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Catalyst-Controlled Chemodivergent Annulation to Indolo/ Pyrrolo-Fused Diazepine and Quinoxaline

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Abstract. Catalyst-controlled chemodivergent annulation between *o*-indolo anilines and diazo compounds has explored for the synthesis of indolo-fused diazepine and quinoxaline. Under the Rh(III) catalyst, reaction proceeded through the free amine assisted C2-H activation followed by amidation leading to the diazepino[1,7-*a*]indole in a highly selective manner. While with Ru(II) catalyst, reaction involves formation Ru-carbene complex followed by $-NH_2$ group insertion and cascade cyclization via metallo-ene type reaction, β-hydride elimination to furnish the indolo[1,2-*a*] quinoxaline as the predominating product. This strategy directs modular approach towards the construction of unique indolo-fused diazepine/quinoxaline as well as pyrrolo-fused diazepine/quinoxaline scaffolds in excellent yields.

Keywords: Catalyst-controlled; Chemodivergent Annulation; Indolo/Pyrrolo-Fused Diazepine and Quinoxaline.

Introduction

Indole and Pyrrole are the most abundant heterocycles in natural products with valuable and diverse biological properties.[1] Especially, indole/pyrrole tethered to other heterocycles such as diazepine and quinoxaline are often considered as important privileged scaffolds in drug discovery. For examples, benzo][1,4]diazepino[1,7-*a*]indole (**I**) have the anti-HCV activity,[2a] whereas diazepino-fused pyrrole Laxivaptan (**II**) show anti-diuretic activity.[2b] Likewise, substituted indolo/pyrrolo[1,2-*a*]quinoxalines at C-4 position (**III**, **IV**, and **V**) exhibit antifungal[3a], anti-HIV[3b], and anti-secretory [3c] activities (Figure 1).

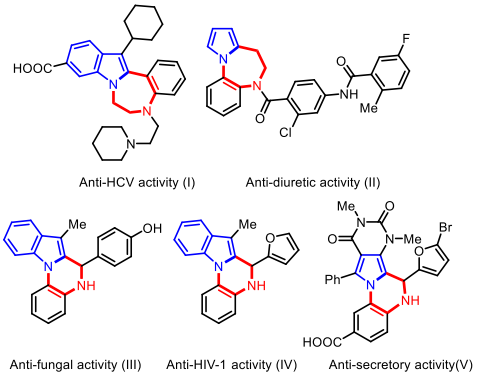
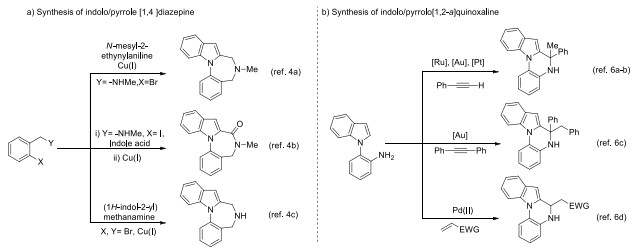


Figure 1. Biological important indole/pyrrole-fused diazepine and quinoxaline derivatives.

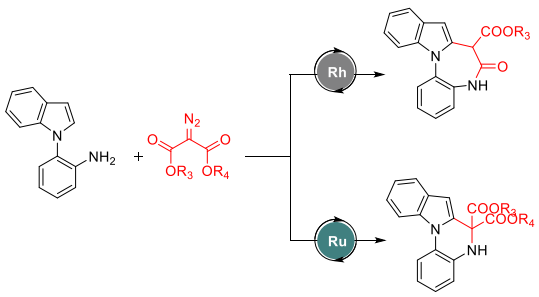
Accordingly, substantial attention focuses on the construction of these fused heterocyclic architectures. Nevertheless, there are few methods reported for the synthesis of these uncommon heterocycles (Scheme 1). For example, Ohta reported one step synthesis of indole-fused benzo-1,4-diazepines through Cu(I) catalyzed domino three component cyclization of 2-ethynylanilines with *o*-bromobenzylamines.[4a] Mangette described the multistep synthesis of indolo/pyrrolodiazepines *via* Cu catalyzed intramolecular *N*-arylation.[4b] Subsequently, Srinivasulu described the S_N^2-CuI catalyzed annulation for the synthesis of benzo[6,7][1,4]diazepino[1,2-*a*]indole.[4c] A classical method to synthesize indolo/pyrrolo-fused quinoxaline involves Pictet–Spengler reaction of *ortho*-indolyl/pyrrolyl anilines with carbonyl compounds.[5] Yu and Patil synthesized indolo/pyrrole[1,2-*a*]quinoxaline by cascade hydroamination/hydroarylation of the *o*-indolo/pyrrolo anilines with terminal alkynes by various metal catalysts.[6a-b] In 2011, Liu group reported Au(I) catalyzed hydroamination and hydroarylation of *o*-indolo/pyrrolo anilines with internal alkyne to synthesize the indolo/pyrrolo[1,2-*a*] quinoxalines.[6c] Xiao achieved indolo-fused

quinoxalines through Pd(II) catalyzed regioselective C-H olefination, and cyclization of *o*-indolo aniline with electron-withdrawing olefins.[6d] Although aforementioned methods are encouraging, it is still highly demand to employ the new straightforward C−H activation strategy to access indolo/pyrrolo-fused diazepine and quinoxaline scaffolds with different substitution patterns.



Scheme 1. Synthesis of indolo/pyrrole-fused diazepine/ quinoxaline derivatives

Over past decades, transition metal catalyzed directed C-H functionalization of indole nucleus has made significant progress and becomes powerful strategy for assembling indole-containing heterocycle.[7] In particularly, heteroatom-assisted selective C2-H functionalization/cascade annulation of indoles is an alternating approach to construct structurally diverse fused-indole heterocyclic scaffolds.[8] Such an example, we have demonstrated that the free amine assisted Pd(II) catalyzed regioselective [5+2] annulation of unprotected indoloanilines with internal alkynes.[9] In connection with our research interest towards the synthesis of structurally diverse important heterocyclic molecules,[10] herein we envisioned that metal catalyzed reaction of *o*-indolo aniline with diazo as coupling partner could deliver the indolo-fused diazepine through free amine assisted C2-H functionalization/cyclization. During our optimization studies, a remarkable chemodivergent annulation observed by switching the catalyst, which enabled facile synthesis of hybrid diazepine/quinoxaline-fused indole heterocycles (Scheme 2).



Scheme 2. A transition metal controlled approach to the different scaffolds

Results and Discussion

We first used 2-(1*H*-indol-1-yl) aniline **1a** as a model substrate and diethyl diazomalonate **2a** as a coupling partner. In the presence of $[Cp^*RhCl_2]_2$ (2.5 mol %)/$AgSbF_6$ (20 mol %) catalyst and AcOH (2.5 equiv.) in EtOH at 60 °C for 1 h, both the C2 (**3aa**) and C3 (**4aa**) alkylated intermediates were obtained in 65 % and 25 % yield respectively (entry 1). When the same reaction was heated for 3 h, the intermediates **3aa** was converted into diazepine derivative **5aa** in 70 % yield along with 20 % of C3-alkylated product **4aa** (entry 2)**.** Interestingly, well-resolved ^1H and ^{13}C NMR spectra of **5aa** have shown substantial peak doubling in acetone-d_6 at room temperature due the existence of rotamers. Variable temperature NMR studies conducted to confirm the interconverting rotamers (See SI, S28-S46). The structure of **5aa** is further established by X-ray crystallographic analysis, which clearly indicates that seven membered diazepine ring is slightly distorted and fused at C2-postion of indole ring (Figure 2).

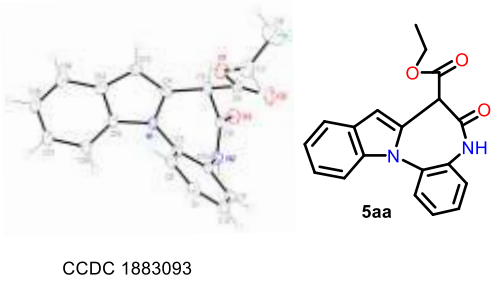


Figure 2. X-ray structure of compound **5aa**

Next, replacing AcOH with PivOH did not observe improvement in yield (entry 3). In the absence of co-additives suppressed the formation of **4aa** and the yield of **5aa** was significantly augmented to 92 % (entry 4). A brief evaluation of other additives and solvents indicated that $AgSbF_6$ and EtOH are good combination in this reaction (entries 5-11). There was no change in yield when temperature raised to 100 °C, but lower yield obtained at 30 °C (entries 12-13). The importance of catalyst and additive also studied, as reactions gave lower yield in the absence of additive, whereas reaction did not proceed in the absence of catalyst (entries 14-15). When $[RhCp^*Cl_2]_2$ was replaced by $[CoCp^*(CO)I_2]$, $PdCl_2$ or $Pd(OAc)_2$, no reaction occurred and starting material **1a** was recovered (entries 16-18). To our surprise, when reaction was performed with $[Ru(p\text{-cymen})Cl_2]_2$ (5 mol%)/$AgSbF_6$(20 mol%)in EtOH at 60 °C for 12 h, the new six membered indole-fused quinoxaline **7aa** (35 %) and *N*-alkylated product **6aa** (55%) were isolated instead of seven membered indole-fused diazepine **5aa** (entry 19). The structure of **7aa** is ascertained by X-ray single crystallography, which demonstrates the newly formed six membered ring adopts the boat conformation and overall structure is planar (Figure 3).

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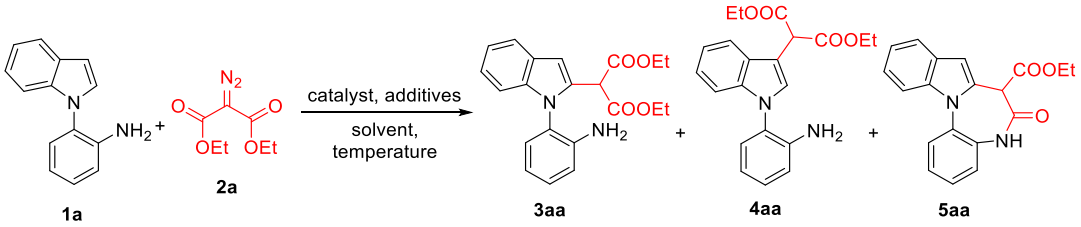
Table 1. Optimization for the synthesis of diazepino[1,7-*a*]indole (**5aa**)[a]



Entry	Catalyst	Additives	Acid	Solvent	Temp (°C)	Time (h)	Yield (%)[b]		
							3aa	**4aa**	**5aa**
1	$[RhCp^*Cl_2]_2$	$AgSbF_6$	AcOH	EtOH	60	1	65	25	0
2	$[RhCp^*Cl_2]_2$	$AgSbF_6$	AcOH	EtOH	60	3	0	20	70
3	$[RhCp^*Cl_2]_2$	$AgSbF_6$	PivOH	EtOH	60	3	0	25	72
4	**$[RhCp^*Cl_2]_2$**	**$AgSbF_6$**	**-**	**EtOH**	**60**	**3**	**0**	**0**	**92**
5	$[RhCp^*Cl_2]_2$	CsOAc	-	EtOH	60	3	0	0	0
6	$[RhCp^*Cl_2]_2$	NaOAc	-	EtOH	60	3	0	0	0
7	$[RhCp^*Cl_2]_2$	$AgNTf_6$	-	EtOH	60	3	0	20	65
8	$[RhCp^*Cl_2]_2$	AgOTf	-	EtOH	60	3	0	35	45
9	$[RhCp^*Cl_2]_2$	$AgSbF_6$	-	DCE	100	6	0	0	72
10	$[RhCp^*Cl_2]_2$	$AgSbF_6$	-	MeOH	60	3	15	0	80
11	$[RhCp^*Cl_2]_2$	$AgSbF_6$	-	ACN	100	3	0	0	0
12	$[RhCp^*Cl_2]_2$	$AgSbF_6$	-	EtOH	100	3	0	0	82
13	$[RhCp^*Cl_2]_2$	$AgSbF_6$	-	EtOH	30	12	0	20	50
14	$[RhCp^*Cl_2]_2$-	-	-	EtOH	60	12	0	15	35
15	-	$AgSbF_6$	-	EtOH	60	3	0	0	0
16	[Co Cp*(CO)I_2]	$AgSbF_6$	AcOH	EtOH	60	10	0	0	0
17	$Pd(OAc)_2$[c]	$Cu(OAc)_2$	-	EtOH	60	10	0	0	0
18	$PdCl_2$[c]	$Cu(OAc)_2$	-	EtOH	60	10	0	0	0
19[d]	$[Ru(p\text{-cymen})Cl_2]_2$[c]	$AgSbF_6$	-	EtOH	60	12	0	0	0

[a] Reaction conditions: **1a** (0.48 mmol), **2a** (0.96 mmol), catalyst (2.5 mol%), additive (20 mol%), solvent (4 mL). [b] Isolated yields. [c] catalyst (5 mol%).[d] Obtained **7aa** in 35% and **6aa** in 55% yield.

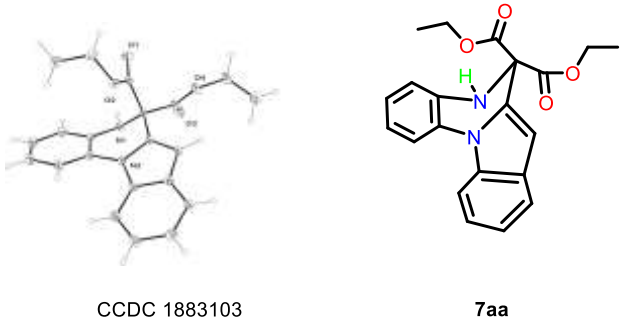


Figure 3. ORTEP diagram of compound **7aa**

With an optimized condition in hand, we next examined the substrate scope of various indolyl/pyrrolyl anilines **1/1'** with diazo compounds **2** (Table 2). The reactions of substrate having electron donating/withdrawing groups on aniline (**1a-1c, 1na-pa**) or indole ring (**1d-1g, 1pa-ra**) with diethyl diazomalonate **2a** proceeded smoothly to deliver the desired products in excellent yield (**5aa-5ga, 5na-5ra**). In the case of indole bearing methyl group at 3-position and electron donating/withdrawing groups on aniline ring (**1g-1k**) furnished the corresponding products (**5ga-5ka**) in excellent yields, where rotamers did not observe presumably due to the steric hindrance of –Me group restricting the rotation of ester group. Heterocyclic *o*-indolyl aniline (**1o**) is also compatible and led to desired product **5oa** in 74 % yield, whereas o*rtho*-methyl substituted *o*-indolyl aniline (**1m**) and free amine protected *o*-indolyl aniline (**1s**) were not successful. Furthermore, replacement of the indole core with the pyrrole provided a new class of pyrrolo-fused diazepine analogues (Table 2b**)**. Various functional group such as -H (**5'a**), -OMe (**5'b)**, -CF_3 (**5'c**), -COOMe (**5'd**) on aniline ring are well-tolerated to furnish pyrrolo[1,2-*d*][1,4]diazepine (**5'aa-5'da)** in good yield. However, 2,4-dimethyl pyrrolyl aniline (**1'e**) and 2-ethyl imidazolyl aniline (**1'f**) are not suitable substrates for this cascade C-H/N-H annulation. This may be because the steric hindrance of 2,4-dimethyl pyrrolyl ring and strong metal-chelating ability of the electron deficient imidazolyl

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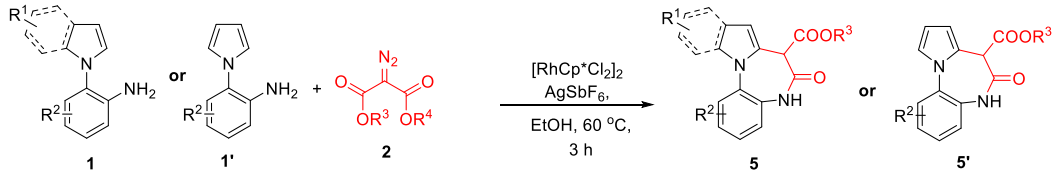
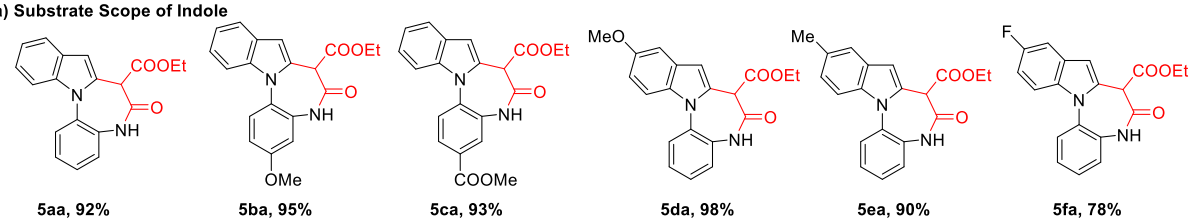
ring inhibit the formation of six-membered rhodacycle intermediate. Afterward, we tested the feasibility of different diazo malonates (Table 2c). The dimethyl, dibenzyl diazomalonates (**2b-c**) reacted efficiently with substrate *o*-indolo and pyrrolo anilines (**1a**, **1'a)** or 2-(3-methyl-1*H*-indolyl)aniline **1g** to afford the corresponding products in excellent yields (**5ab-ac, 5gb-gc,** and **5'ac**), whereas diitertbuty diazomalonates (**2d**) yielded the desired product in good yields (**5ad, 5gd,** and **5'ad**).

Table 2. A Rh(III) catalyzed synthesis of indolo/pyrrolo-fused diazepine (**5**)[a,b]

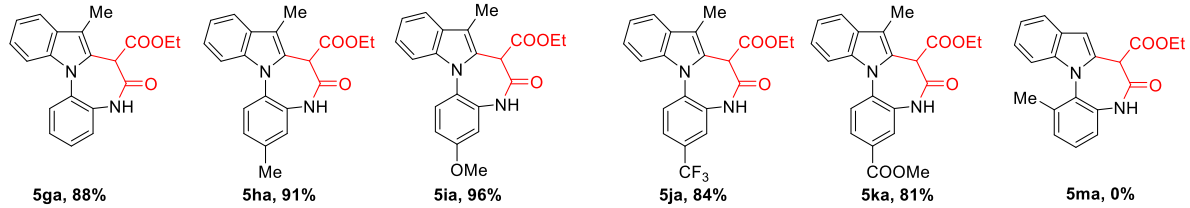


1 1' 2 5 5'

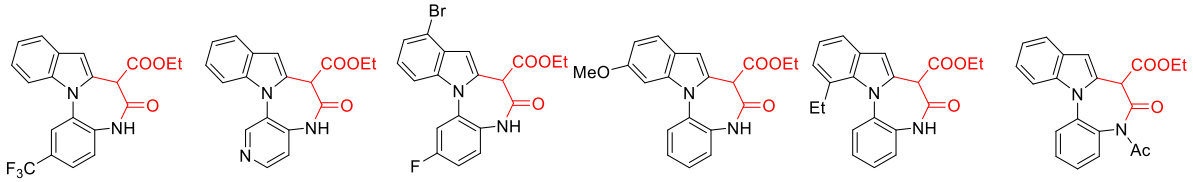
a) Substrate Scope of Indole



5aa, 92% **5ba, 95%** **5ca, 93%** **5da, 98%** **5ea, 90%** **5fa, 78%**

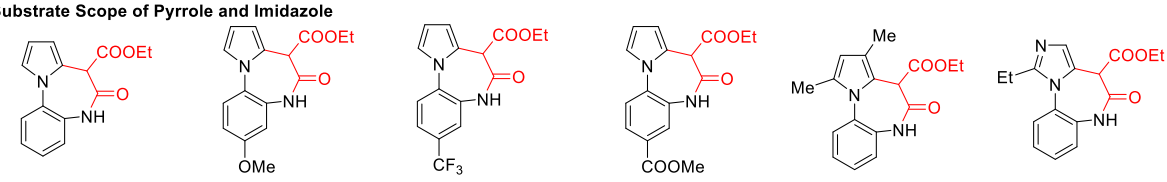


5ga, 88% **5ha, 91%** **5ia, 96%** **5ja, 84%** **5ka, 81%** **5ma, 0%**



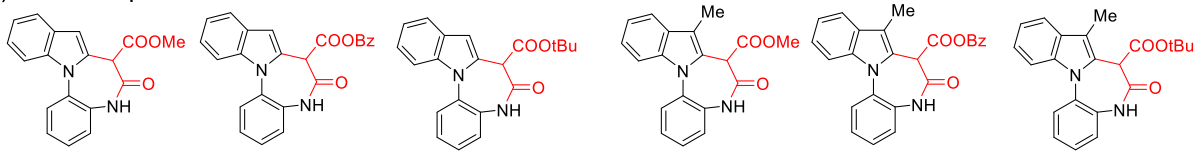
5na, 86% **5oa, 74%** **5pa, 92%** **5qa, 88%** **5ra, 85%** **5sa, 0%**

b) Substrate Scope of Pyrrole and Imidazole

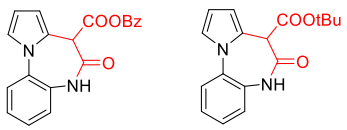


5'aa, 85% **5'ba, 89 %** **5'ca, 85 %** **5'da, 77%** **5'ea, 0%** **5'fa, 0%**

c) Substrate Scope of Diazo



5ab, 91% **5ac, 87%** **5ad, 65%** **5gb, 91%** **5gc, 81%** **5gd, 70%**



5'ac 75% **5'ad, 48%**

[a] Reaction conditions: **1** (0.48 mmol), **2** (0.96 mmol), $[RhCp^*Cl_2]_2$ (2.5 mol%), $AgSbF_6$ (20 mol%), EtOH (4 mL), 60 °C, 3h. [b] Isolated yields.

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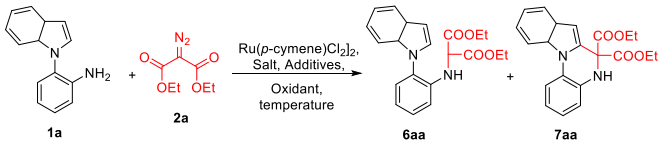
Table 3. Optimization for the synthesis of Indolo[1,2-*a*]quinoxalines (**7aa**)[a]



Entry	Additive	Solvent	Time	Yield(%)[b]	
				7aa	**6aa**
1[c]	AcOH	EtOH	12	13	73
2[c]	PivOH	EtOH	12	10	70
3[c]	NaOAc	EtOH	12	61	0
4[c]	$Cu(OAc)_2$	EtOH	12	0	trace
5	NaOAc	EtOH	12	75	0
6	KOAc	EtOH	12	72	0
7	CsOAc	EtOH	12	65	0
8	NaOPiv	EtOH	12	52	0
9	CsOPiv	EtOH	12	58	0
10	NaOAc	MeOH	12	70	0
11	NaOAc	TFE	12	80	0
12	NaOAc	CH_3CN	12	trace	0
13	NaOAc	DCE	12	45	0
14[d]	**NaOAc**	**TFE**	**6**	**87**	**0**
15[d],[e]	NaOAc	TFE	6	85	0
16	-	TFE	24	0	0

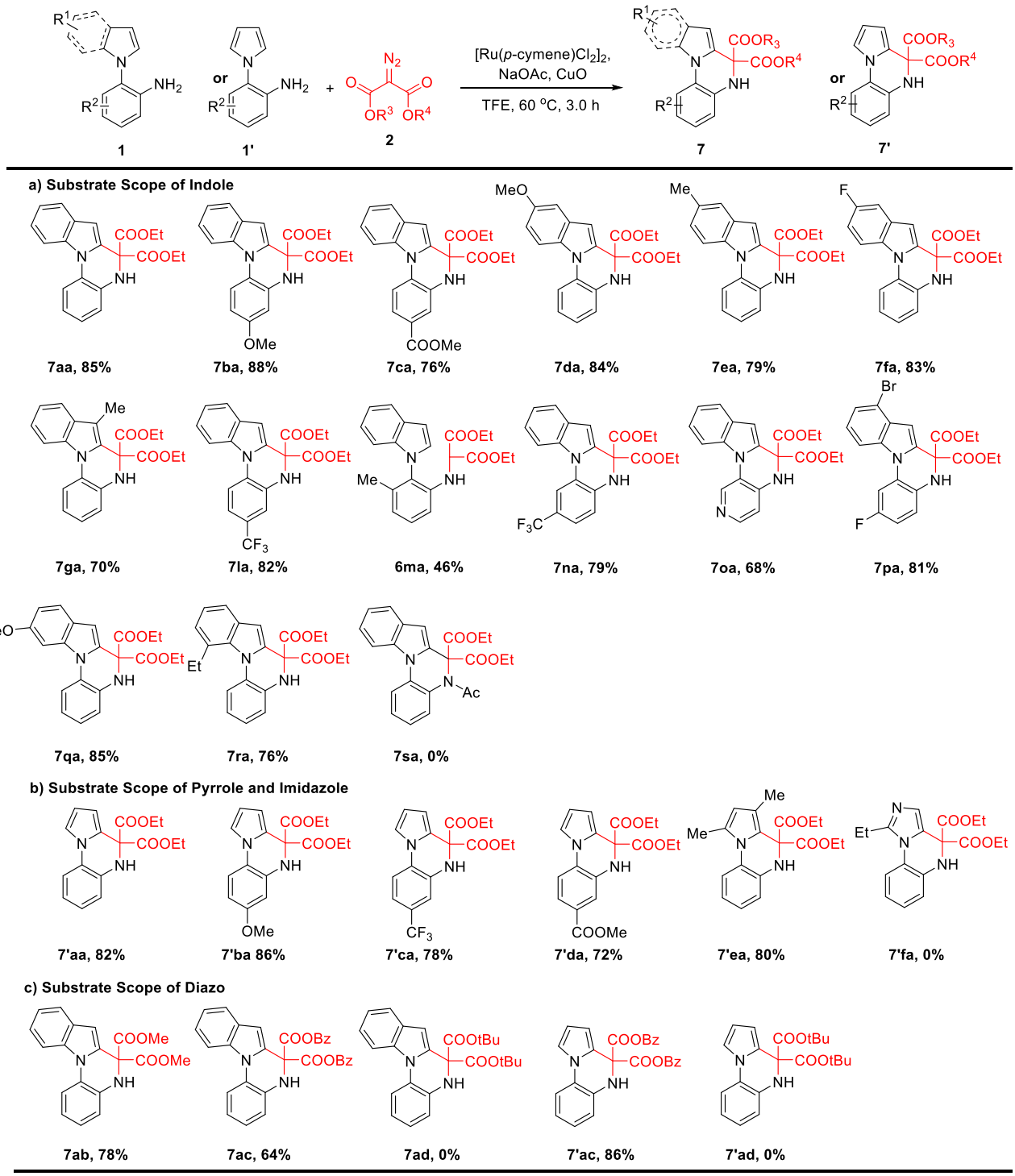
[a] Reaction conditions: **1a** (0.48 mmol), **2a** (.96 mmol), catalyst (5 mol%), additive (20 mol%), oxidant (0.96 mmol), solvent (4 mL) at 60 °C. [b] Isolated yields. [c] $AgSbF_6$ (20 mol%) used as a salt. [d] CuO used as an oxidant.[e] At 100 °C.

Next, we move our attention to find out the reaction condition for serendipity discovered indolo[1,2-*a*]quinoxaline **7aa** by Ru(II) as a catalyst**.** Initially, various additives such as PivOH, AcOH, $Cu(OAc)_2$, and NaOAc were evaluated (Table 3, entries 2-5). Among them, NaOAc afforded the **7aa** in 61 % yield without formation of *N*-alkylated product **6aa (**entry 4). In the absence of $AgSbF_6$, **7aa** increased to 75 % yield (Table 3, entry 5). Replacing NaOAc with KOAc, CsOAc, NaOPiv, and CsOPiv led to reduction in the yields (entries 6-9). Subsequent solvent screening demonstrated 2,2,2,-trifluoroethanol (TFE) to give **7aa** in 80 % yield (entry 11). Respectable improvement in the yield and reaction time observed when CuO used as an oxidant, afforded **7aa** in 87 % yield in 6 h (entry 14). Rising the temperature to 100 °C did not affect the product formation (entry 15). No product formation observed when reaction conducted without a catalyst (entry 16). Briefly screening showed that diethyl indolo[1,2-*a*]quinoxaline-6,6(5*H*)-dicarboxylate **7aa** was obtained in 87% yield when the *o*-indolo aniline **1aa** and diethyl diazo malonate **2aa** in TFE were treated with [Ru(*p*-cymene)Cl_2]$_2$ (5 mol%), additive NaOAc (20 mol%), and oxidant CuO (2.0 equiv) at 60 °C for 6h (entry 14).

Next, we studied the reaction scope of various substituted *o*-indolyl aniline **1** with diethyl diazomalonate **2a** (Table 4a). Various electron donating/withdrawing groups, halo substituent on aniline moiety or indole moiety of *o*-indolyl aniline are well-tolerated to construct the series of indolo[1,2-*a*]quinoxalines (**7aa-ga, 7la, 7na-ra**) in moderate to excellent yields. However, a methyl group at *ortho* position of *o*-indolyl aniline **1m** failed to give the desired product, where *N*-alkylated product **6ma** obtained in 46 % yield. No product formation was observed with NH-substituted *o*-indolyl aniline (**1s**). The *o*-pyrrolyl aniline having different substituents on aniline moiety were efficiently engaged in reaction to led to the corresponding pyrrolo[1,2-*a*]quinoxaline (Table 4b**, 7'aa-da**) in moderate to excellent yield. In addition, pyrrole bearing methyl group on 2,4 position **1'e** smoothly furnished the expected product **7'ea** in 80 % yield. No product formation observed with the *o*-imidazolyl aniline (**1'f**) and starting material remained unreacted. We also investigated scope and reactivity of the various diazo compounds **2** with *o*-indolyl/pyrrolyl aniline **1a** and **1'a** (Table 4c). The reaction of dimethyl diazomalonate **2b** or dibenzyl 2-diazomalonate **2c** with *o*-indolyl aniline **1a** provided the products **7ab** and **7ac** in 78 % and 64 % yield respectively. Moreover, *o*-pyrrolyl aniline **1'a** smoothly reacted dibenzyl 2-diazomalonate **2c** to furnish the desired product **7'ac** in excellent yield. The di-*tert*-butyl diazomalonate **2d** did not react with *o*-indolyl/pyrrolyl aniline (**1a**/**1'a)** and the reaction becomes sluggish.

To shed light on mechanism of this catalyst controlled chemodivergent annulation, a series of control experiments were performed (Scheme 3). The treatment of C2-alkylated intermediate **3aa** under the Rh catalyzed reaction condition resulted **5aa** in 91 % yield (Scheme 3a, right). Similarly, formation of **5aa** was observed in 70 % yield instead of indolo [1,2-*a*]quinoxaline **7aa** under the Ru catalyzed reaction condition (Scheme 3a, left). These results suggest the formation of **5aa** takes place through the C2-H activation followed by amide bond formation, whereas formation of **6aa** is not due to the Ru-catalyzed C2−H bond activation. Next, we perform the reaction of diazo malonate **2a** with the [Ru(*p*-cymene)Cl_2]$_2$ and NaOAc in TFE at room temperature to deliver the Ru-carbene complex **B** (Scheme 3b). Then, the reaction between Ru-carbene complex **B** and *o*-indolo aniline in the presence oxidant CuO in TFE at 60 °C afforded the product **7aa** in the 50 % yield along with *N*-alkylated product **6aa** in 15 % yield (Scheme 3c). This result may indicate the synthesis of indolo [1,2-*a*]quinoxaline is initiated by the formation of Ru-carbene complex **B**. Afterward, we carried out the competition experiments of Ru and Rh catalyst using substrate **1a** and **2a**. The Ru-catalyzed product **7aa** obtained in 75 % yield, but no Rh-catalyzed product **5aa** observed (Scheme 3d) which may be due to the rapid formation of Ru-carbene complex **B** to dominate

Table 4. A Ru(II) catalyzed synthesis of indolo/pyrrolo-fused quinoxaline (**7**)[a,b]



[a]Reaction conditions: **1a** (0.48 mmol), **2a** (0.96 mmol), [Ru(*p*-cymene)Cl_2]$_2$ (5 mol%), NaOAc (20 mol%), CuO (0.96 mmol), TFE (4 mL), 60 °C, 6 h. [b] Isolated yields.

reaction progress.

On the basis of the experimental results and precedent literature evidence,[11] a plausible mechanism for the synthesis of diazepino [1,7-*a*]indole is depicted in Scheme 4. First, active dicationic Rh(III) species [RhCp*X_2] was generated from [RhCp*Cl_2]$_2$ and $AgSbF_6$. Coordination of a free amine group of *o*-indolyl aniline **1a** to [RhCp*X_2] species **I** followed by selective C_2-H cleavage afforded six membered rhodacycle intermediate **II**. Subsequently, coordination of incoming diazo ester **2a** to Rh(III) species **II** followed by extrusion of nitrogen gave the metal-carbene species **IV.** Later migratory insertion of the Rh-C bond into the carbene moiety afford seven membered rhodacycle intermediate **V**, which would undergo the protonolysis to form C2 alkylated intermediate **VI**. Finally, free amine group proceeded

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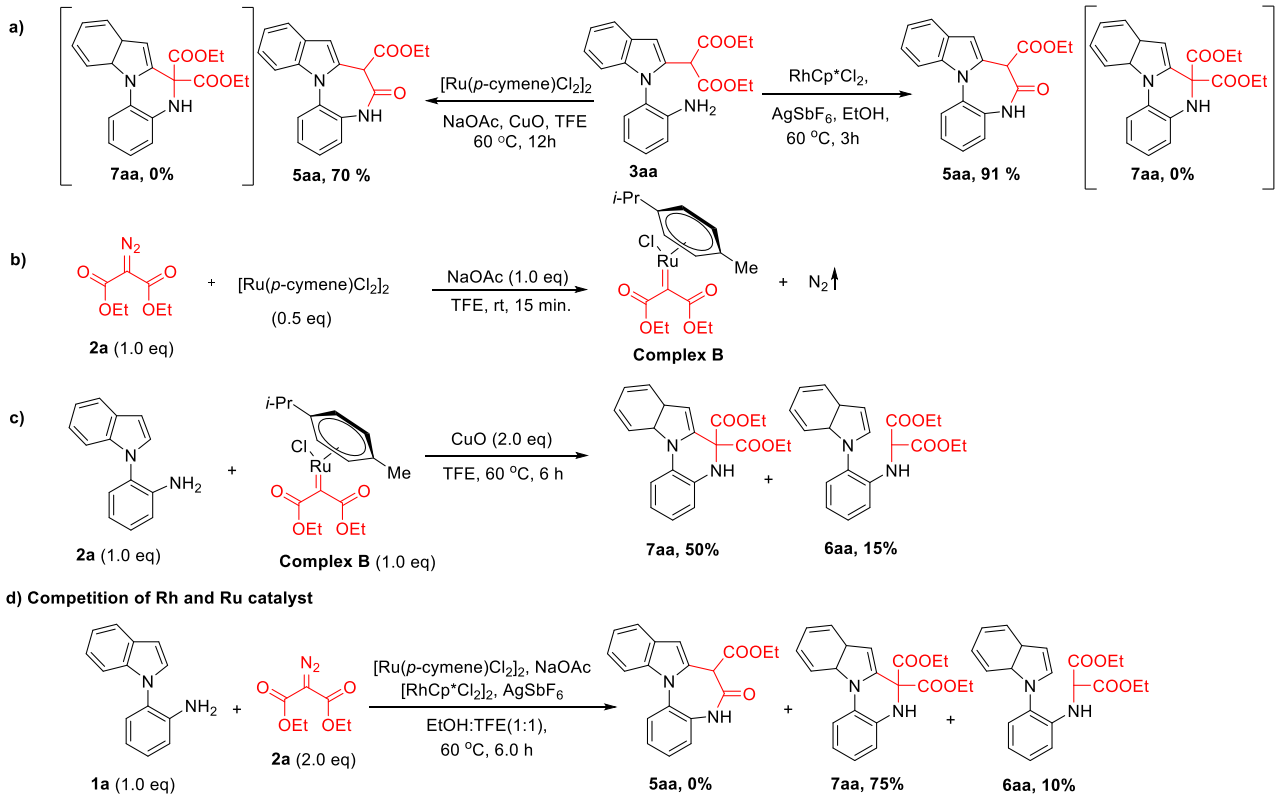
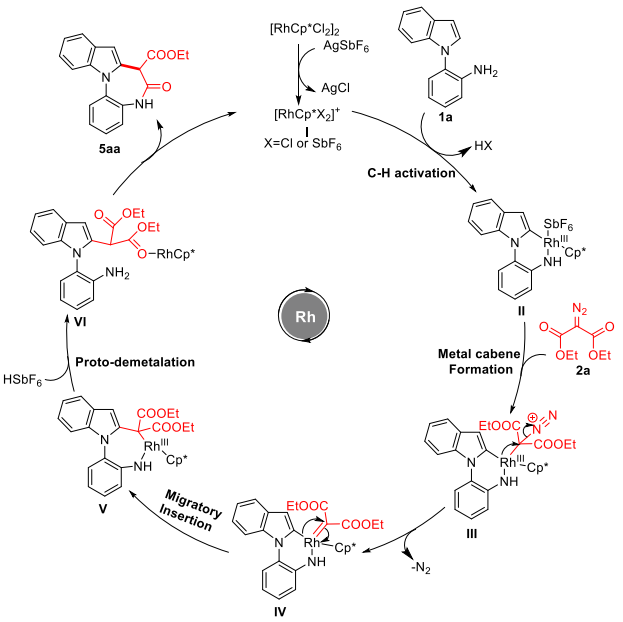
Scheme 3. A mechanistic study to probe the reaction pathway

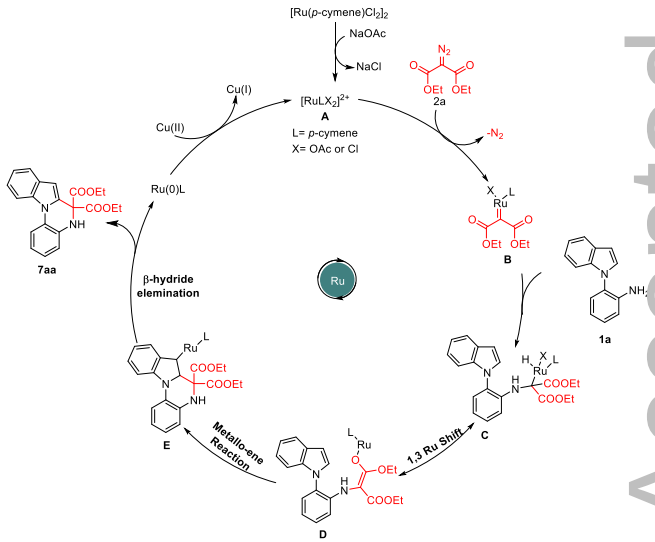


nucleophilic attack towards the carbonyl group in ester moiety **VI** where $[RhCp^*]^{2+}$ acted as a Lewis acid to activate the carbonyl group to furnish corresponding product **5aa** with regeneration of active catalyst **I**.

Scheme 4: A plausible mechanism leading to the formation of diazepino [1,7-*a*]indole **5aa**



Scheme 5. A plausible pathway for the formation of indolo [1,2-*a*]quinoxaline **7**



Although the formation of **7** remains unclear at this stage, referring to the previous literatures[12] and our experimental results, a plausible mechanism for the formation of **7aa** is proposed in Scheme 5. A [Ru(*p*-cymene)Cl_2]$_2$ complex generates the active [Ru(*p*-cymene)X_2] species **A** which forms the Ru-carbene intermediate **B** by elimination of –N_2. Next, addition of free amine group of *o*-indolo aniline to ruthenium

carbene intermediate **B** to give the *N*-ylide **C**[13]. After 1,3 Ru shift followed by metallo-ene reaction takes place to afford the intermediate **E**. Finally, β-hydride elimination furnishes the indolo-fused quinoxaline **7** along with Ru(0) intermediate which was further reoxidized by CuO to regenerates the active catalyst **A** to continue the catalytic cycle.[13b-c]

Conclusion

We have successfully explored catalyst-controlled chemodivergent annulation strategy to access diazepino [1,7-*a*]indole and indolo [1,2-*a*]quinoxaline from reaction of readily available *o*-indolo anilines with diazo esters as a coupling partner. Notably, the product formation is exclusively dependent on choice of transition metal catalysts. In the presence of Rh(III) catalyst, indolo-fused diazepine was selectively created *via* selective C_2-H alkylation and subsequently the amide bond formation was proceeded. On other hand with Ru as a catalyst, the indolo-fused quinoxaline afforded through insertion of N-H bond to ruthenium carbene followed by cyclization through metallo-ene type reaction. A variety of *o*-indolo/pyrrolo anilines and diazo compounds are amenable to the current catalyst-controlled system to afford the indolo/pyrrolo-fused diazepine and quinoxaline in excellent yields. Further detailed mechanistic investigation for formation of indolo [1,2-*a*]quinoxalines is underway in our laboratory.

Experimental Section

A representative procedure for the synthesis of Ethyl 6-oxo-6,7-dihydro-5*H*-benzo[2,3][1,4]diazepino[1,7-*a*] indole-7-carboxylate (5aa)

A seal reaction tube was charged with *o*-indolo aniline **1a** (100 mg, 0.48 mmol), diethyl malonate **2a** (178 mg, 0.96 mmol), $[RhCp^*Cl_2]_2$ (7.0 mg, 2.5 mol %), $AgSbF_6$ (32 mg, 20 mol %), in EtOH (4.0 mL). The mixture was stirred at 60 °C for 3 h. After completion of reaction, the reaction mixture was diluted with EtOAc and filtered through the celite. The solvent was removed under vacuum, and the residue was purified by silica gel chromatography using hexane/ethyl acetate (90:10 %) to afford product dihydro-5*H*-benzo[2,3][1,4]diazepino[1,7-*a*]indole **5aa** as a white solid (141 mg, 92% yield).

Mp 215-217 °C; 74:26 rotamer ratio at room temperature in C_3D_6O; ^{1}H NMR (400 MHz, C_3D_6O) δ 9.46 (s, 0.26H), 9.31 (s, 1H), 7.87 (dd, *J* = 8.0, 3.6 Hz, 0.42H), 7.85-7.80 (m, 1H), 7.70-760 (m, 3H), 7.51-7.56 (m, 1H), 7.41-7.38 (m, 3H), 7.29 – 7.13 (m, 3H), 6.74 (s, 1H), 5.10 (s, 1H), 4.7 (s, 0.26H), 4.31 (q, *J* = 8.2 Hz, 0.8H), 3.79 (q, *J* = 7.9 Hz,, 2H), 1.34 – 1.21 (m, 1.4H), 0.83 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, C_3D_6O) δ 167.0, 166.5, 165.9, 135.9, 135.3, 134.8, 133.9, 131.23, 130.6, 129.5, 127.2, 127.1, 126.0, 125.7, 125.2, 124.9, 123.9, 123.9, 123.7, 122.5, 122.3, 121.0, 121.0, 120.9, 110.6, 103.1, 100.8, 61.4, 60.9, 53.4, 48.7, 13.5, 13.1; MS (ESI): *m/z* 321; HRMS (ESI, m/z) Calcd. $C_{19}H_{17}N_2O_3$ $[M+H]^+$: 321.1234; Found 321.1240 $(M+H)^+$

^{1}H NMR (600 MHz, DMSO-d_6 at 100 °C) δ 9.91 (s, 1H), 7.69 (s, 1H), 7.64 (d, *J* = 7.9 Hz, 1H), 7.58 (d, *J* = 8.3 Hz, 1H), 7.39-7.32 (m, 3H), 7.21 (t, *J* = 7.8 Hz, 1H), 7.16 (t, *J* = 7.5 Hz, 1H), 6.69 (s, 1H), 5.10 (s, 1H), 3.74 (s, 2H), 0.80 (s, 3H).

A representative procedure for the synthesis of diethyl indolo[1,2-*a*]quinoxaline-6,6(5*H*)-dicarboxylate (7aa)

A seal reaction tube was charged with *o*-indolo aniline **1a** (100 mg, 0.48 mmol), diethyl malonate **2a** (178 mg, 0.96 mmol), $[Ru(p\text{-cymene})Cl_2]_2$ (29.0 mg, 10 mol %), NaOAC (8.0 mg, 20 mol %), CuO (75 mg, 0.96 mmol) in 2,2,2-Trifluoroethanol (TFE) (5.0 mL). The mixture was stirred at 60 °C for 6 h. After completion of reaction, reaction mixture was diluted with EtOAc and filtered through the celite. The solvent was removed under vacuum, and the residue was purified by silica gel chromatography using hexane/ethyl acetate (98:2 %) to afford product diethyl indolo[1,2-*a*]quinoxaline-6,6(5*H*)-dicarboxylate **7aa** as white solid (140 mg, 85 % yield).

Mp 110-113 °C; ^{1}H NMR (400 MHz, C_3D_6O) δ 8.10 (d, *J* = 8.4 Hz, 1H), 7.97 (d, *J* =7.6 Hz, 1H), 7.68 (d, *J* =7.6 Hz, 1H),7.34 – 7.28 (m, 2H), 7.22 – 7.17 (t, *J* =7.44 Hz, 1H), 7.10 – 7.01 (q, *J* = 7.4 Hz, 2H), 6.83 (s, 1H), 6.32 (s, 1H), 4.27 (q, *J* = 7.1 Hz, 4H), 1.23 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (101 MHz, C_3D_6O) δ 167.1, 134.5, 134.0, 131.9, 129.3, 126.4, 124.3, 123.2, 121.4, 121.0, 120.3, 116.6, 116.4, 101.8, 101.7, 62.2, 13.4; MS (ESI) *m/z*: 365 (MH^+); HRMS (ESI, m/z) Calcd. $C_{21}H_{20}N_2NaO_4$ $[M+Na]^+$: 387.1315; Found 387.1318 $(M+Na)^+$.

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[14] CCDC 1883093 (**5aa**) and CCDC 1883103 (**7aa**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

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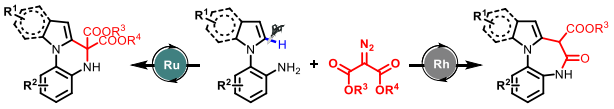
FULL PAPER

Catalyst-Controlled Chemodivergent Annulation to Indolo/Pyrrolo-Fused Diazepine and Quinoxaline



Adv. Synth. Catal. **Year**, *Volume*, Page – Page

Sandip Dhole, Wei-Jung Chiu, Chung-Ming Sun*