, 123.62, 121.75, 121.68, 120.34, 119.87, 110.44, 110.18, 105.07, 64.19, 63.20, 53.85, 50.14, 40.17, 38.69, 31.07, 31.03, 26.24, 25.74; IR (KBr plate, cm^{-1}) ν_{max} 481.49, 742.26, 801.56, 977.01, 1093.63, 1145.37, 1323.25, 1419.59, 1457.74, 1507.49, 1540.76, 1636.17, 2927.71, 3241.54; HRMS (ESI-TOF) m/z $[M+H]^+$, Calcd for $C_{20}H_{27}O_3N_2S$ 375.1737. Found: 375.1730.

*4.2.10. N-((9-Tosylpyrano[3,4-b]indol-4(1H,3H,9H)-ylidene)methyl)methane-sulfonamide (**2j**).* White solid (38.1 mg, 44% yield); m.p. 64-69 ^{o}C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.68 (d, *J* = 8.8 Hz, 1H), 8.06 (d, *J* = 8.3 Hz, 1H), 7.80 (d, *J* = 8.3 Hz, 2H), 7.69 (d, *J* = 7.1 Hz, 1H), 7.44 – 7.27 (m, 4H), 6.72 (d, *J* = 8.6 Hz, 1H), 5.12 (s, 2H), 4.45 (s, 2H), 3.14 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 146.22, 135.79, 134.19, 133.04, 130.83, 127.05, 126.62, 125.35, 124.92, 120.79, 118.07, 115.10, 114.50, 111.90, 64.35, 63.31, 41.42, 21.49; IR (KBr plate, cm^{-1}) ν_{max} 518.85, 580.42, 666.07, 748.72, 858.73, 973.71, 1090.13, 1151.83, 1250.83, 1348.89, 1451.75, 1645.46, 2925.79; HRMS (ESI-TOF) m/z [M+H]$^{+}$, Calcd for $C_{20}H_{21}O_5N_2S_2$ 433.0886. Found: 433.0888.

*4.2.11. N-((9-Benzylpyrano[3,4-b]indol-4(1H,3H,9H)-ylidene)methyl)methane-sulfonamide (**2k**).* White solid (53.8 mg, 73% yield); m.p. 177-178 ^{o}C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.22 (d, *J* = 8.7 Hz, 1H), 7.69 (d, *J* = 6.5 Hz, 1H), 7.51 (d, *J* = 7.1 Hz, 1H), 7.30 (t, *J* = 7.0 Hz, 2H), 7.25 (d, *J* = 6.5 Hz, 1H), 7.19 – 7.11 (m, 2H), 7.06 (d, *J* = 7.1 Hz, 2H), 6.54 (d, *J* = 8.6 Hz, 1H), 5.35 (s, 2H), 4.83 (s, 2H), 4.47 (s, 2H), 3.09 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 138.15, 137.18, 135.67, 129.18, 127.85, 126.95, 123.68, 122.09, 120.72, 120.03, 117.26, 112.94, 110.83, 106.23, 64.27, 62.72, 60.24, 46.56, 21.23, 14.56; IR (KBr plate, cm^{-1}) ν_{max} 519.44, 737.77, 976.03, 1094.91, 1137.75, 1322.36, 1457.01, 1541.47, 1652.76, 3259.95; HRMS (ESI-TOF) m/z [M+H]$^{+}$, Calcd for $C_{20}H_{21}O_3N_2S$ 369.1267. Found: 369.1263.

*4.2.12. N-((10-Methyl-1-oxo-3,4-dihydro-1H-oxepino[3,4-b]indol-5(10H)-ylidene) methyl)methane-sulfonamide (**2l**).* White solid (39.1 mg, 61% yield); m.p. 83-87 ^{o}C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.27 (s, 1H), 8.31 (d, *J* = 7.7 Hz, 1H), 7.69 (d, *J* = 8.1 Hz, 1H), 7.38 (dt, *J* = 14.7, 7.1 Hz, 2H), 5.78 (s, 1H), 4.68 – 4.52 (m, 1H), 4.31 (dd, *J* = 16.8, 9.3 Hz, 1H), 3.85 (s, 3H), 3.15 (s, 3H), 3.01 (dt, *J* = 19.5, 9.9 Hz, 1H), 2.89 – 2.67 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 211.59, 163.85, 145.53, 138.50, 124.97, 124.93, 123.88, 122.54, 111.65, 111.10, 75.19, 65.59, 40.87, 36.54,

32.30; IR (KBr plate, cm^{-1}) ν_{max} 512.69, 785.44, 965.35, 1138.49, 1299.74, 1473.38, 1558.97, 1716.58, 2925.76, 3446.42; HRMS (ESI-TOF) m/z $[M+H]^+$, Calcd for $C_{15}H_{17}O_4N_2S$ 321.0904. Found: 321.0899.

4.3 One-pot synthesis of pyranoindole starting from alkyne

To an oven dried schlenk tube charged with alkyne (0.2 mmol) and CuTC (0.02 mmol) in toluene, was added mesyl azide (0.2 mmol) and stirred at room temperature. After 8 h alkyne was completed converted to the corresponding *N*-sulfonyl triazole and $Rh_2(Oct)_4$ (0.004 mmol) was added and stirred at 100 °C. After completion, the reaction mixture was directly purified by flash column chromatography with ethyl acetate and petroleum ether as eluents to achieve the desired pyranoindole derivative **2a** (31.5 mg, 54% yield).

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