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EXPERIMENTAL INVESTIGATION OF TETRACYCLIC COMPOUNDS CONTAINING A NINE-MEMBERED SULTAM VIA COBALT ALKYNE COMPLEXES

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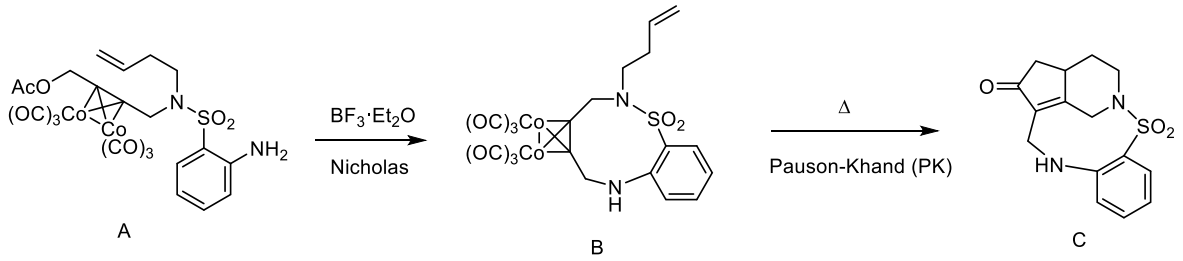
Abstract – The synthesis, reactivity, and stereochemistry of nine-membered sultams fused with cobalt alkyne complexes using sequential Nicholas and Pauson–Khand reactions are reported. Novel tetracyclic compounds containing nine-membered sultam moieties were characterized by NMR spectroscopy and X-ray crystallography.

INTRODUCTION

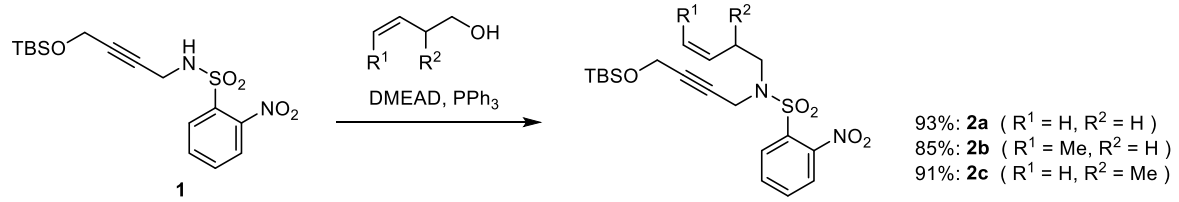
Dicobalt hexacarbonyl alkyne complex-mediated cyclization reactions are among the methods available to construct medium-sized rings and bicyclic systems.[1] The Nicholas[2] and Pauson–Khand (PK) reactions[3] have been extensively studied and remain of great importance in this respect, with applications in the synthesis of structurally complex molecules, including bioactive natural products.[4] In addition, studies on the combined use of the Nicholas and PK reactions have been attempted by several groups.[5] The Shea group reported the scope and limitations of this approach for the synthesis of medium-sized heterocyclic ring systems, wherein they demonstrated difficulty in constructing a nitrogen-embedded, nine-membered ring framework.[5a] Recently, our group successfully constructed a sulfonamide-embedded, nine-membered ring compound fused with dicobalt hexacarbonyl moiety B, which was synthesized from dicobalt alkyne complex A by a BF_3-induced Nicholas reaction.[6] As a result of the bent and strained structure of B, a subsequent intramolecular PK reaction occurred upon heating without the addition of any reagents to afford tetracycle C in sufficient yield (**Scheme 1**). Encouraged by this novel synthetic route and the reactivity of these medium-sized sultams (B and C), which are synthetically important building blocks in drug discovery,[7] we decided to investigate their chemical properties. Herein, we report the detailed syntheses of tetracyclic compounds containing a nine-membered sultam via sequential cobalt alkyne complex-mediated cyclization reactions.



Scheme 1. Synthesis of tetracyclic compound C through sequential reactions of cobalt complex A via intermediate B

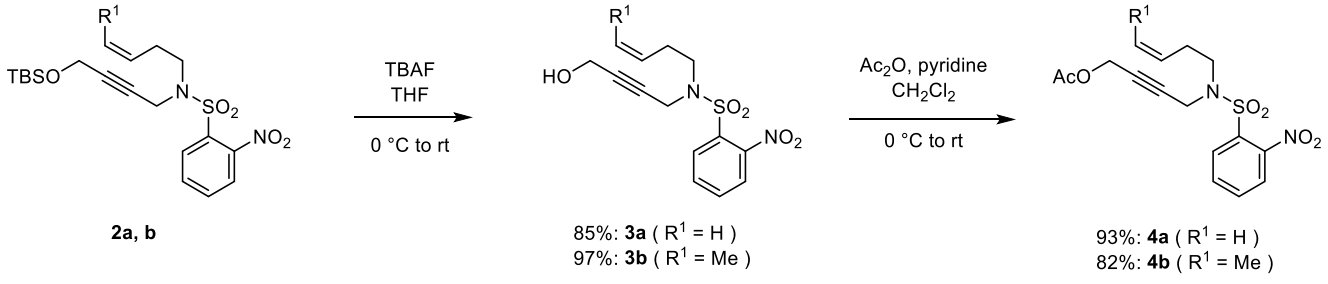
RESULTS AND DISCUSSION

The preparation of the various cobalt precursors was based on a previously established, diverse synthetic route.[6] First, enyne-sulfonamides **2a–c** were prepared from sulfonamide **1** with one of three alcohols, but-3-en-1-ol, *cis*-pent-3-en-1-ol, or 2-methylbut-3-en-1-ol, in the presence of di-2-methoxyethyl azodicarboxylate (DMEAD) and PPh_3. DEMAD, as reported by the Sugimura group,[8] is a useful reagent for the Mitsunobu[9] and Fukuyama *o*-nitrobenzenesulfonamide (nosylamide) protocol,[10] allowing for a facile purification process. Compounds **2a–c** were readily produced in 85%–93% yields by adopting this protocol (**Scheme 2**).



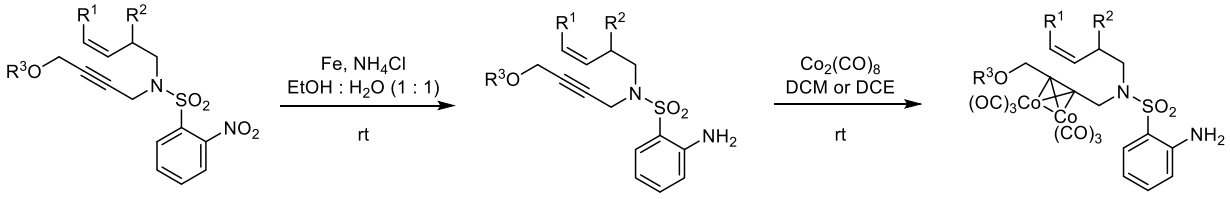
Scheme 2. Synthesis of enyne-sulfonamides **2a–c** using the Mitsunobu and Fukuyama protocol with DMEAD

To test the reactivity of the propargyl group, the *tert*-butyldimethylsilyl (TBS) group was transformed into an acetyl (Ac) group, as the acetoxyl moiety is an excellent leaving group for the Nicholas reaction.[2] The TBS groups were removed from **2a** and **2b** by adding tetrabutylammonium fluoride (TBAF) in tetrahydrofuran (THF) at 0 °C to give corresponding propargyl alcohols **3a** and **3b**. Compounds **3a** and **3b** were then converted into **4a** and **4b** in sufficient yields using anhydrous acetic acid with pyridine in CH_2Cl_2 at 0 °C (**Scheme 3**).



Scheme 3. Conversion of TBS into Ac via propargyl alcohols

Chemoselective reduction of the nitro groups on **2a–c**, **3a**, and **4a**,**b** was achieved using Fe in the presence of NH_4Cl in aqueous ethanol, a process developed by the Ramadas group[11a] and Xiao group,[11b] to give aniline derivatives **5a–f** in 88%–95% yields without any intermediates or side products. Subsequent dicobalt alkyne complexation of **5a–f** was performed under simple conditions, mixing with a stoichiometric amount of dicobalt octacarbonyl [$Co_2(CO)_8$] in dichloromethane (DCM) or 1,2-dichloroethane (DCE) at ambient temperature for 2 h. Cobalt alkyne complexes **6a–f** could all be isolated in excellent yields using silica gel chromatography; however, the PK cyclization gradually occurred in the warm water bath during evaporation (**Scheme 4**).



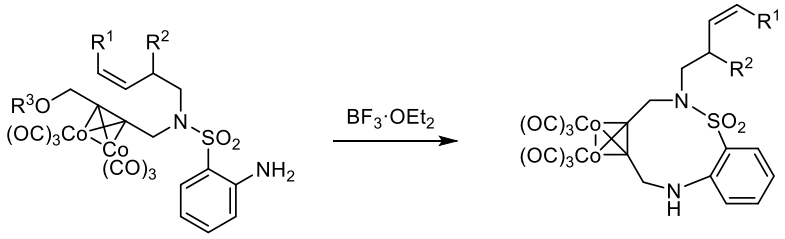
2a-c, 3a, 4a,4b

96%: **5a** (R^1 = H, R^2 = H, R^3 = TBS)
92%: **5b** (R^1 = Me, R^2 = H, R^3 = TBS)
96%: **5c** (R^1 = H, R^2 = Me, R^3 = TBS)
88%: **5d** (R^1 = H, R^2 = H, R^3 = H)
93%: **5e** (R^1 = H, R^2 = H, R^3 = Ac)
95%: **5f** (R^1 = Me, R^2 = H, R^3 = Ac)

98%: **6a** (R^1 = H, R^2 = H, R^3 = TBS)
99%: **6b** (R^1 = Me, R^2 = H, R^3 = TBS)
93%: **6c** (R^1 = H, R^2 = Me, R^3 = TBS)
88%: **6d** (R^1 = H, R^2 = H, R^3 = H)
96%: **6e** (R^1 = H, R^2 = H, R^3 = Ac)
99%: **6f** (R^1 = Me, R^2 = H, R^3 = Ac)

Scheme 4. Nitro group reduction and complexation with cobalt carbonyl reagents

Once we obtained **6a–f**, we began investigating the formation of nine-membered sultams with the cobalt alkyne complexes through an endo-type Nicholas cyclization reaction.[2] The reaction conditions were found to be optimized when 2.4 equiv of boron trifluoride diethyl etherate in dilute DCE was used. Use of 1.2 equiv of BF_3 required a longer reaction time, most likely due to the existence of the amino groups in **6a–f**. Subsequently, **6a–f** were converted into nine-membered sultams **7a–f** using the optimized reaction conditions, i.e., BF_3 (2.4 equiv) in DCE (0.005M) at 0 °C for 30 min. Interestingly, there was no difference in whether OTBS (**6a**), OH (**6d**), or OAc (**6e**) was used as the leaving group at the propargylic position, affording **7a**, **7d**, and **7e**, respectively. Thus, we demonstrated that the Nicholas reaction could proceed even in the presence of the OTBS moiety as a protecting group. Therefore, there is no longer a need to exchange TBS for Ac, as in **Scheme 3** (**Scheme 5**).

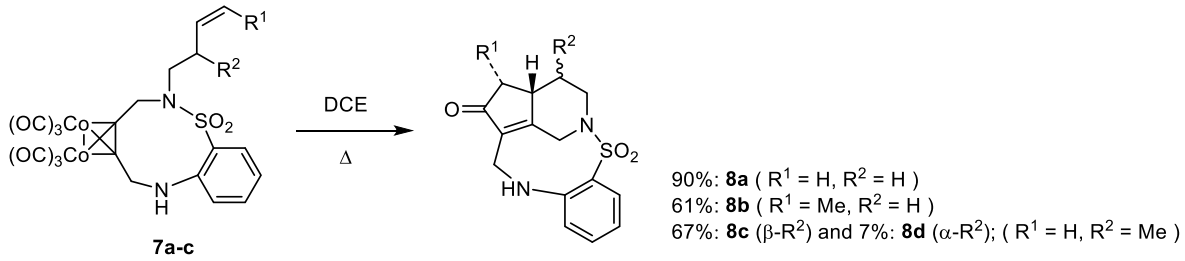


6a (R^1 = H, R^2 = H, R^3 = TBS)
6b (R^1 = Me, R^2 = H, R^3 = TBS)
6c (R^1 = H, R^2 = Me, R^3 = TBS)
6d (R^1 = H, R^2 = H, R^3 = H)
6e (R^1 = H, R^2 = H, R^3 = Ac)
6f (R^1 = Me, R^2 = H, R^3 = Ac)

82%: **7a** (R^1 = H, R^2 = H) from **6a**
84%: **7b** (R^1 = Me, R^2 = H) from **6b**
72%: **7c** (R^1 = H, R^2 = Me) from **6c**
69%: **7a** (R^1 = H, R^2 = H) from **6d**
72%: **7a** (R^1 = H, R^2 = H) from **6e**
77%: **7b** (R^1 = Me, R^2 = H) from **6f**

Scheme 5. BF_3-induced endocyclic Nicholas reaction for construction of nine-membered sultams

Next, we investigated the reactivity of the cobalt alkyne moiety with alkenes on **7a–c** under intramolecular PK cyclization conditions.[3] First, terminal alkene **7a** was successfully converted to cyclopentenone **8a** in 90% yield by simply heating at 60 °C for 30 min. In contrast, the PK cyclization of internal alkene **7b** required reaction at 80 °C for 1 h to completely consume the cobalt complex and afford **8b** as a single isomer in 61% yield. Thus, the methyl group on the alkene inhibited access between the alkene and cobalt moieties. Moreover, we previously reported that a methyl group at the allylic position affected the PK cyclization process, resulting in two diastereoisomers.[12] Therefore, the attempted PK cyclization of **7c** gave two isomers (**8c** and **8d**) in about 10:1 ratio, demonstrating that repulsion between the methyl group and alkene moiety influenced the cyclization process (**Scheme 6**).



Scheme 6. Heat-induced intramolecular PK reaction of **7a–c**

The stereochemistry and conformations of **8b** and **8c** were confirmed using single crystal X-ray analysis, as illustrated in **Figure 1**.[13] The results indicated that the piperidine and aromatic rings were in close proximity due to the bent nine-membered ring conformation. The corresponding NMR spectroscopic data supported this observation. For example, the corresponding methyl peak in **8d** (α-isomer) was observed at −0.17 ppm (d, J = 7.6 Hz, 3H) in the ^{1}H NMR spectrum, as a result of the ring current effect.

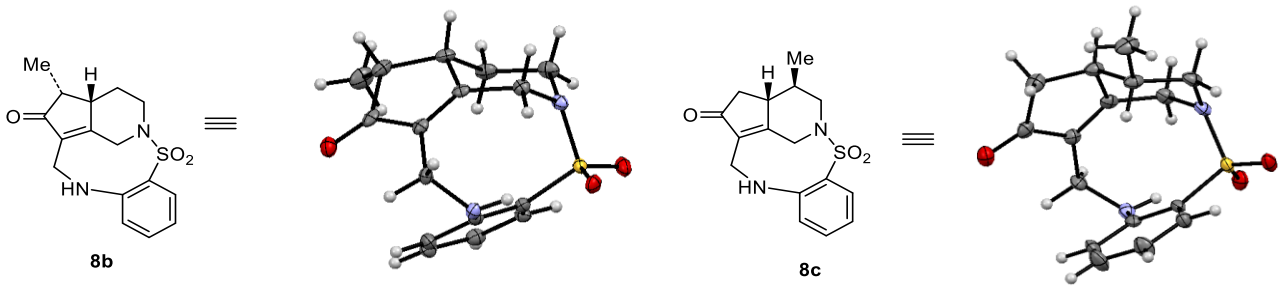
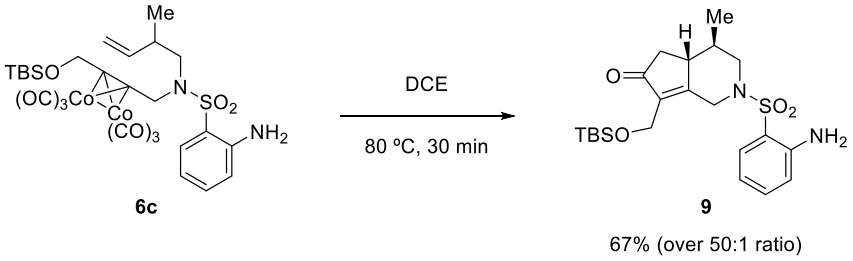


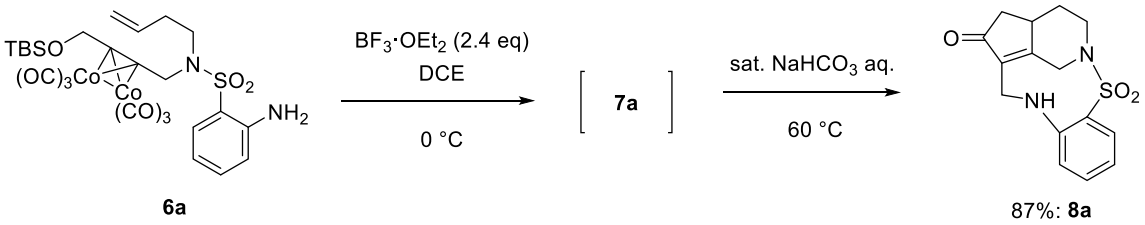
Figure 1. X-Ray crystal structures of **8b** and **8c**

To compare the diastereoselectivity of **8c**:**8d** = ca. 10:1, we attempted the PK reaction of acyclic, alkyne cobalt complex **6c**. Under the same reaction conditions, the major product, **9**, was obtained in 67% yield with trace amounts of a minor product (over 50:1 ratio). The stereochemistry of **9** was confirmed by NMR spectroscopic measurements and was also supported by our previously reported compounds.[12] These results indicate that diastereoselectivity generation is influenced by the nine-membered ring conformation throughout the PK reaction process (**Scheme 7**).



Scheme 7. PK reaction of **6c** to produce **9** as the major stereoisomer

We also explored a one-pot procedure from **6a** to **8a**. After several attempts, we found that adding saturated aqueous $NaHCO_3$ after the completion of the Nicholas reaction followed by heating afforded **8a** in 87% yield without isolation and purification of **7a**. When the $NaHCO_3$ and heating were removed, the yield of **8a** decreased to below 40%. Therefore, we demonstrated that the PK step from **7a** proceeds smoothly under basic aqueous conditions, which avoid the decomposition of **7a** (**Scheme 8**).



Scheme 8. One-pot procedure of sequential cobalt reactions from **6a** to **8a**

In conclusion, we investigated the combined use of the Nicholas and PK reactions to synthesize unique tetracyclic molecules **8a–d.** In the Nicholas reaction, OTBS, OH, and OAc groups could function as leaving groups. Through the PK reaction, the diastereoselectivity of nine-membered ring fused cobalt complex **7c** was different from that of acyclic **6c**. We also successfully demonstrated a one-pot procedure for sequential cobalt reactions. We expect that these results will allow for the enhancement of the chemistry toward medium-sized heterocyclic sultams in drug discovery.

EXPERIMENTAL

General. Melting points were measured using a Yanaco micro-melting point apparatus. IR spectra were obtained using a PerkinElmer Spectrum 100 FT-IR spectrometer. ^1H and ^{13}C NMR spectra were recorded using JEOL JNM-ECA-600 spectrometer (^1H: 600 MHz; ^{13}C: 150 MHz) in $CDCl_3$. The chemical shifts were reported in ppm (δ) using tetramethylsilane (TMS) as an internal standard. Coupling constants (*J*) were reported in hertz (Hz) using the following abbreviations for the multiplicity: s, singlet; d, doublet; t, triplet; m, multiplet; comp, complex, i.e., overlapping multiplets of magnetically nonequivalent protons; br, broad. Mass spectra were measured using a JEOL JMS-600 spectrometer.

***N*-[4-(*tert*-Butyldimethylsilyloxy)-but-2-ynyl]-2-nitrobenzenesulfonamide (1)** Following the procedure used in our previous experiments,[6] **1** was prepared through a four-step sequence from 2-nitrobenznenesulfonamide and obtained as a colorless oil. The structure was confirmed by comparison to an authentic sample.[6] ^{1}H NMR: δ 8.19–8.15 (m, 1H), 7.91–7.87 (m, 1H), 7.76–7.71 (comp, 2H), 5.62 (t, *J* = 6.0 Hz, 1H), 4.02 (dt, *J* = 6.0, 1.7 Hz, 2H), 3.96 (t, *J* = 1.7 Hz, 2H), 0.82 (s, 9H), 0.00 (s, 6H).

General procedure for synthesis of enyne-amides (2a–c)

To a stirred solution of **1** (1 equiv), alcohol (1.1–1.3 equiv), and PPh_3 (1.2 equiv) in anhydrous toluene (5 mL per 1 mmol) was slowly added DMEAD (1.2 equiv) at 0 °C. After stirring for 24 h at ambient temperature, the reaction mixture was treated with H_2O. The aqueous layer was separated from the organic layer and extracted with Et_2O. The combined organic layers were dried with $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography by eluting with hexane:EtOAc (6:1 to 3:1) to give the corresponding enyne-amide (**2a–c**).

***N*-(But-3-en-1-yl)-*N*-[4-(*tert*-butyldimethylsilyloxy)-but-2-yn-1-yl]-2-nitrobenzenesulfonamide (2a)**:[6] Obtained in 93% yield as a colorless oil. ^{1}H NMR: δ 8.03 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.70–7.64 (comp, 2H), 7.62 (dd, *J* = 7.6, 1.4 Hz, 1H), 5.70 (ddt, *J* = 17.2, 10.3, 6.9 Hz, 1H), 5.08 (dd, *J* = 17.2, 1.4 Hz, 1H), 5.02 (dd, *J* = 10.3, 1.4 Hz, 1H), 4.23 (s, 2H), 4.17 (s, 2H), 3.46 (t, *J* = 7.2 Hz, 2H), 2.34 (dt, *J* = 7.2, 6.9 Hz, 2H), 0.86 (s, 9H), 0.04 (s, 6H).

(*Z*)-*N*-[4-(*tert*-Butyldimethylsilyloxy)-but-2-yn-1-yl]-2-nitro-*N*-(pent-3-en-1-yl)benzenesulfonamide (2b): Obtained in 85% yield as a yellow oil. ^{1}H NMR: δ 8.02 (dd, *J* = 7.2, 1.8 Hz, 1H), 7.70–7.64 (comp, 2H), 7.62 (dd, *J* = 6.6, 1.8 Hz, 1H), 5.56–5.48 (m, 1H), 5.33–5.26 (m, 1H), 4.25 (s, 2H), 4.18 (s, 2H), 3.41 (t, *J* = 1.8 Hz, 2H), 2.34 (q, *J* = 7.2 Hz, 2H), 1.59 (d, *J* = 6.0 Hz, 3H), 0.86 (s, 9H), 0.05 (s, 6H). ^{13}C NMR: δ 148.3, 133.6, 133.2, 131.7, 130.9, 127.2, 125.5, 124.3, 84.5, 77.8, 51.6, 46.3, 36.9, 25.8 (3C), 25.6, 18.3, 12.7, -5.2 (2C). IR (neat): 2929, 2857, 1544, 1471, 1439, 1359, 1254, 1164 cm^{-1}. CIMS *m/z*: $[M + H]^+$ calcd for $C_{21}H_{33}N_2O_5SiS$, 453.1879; found, 453.1906.

***N*-[4-(*tert*-Butyldimethylsilyloxy)-but-2-yn-1-yl]-*N*-(2-methylbut-3-en-1-yl)-2-nitrobenzenesulfonamide (2c)**: Obtained in 91% yield as a colorless oil. ^{1}H NMR: δ 8.02 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.69–7.64 (comp, 2H), 7.61 (dd, *J* = 6.9, 2.1 Hz, 1H), 5.65 (ddd, *J* = 17.5, 10.3, 7.6 Hz, 1H), 5.06 (d, *J* = 17.5 Hz, 1H), 4.98 (d, *J* = 10.3, 1H), 4.23 (t, *J* = 2.1 Hz, 2H), 4.14 (t, *J* = 2.1 Hz, 2H), 3.31 (d, *J* = 7.6 Hz, 2H), 2.51 (dtq, *J* = 7.6, 7.6, 6.6 Hz, 1H), 1.00 (d, *J* = 6.6 Hz, 3H), 0.86 (s, 9H), 0.04 (s, 6H). ^{13}C NMR: δ 148.4, 140.5, 133.6, 133.1, 131.6, 131.0, 124.2, 115.5, 84.6, 77.4, 52.0, 51.5, 37.1, 36.3, 25.8 (3C), 18.3, 17.5, -5.1 (2C). IR (neat): 2957, 2930, 2858, 1545, 1463, 1359, 1254, 1164 cm^{-1}. CIMS *m/z*: $[M + H]^+$ calcd for $C_{21}H_{33}N_2O_5SiS$, 453.1879; found, 453.1885.

General procedure for synthesis of alcohols (3a, 3b)

To a stirred solution of silyl ether (**2a** or **2b**) in THF (4 mL per 1 mmol) was slowly added TBAF (1 M in THF, 1.2 equiv) at 0 °C. The mixture was stirred for 0.5–1 h at room temperature and treated with H_2O. The aqueous layer was extracted with EtOAc and the combined organic layers were washed with brine, dried with $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography by eluting with hexane:EtOAc (1:2) to give the corresponding alcohol (**3a** or **3b**).

***N*-(But-3-en-1-yl)-*N*-(4-hydroxybut-2-yn-1-yl)-2-nitrobenzenesulfonamide (3a)**:[6] Obtained in 85% yield as a colorless oil. ^{1}H NMR: δ 8.06 (dd, *J* = 7.6, 2.1 Hz, 1H), 7.72–7.66 (comp, 2H), 7.64 (dd, *J* = 7.6, 2.1 Hz, 1H), 5.70 (ddt, *J* = 17.2, 10.3, 6.9 Hz, 1H), 5.09 (ddt, *J* = 17.2, 3.4, 1.4 Hz, 1H), 5.03 (dd, *J* = 10.3, 1.4 Hz, 1H), 4.22 (s, 2H), 4.13 (d, *J* = 5.5 Hz, 2H), 3.46 (t, *J* = 7.6 Hz, 2H), 2.34 (dt, *J* = 7.6, 6.9 Hz, 2H), 1.55–1.43 (br s, 1H).

(*Z*)-*N*-(4-Hydroxybut-2-yn-1-yl)-2-nitro-*N*-(pent-3-en-1-yl)benzenesulfonamide (3b): Obtained in 97% yield as a colorless oil. ^{1}H NMR: δ 8.05–7.97 (m, 1H), 7.71–7.65 (m, 2H), 7.64–7.59 (m, 1H), 5.52–5.44 (m, 1H), 5.30–5.21 (m, 1H), 4.19 (s, 2H), 4.13–4.07 (m, 2H), 3.36 (t, *J* = 7.2 Hz, 2H), 2.30 (dt, *J* = 6.6, 6.6 Hz, 2H), 1.54 (dd, *J* = 7.2, 2.4 Hz, 3H). ^{13}C NMR: δ 148.2, 133.9, 132.8, 131.9, 130.9, 127.2, 125.5, 124.3, 84.1, 78.7, 50.7, 46.5, 36.9, 25.6, 12.9. IR (neat): 3414, 2920, 1729, 1535, 1439, 1351, 1161 cm^{-1}. CIMS *m/z*: $[M + H]^+$ calcd for $C_{15}H_{19}N_2O_5S$, 339.1014; found, 339.0997.

General procedure for synthesis of acetates (4a, b)

To a stirred solution of alcohol (**3a** or **3b**) in the presence of pyridine (1.5–2.0 equiv) in anhydrous CH_2Cl_2 (4 mL per 1 mmol) was slowly added Ac_2O (1.2–1.5 equiv) at 0 °C. The mixture was stirred for 24 h at room temperature and treated with saturated aqueous $NaHCO_3$. The aqueous layer was separated from the CH_2Cl_2 layer and extracted with additional CH_2Cl_2. The combined organic layers were washed with 1 M aqueous HCl, washed with brine, dried with $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography by eluting with hexane:EtOAc (2:1) to give the corresponding acetate (**4a** or **4b**).

4-[*N*-(But-3-en-1-yl)-2-nitrophenylsulfonamide]-but-2-yn-1-yl acetate (4a):[6] Obtained in 93% yield as a colorless oil. ^{1}H NMR: δ 8.04–7.99 (m, 1H), 7.72–7.66 (comp, 2H), 7.65–7.60 (m, 1H), 5.69 (ddt, *J* = 17.2, 10.3, 6.9 Hz, 1H), 5.08 (dd, *J* = 17.2, 1.4 Hz, 1H), 5.02 (dd, *J* = 10.3, 1.4 Hz, 1H), 4.51 (s, 2H), 4.23 (s, 2H), 3.44 (t, *J* = 6.9 Hz, 2H), 2.33 (dt, *J* = 7.6, 6.9 Hz, 2H), 2.04 (s, 3H).

(*Z*)-4-[2-Nitro-*N*-(pent-3-en-1-yl)phenylsulfonamide]-but-2-yn-1-yl acetate (4b): Obtained in 82% yield as a colorless oil. ^{1}H NMR: δ 8.04–8.00 (m, 1H), 7.71–7.66 (comp, 2H), 7.65–7.61 (m, 1H), 5.55–5.48 (m, 1H), 5.32–5.25 (m, 1H), 4.52 (t, *J* = 1.8 Hz, 2H), 4.24 (t, *J* = 1.8 Hz, 2H), 3.38 (t, *J* = 6.9 Hz, 2H), 2.33 (dt, *J* = 7.6, 6.9 Hz, 2H), 2.04 (s, 3H), 1.58 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR: δ 170.1, 148.3, 133.7, 133.0, 131.8, 130.9, 127.2, 125.4, 124.3, 80.0, 79.8, 51.9, 46.5, 36.9, 25.6, 20.8, 12.9. IR (neat): 2937,

1741, 1550, 1438, 1356, 1222, 1163 cm^{-1}. CIMS *m/z*: $[M + H]^+$ calcd for $C_{17}H_{21}N_2O_6S$, 381.1120; found, 381.1106.

General procedure for synthesis of aniline derivatives (5a–f)

To a stirred suspension of a 2-nitrobenzene derivative (**2a–c**, **3a**, **4a**,**b**) in the presence of NH_4Cl (10 equiv) in EtOH:H_2O (1:1, 20 mL per 1 mmol) was added iron powder (10 equiv) at room temperature. The reaction mixture was stirred vigorously for 24 h and filtered through a Celite pad with EtOAc. After removal of EtOH and EtOAc from the filtrate under reduced pressure, the water layer was extracted with EtOAc. The organic layer was dried with $MgSO_4$ and concentrated under reduced pressure to give the corresponding aniline derivative (**5a–f**).

2-Amino-*N*-but-3-enyl-*N*-[4-(*tert*-butyldimethylsilyloxy)-but-2-ynyl]benzenesulfonamide (5a): Obtained in 96% yield as a colorless oil. ^{1}H NMR: δ 7.60 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.27–7.23 (m, 1H), 6.71 (dd, *J* = 8.3, 6.9 Hz, 1H), 6.67 (d, *J* = 8.3 Hz, 1H), 5.72 (ddt, *J* = 17.2, 10.3, 6.9 Hz, 1H), 5.07 (d, *J* = 17.2 Hz, 1H), 5.04–5.00 (comp, 3H), 4.13 (s, 2H), 4.13 (s, 2H), 3.33 (t, *J* = 7.6 Hz, 2H), 2.30 (dt, *J* = 7.6, 6.9 Hz, 2H), 0.86 (s, 9H), 0.05 (s, 6H). ^{13}C NMR: δ 146.0, 134.6, 134.0, 130.2, 120.4, 117.6, 117.2, 117.1, 83.9, 77.6, 51.5, 45.8, 36.7, 32.1, 25.8 (3C), 18.2, -5.2 (2C). IR (neat): 3483, 3380, 2929, 2857, 1617, 1483, 1453, 1340, 1320, 1139 cm^{-1}. CIMS *m/z*: $[M + H]^+$ calcd for $C_{20}H_{33}N_2O_3SiS$, 409.1981; found, 409.1954.

(*Z*)-2-Amino-*N*-[4-(*tert*-butyldimethylsilyloxy)-but-2-yn-1-yl]-*N*-(pent-3-en-1-yl)benzenesulfonamide (5b): Obtained in 92% yield as a yellow oil. ^{1}H NMR: δ 7.60 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.24 (ddd, *J* = 8.3, 6.9, 1.4 Hz, 1H), 6.70 (ddd, *J* = 8.3, 6.9, 1.4 Hz, 1H), 6.67 (dd, *J* = 8.3, 1.4 Hz, 1H), 5.56–5.49 (m, 1H), 5.34–5.28 (m, 1H), 5.02 (s, 2H), 4.14 (t, *J* = 1.7 Hz, 2H), 4.12 (t, *J* = 1.7 Hz, 2H), 3.28 (t, *J* = 7.6 Hz, 2H), 2.30 (dt, *J* = 7.6, 7.2 Hz, 2H), 1.59 (d, *J* = 6.9 Hz, 3H), 0.86 (s, 9H), 0.05 (s, 6H). ^{13}C NMR: δ 146.2, 134.1, 130.2, 126.7, 126.0, 120.5, 117.6, 117.3, 83.9, 77.8, 51.6, 46.0, 36.8, 25.9 (3C), 25.6, 18.3, 13.0, -5.1 (2C). IR: 3479, 3379, 2929, 2857, 1617, 1566, 1483, 1453, 1339, 1320, 1255, 1143, 1079 cm^{-1}. CIMS *m/z*: $[M + H]^+$ calcd for $C_{21}H_{35}N_2O_3SiS$, 423.2137; found, 423.2145.

2-Amino-*N*-[4-(*tert*-butyldimethylsilyloxy)-but-2-yn-1-yl]-*N*-(2-methylbut-3-en-1-yl)-benzenesulfonamide (5c): Obtained in 96% yield as a yellow oil. ^{1}H NMR: δ 7.60 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.25 (ddd, *J* = 8.3, 7.3, 1.4 Hz, 1H), 6.71 (dd, *J* = 8.3, 7.3 Hz, 1H), 6.66 (d, *J* = 8.3 Hz, 1H), 5.68 (ddd, *J* = 18.4, 10.3, 7.6 Hz, 1H), 5.04 (d, *J* =18.4 Hz, 1H), 5.03 (s, 2H), 4.99 (d, *J* = 10.3 Hz, 1H), 4.13–4.08 (comp, 4H), 3.19–3.12 (m, 2H), 2.47 (dtq, *J* = 7.6, 7.6, 6.9 Hz, 1H), 0.99 (d, *J* = 6.9 Hz, 3H), 0.86 (s, 9H), 0.05 (s, 6H). ^{13}C NMR: δ 146.2, 141.0, 134.1, 130.3, 120.5, 117.6, 117.2, 115.0, 84.0, 77.6, 51.8, 51.6, 37.2, 36.2, 25.9 (3C), 18.3, 17.5, -5.1 (2C). IR (neat): 3479, 3380, 2957, 2929, 2858, 1617, 1484, 1454, 1341, 1321, 1254, 1137, 1077 cm^{-1}. CIMS *m/z*: $[M + H]^+$ calcd for $C_{21}H_{35}N_2O_3SiS$, 423.2137; found 423.2165.

2-Amino-*N*-(but-3-en-1-yl)-*N*-(4-hydroxybut-2-yn-1-yl)benzenesulfonamide (5d): Obtained in 88% yield as a colorless oil. ^{1}H NMR: δ 7.61 (d, *J* = 8.3, 1H), 7.30–7.24 (m, 1H), 6.72 (d, *J* = 8.3, 6.9 Hz, 1H), 6.69 (d, *J* = 8.3 Hz, 1H), 5.72 (ddt, *J* = 17.2, 10.3, 6.9 Hz, 1H), 5.20–4.92 (comp, 4H), 4.11 (s, 2H), 4.04 (s, 2H), 3.34 (t, *J* = 7.3 Hz, 2H), 2.29 (dt, *J* = 7.3, 6.9 Hz, 2H), 1.93–1.57 (br s, 1H). ^{13}C NMR: δ 146.3, 134.6, 134.2, 130.5, 120.4, 117.7, 117.3, 117.2, 83.6, 78.8, 50.9, 46.1, 36.7, 32.2. IR (neat): 3482, 3379, 2927, 1617, 1484, 1453, 1319, 1139 cm^{-1}. CIMS *m/z*: $[M + H]^+$ calcd for $C_{14}H_{19}N_2O_3S$, 295.1116; found, 295.1123.

4-[(2-Aminobenzenesulfonyl)-but-3-enylamino]but-2-ynyl acetate (5e):[6] Obtained in 93% yield as a colorless oil. ^{1}H NMR: δ 7.59 (dd, *J* = 8.4, 1.4 Hz, 1H), 7.27–7.22 (m, 1H), 6.73–6.65 (comp, 2H), 5.71 (ddt, *J* = 17.2, 10.7, 6.9 Hz, 1H), 5.07 (dd, *J* = 17.2, 1.4 Hz, 1H), 5.05 (br s, 2H), 5.01 (d, *J* = 10.7 Hz, 1H), 4.45 (t, *J* = 2.1 Hz, 2H), 4.12 (t, *J* = 2.1 Hz, 2H), 3.31 (t, *J* = 6.9 Hz, 2H), 2.29 (dt, *J* = 6.9, 6.9 Hz, 2H), 2.04 (s, 3H).

(*Z*)-4-[2-Amino-*N*-(pent-3-en-1-yl)phenylsulfonamide]-but-2-yn-1-yl acetate (5f): Obtained in 95% yield as a light yellow oil. ^{1}H NMR: δ 7.61 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.26 (ddd, *J* = 8.5, 7.6, 1.4 Hz, 1H), 6.72 (dd, *J* = 8.0, 7.6 Hz, 1H), 6.68 (d, *J* = 8.5 Hz, 1H), 5.56–5.49 (m, 1H), 5.35–5.28 (m, 1H), 5.03 (br s, 2H), 4.47 (t, *J* = 2.1 Hz, 2H), 4.15 (t, *J* = 2.1 Hz, 2H), 3.26 (t, *J* = 7.6 Hz, 2H), 2.29 (dt, *J* = 7.6, 7.6 Hz, 2H), 2.05 (s, 3H), 1.59 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR: δ 170.2, 146.2, 134.2, 130.3, 126.5, 125.9, 120.4, 117.7, 117.3, 80.0, 79.2, 52.1, 46.2, 36.8, 25.6, 20.8, 12.9. IR (neat): 3481, 3380, 3017, 2936, 1736, 1616, 1483, 1453, 1320, 1220, 1145 cm^{-1}. CIMS *m/z*: $[M + H]^+$ calcd for $C_{17}H_{23}N_2O_4S$, 351.1378; found, 351.1353.

General procedure for synthesis of cobalt complexes (6a–f)

To a stirred solution of an alkyne derivative (**5a–f**) in anhydrous CH_2Cl_2 or $ClCH_2CH_2Cl$ (10 mL per 1 mmol) was added dicobalt octacarbonyl (1.05 equiv) at room temperature under an Ar atmosphere. After stirring for 2 h, the solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography by eluting with $CHCl_3$ or hexane:EtOAc (20:1 to 6:1) to give the corresponding cobalt complex (**6a–f**).

Cobalt complex with 5a (6a): Obtained in 98% yield as a dark red oil. ^{1}H NMR: δ 7.67 (d, *J* = 8.3 Hz, 1H), 7.30 (dd, *J* = 8.3, 7.3 Hz, 1H), 6.76 (dd, *J* = 7.6, 7.3 Hz, 1H), 6.71 (d, *J* = 7.6 Hz, 1H), 5.59 (ddt, *J* = 16.5, 9.6, 6.9 Hz, 1H), 5.03–4.93 (comp, 4H), 4.82 (s, 2H), 4.65 (s, 2H), 3.44 (t, *J* = 7.6 Hz, 2H), 2.20 (dt, *J* = 7.6, 6.9 Hz, 2H), 0.93 (s, 9H), 0.12 (s, 6H). ^{13}C NMR: δ 199.4 (6C), 145.7, 134.3, 134.1, 130.0, 121.7, 117.8, 117.6, 117.3, 98.3, 89.7, 63.7, 49.5, 46.4, 31.6, 25.9 (3C), 18.4, -5.6 (2C). IR (neat): 3482, 3379, 2929, 2857, 2093, 2051, 2018, 1617, 1483, 1454, 1337, 1143 cm^{-1}. The corresponding molecular ion was not detected using either EIMS or CIMS methods.

Cobalt complex with 5b (6b): Obtained in 99% yield as a dark red oil. ^{1}H NMR: δ 7.73–7.63 (m, 1H), 7.33–7.20 (m, 1H), 6.80–6.68 (comp, 2H), 5.51–5.42 (m, 1H), 5.22–5.13 (m, 1H), 5.00 (br s, 2H), 4.82 (br s, 2H), 4.67 (br s, 2H), 3.42–3.32 (m, 2H), 2.24–2.14 (m, 2H), 1.57–1.45 (m, 3H), 0.92 (br s, 9H), 0.11 (br s, 6H). ^{13}C NMR: δ 199.5 (6C), 145.8, 134.2, 130.0, 126.9, 125.7, 121.9, 117.8, 117.7, 98.5, 89.9, 63.8, 49.5, 46.6, 25.9 (3C), 25.0, 18.5, 12.8, -5.5 (2C). IR: 3485, 3380, 2930, 2859, 2093, 2050, 2005, 1617, 1569, 1483, 1454, 1336, 1320, 1258, 1142 cm^{-1}. The corresponding molecular ion was not detected using either EIMS or CIMS methods.

Cobalt complex with 5c (6c): Obtained in 93% yield as a dark red oil. ^{1}H NMR: δ 7.67 (d, *J* = 7.3 Hz, 1H), 7.33–7.23 (m, 1H), 6.75 (dd, *J* = 7.3, 6.2 Hz, 1H), 6.69 (d, *J* = 7.6 Hz, 1H), 5.46 (ddd, *J* = 17.2, 9.6, 8.3 Hz, 1H), 4.97 (br s, 2H), 4.91–4.67 (comp, 6H), 3.35–3.17 (m, 2H), 2.39–2.28 (m, 1H), 0.93 (s, 9H), 0.82 (d, *J* = 6.2 Hz, 3H), 0.11 (s, 6H). ^{13}C NMR: δ 199.5 (6C), 145.8, 140.7, 134.2, 130.2, 122.0, 117.7, 117.6, 115.3, 98.7, 89.1, 63.8, 51.8, 50.0, 36.4, 26.0 (3C), 18.5, 17.5, -5.5 (2C). IR (neat): 3486, 3382, 2955, 2931, 2858, 2092, 2048, 2009, 1857, 1618, 1485, 1455, 1335, 1320, 1257, 1140, 1066 cm^{-1}. The corresponding molecular ion was not detected using either EIMS or CIMS methods.

Cobalt complex with 5d (6d): Obtained in 88% yield as a dark red oil. ^{1}H NMR: δ 7.66 (d, *J* = 7.6 Hz, 1H), 7.37–7.28 (m, 1H), 6.82–6.74 (m, 1H), 6.73 (d, *J* = 7.6 Hz, 1H), 5.61–5.47 (m, 1H), 5.10–4.80 (comp, 6H), 4.69 (s, 2H), 3.45–3.30 (comp, 3H), 2.18–2.08 (m, 2H). ^{13}C NMR: δ 199.3 (6C), 145.9, 134.7, 134.0, 130.1, 120.8, 118.0, 117.9, 117.7, 97.2, 90.4, 63.7, 50.1, 47.1, 31.8. IR (neat): 3481, 3384, 2934, 2093, 2050, 2002, 1617, 1483, 1454, 1319, 1139 cm^{-1}. The corresponding molecular ion was not detected using either EIMS or CIMS methods.

Cobalt complex with 5e (6e):[6] Obtained in 96% yield as a dark red oil. ^{1}H NMR: δ 7.65 (d, *J* = 7.9 Hz, 1H), 7.30 (dd, *J* = 8.3, 7.6 Hz, 1H), 6.77 (dd, *J* = 7.9, 7.6 Hz, 1H), 6.72 (d, *J* = 8.3 Hz, 1H), 5.62–5.53 (m, 1H), 5.34 (s, 2H), 5.03–4.93 (comp, 4H), 4.64 (s, 2H), 3.40 (t, *J* = 7.6 Hz, 2H), 2.19 (dt, *J* = 8.3, 7.6 Hz, 2H), 2.12 (s, 3H).

Cobalt complex with 5f (6f): Obtained in 99% yield as a dark red oil. ^{1}H NMR: δ 7.67 (d, *J* = 8.3 Hz, 1H), 7.29 (dd, *J* = 8.3, 7.6 Hz, 1H), 6.77 (dd, *J* = 8.3, 7.6 Hz, 1H), 6.71 (d, *J* = 8.3 Hz, 1H), 5.51–5.44 (m, 1H), 5.35 (s, 2H), 5.20–5.13 (m, 1H), 5.00 (br s, 2H), 4.67 (s, 2H), 3.33 (t, *J* = 8.0 Hz, 2H), 2.18 (dt, J = 8.0, 7.6 Hz, 2H), 2.12 (s, 3H), 1.50 (d, *J* = 6.2 Hz, 3H). ^{13}C NMR: δ 199.0 (6C), 170.7, 145.9, 134.3, 130.0, 127.1, 125.4, 121.6, 117.9, 117.8, 91.4, 90.7, 64.9, 49.5, 47.0, 25.1, 20.6, 12.8. IR (neat): 3480, 3383, 2096, 2056, 2023, 1740, 1617, 1483, 1454, 1374, 1336, 1264, 1220, 1143 cm^{-1}. The corresponding molecular ion was not detected using either EIMS or CIMS methods.

General procedure for synthesis of nine-membered ring products (7a–c)

To a stirred solution of a cobalt alkyne complex (**6a–f**) in anhydrous CH_2Cl_2 or $ClCH_2CH_2Cl$ (200 mL per 1 mmol) was slowly added $BF_3{\cdot}Et_2O$ (2.4 equiv) at 0 °C. The mixture was stirred for 0.5–2 h to

consume the starting materials, as monitored by TLC, and was quenched with saturated aqueous $NaHCO_3$ at 0 °C. The organic layer was separated from the aqueous layer, dried with $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography by eluting with hexane:EtOAc (10:1) or CH_2Cl_2 to give the corresponding nine-membered ring derivative (**7a–c**).

Nine-membered sultam with cobalt complex (7a):[6] Obtained in 82% yield from **6a**, 69% yield from **6d**, and 72% yield from **6e** as a dark red oil. ^{1}H NMR: δ 7.77 (d, *J* = 7.9 Hz, 1H), 7.43 (dd, *J* = 7.7, 7.6 Hz, 1H), 7.19 (d, *J* = 7.7 Hz, 1H), 6.90 (dd, *J* = 7.9, 7.6 Hz, 1H), 6.16 (dd, *J* = 6.9, 6.9 Hz, 1H), 5.80 (ddt, *J* = 17.2, 10.3, 6.9 Hz, 1H), 5.17 (d, *J* = 17.2 Hz, 1H), 5.11 (d, *J* = 10.3 Hz, 1H), 4.90–4.60 (comp, 3H), 3.09–3.01 (br s, 2H), 2.53 (dt, *J* = 7.6, 6.9 Hz, 2H).

Nine-membered sultam with cobalt complex (7b): Obtained in 84% yield from **6b** and 77% yield from **6f** as a dark red oil. ^{1}H NMR: δ 7.78 (d, *J* = 7.6 Hz, 1H), 7.42 (dd, *J* = 8.0, 7.6 Hz, 1H), 7.18 (d, *J* = 8.0 Hz, 1H), 6.90 (dd, *J* = 7.6, 7.6 Hz, 1H), 6.17 (t, *J* = 7.1 Hz, 1H), 5.68–5.56 (m, 1H), 5.44–5.34 (m, 1H), 5.00–4.60 (comp, 4H), 3.09–2.92 (m, 2H), 2.58–2.50 (m, 2H), 1.69 (d, *J* = 6.2 Hz, 3H). ^{13}C NMR: δ 198.6 (6C), 146.5, 134.4, 130.1, 129.5, 127.6, 125.7, 122.5, 120.9, 96.0, 89.5, 53.9, 48.8, 47.2, 27.3, 12.9. IR (neat): 3370, 2928, 2092, 2051, 2005, 1594, 1578, 1503, 1462, 1336, 1148 cm^{-1}. The corresponding molecular ion was not detected using either EIMS or CIMS methods.

Nine-membered sultam with cobalt complex (7c): Obtained in 72% yield from **6c** as a dark red oil. ^{1}H NMR: δ 7.76 (d, *J* = 8.0 Hz, 1H), 7.43 (dd, *J* = 8.0, 7.3 Hz, 1H), 7.19 (d, *J* = 8.0 Hz, 1H), 6.91 (dd, *J* = 8.0, 7.3 Hz, 1H), 6.17 (s, 1H), 5.74 (ddd, *J* = 17.6, 9.6, 8.3 Hz, 1H), 5.17 (d, *J* = 17.6 Hz, 1H), 5.09 (d, *J* = 9.6 Hz, 1H), 5.00–4.54 (comp, 4H), 2.96–2.83 (m, 2H), 2.82–2.71 (m, 1H), 1.07 (d, J = 6.9 Hz, 3H). ^{13}C NMR: δ 198.6 (6C), 146.6, 140.8, 134.5, 130.4, 129.4, 122.7, 121.0, 115.8, 95.8, 88.9, 54.1, 52.5, 49.2, 37.9, 17.7. IR (neat): 3374, 2972, 2930, 2092, 2052, 2017, 1594, 1463, 1336, 1149 cm^{-1}. The corresponding molecular ion was not detected using either EIMS or CIMS methods.

General procedure for synthesis of tetracycles (8a–d)

A solution of sultam (**7a–c**) in anhydrous DCE (200 mL per 1 mmol) was heated to either 60 °C or 80 °C and stirred for 0.5–1 h. The reaction mixture was cooled to room temperature and filtered through a filter paper to remove the insoluble black materials. The filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography by eluting with hexane:EtOAc (1:1 to 0:1) to give the corresponding tetracycle (**8a–d**).

(*E*)-2,3,11,12-Tetrahydro-3,5-ethanobenzo[*h*]cyclopenta[*d*][1,2,7]thiadiazonin-1-(4*H*)-one 6,6-dioxide (8a):[6] Obtained in 90% yield as a white solid. mp 255 °C dec. ^{1}H NMR: δ 7.71 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.35 (ddd, *J* = 7.9, 7.0, 1.4 Hz, 1H), 7.10 (d, *J* = 7.9 Hz, 1H), 6.91 (dd, *J* = 7.8, 7.0 Hz, 1H), 5.57 (dd, *J* = 11.0, 6.2 Hz, 1H), 5.05 (dd, *J* = 15.1, 2.1 Hz, 1H), 4.44 (dd, *J* = 16.1, 11.0 Hz, 1H), 3.95–3.90 (m, 1H), 3.83 (dd, *J* = 16.1, 6.2 Hz, 1H), 3.79 (d, *J* =15.1 Hz, 1H), 3.29 (ddd, *J* = 15.5, 13.1, 2.8 Hz,

1H), 2.71–2.66 (m, 1H), 2.44 (dd, *J* = 19.4, 6.2 Hz, 1H), 1.83 (dddd, *J* = 13.1, 4.8, 2.8, 2.1 Hz, 1H), 1.54 (d, *J* = 19.4 Hz, 1H), 0.13 (dddd, *J* = 15.3, 13.1, 13.1, 4.5 Hz, 1H).

(2*R/S*,3*S/R*,*E*)-2-Methyl-2,3,11,12-tetrahydro-3,5-ethanobenzo[*h*]cyclopenta[*d*][1,2,7]thiadiazonin-1-(4*H*)-one 6,6-dioxide (8b): Obtained in 61% yield as a white solid. mp 260 °C dec. ^{1}H NMR: δ 7.70 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.33 (ddd, *J* = 8.1, 7.9, 1.7 Hz, 1H), 7.11 (dd, *J* = 8.3, 1.4 Hz, 1H), 6.90 (dd, *J* = 7.6, 6.9 Hz, 1H), 5.59 (br s, 1H), 5.05 (dd, *J* = 15.2, 2.1 Hz, 1H), 4.45 (dd, *J* = 15.8, 11.0 Hz, 1H), 3.95 (ddd, *J* = 15.8, 2.8, 2.8 Hz, 1H), 3.84 (dd, *J* = 15.8, 6.2 Hz, 1H), 3.79 (d, *J* = 15.2 Hz, 1H), 3.28 (ddd, *J* = 15.8, 13.1, 2.8 Hz, 1H), 2.75 (ddd, *J* = 11.4, 6.5, 5.5 Hz, 1H), 2.40 (ddd, *J* = 15.1, 7.6, 7.6 Hz, 1H), 1.64–1.56 (m, 1H), 0.67 (d, *J* = 7.6 Hz, 3H), 0.12–0.03 (m, 1H). ^{13}C NMR: δ 209.1, 168.7, 147.0, 138.1, 134.2, 131.5, 128.8, 124.0, 121.7, 46.9, 46.3, 43.3, 42.5, 39.4, 32.2, 8.9. IR (neat): 3392, 2928, 1700, 1463, 1333, 1149 cm^{-1}. CIMS *m/z*: $[M + H]^+$ calcd for $C_{16}H_{19}N_2O_3S$, 319.1116; found, 319.1118.

(3*R/S*,14*R/S*,*E*)-14-Methyl-2,3,11,12-tetrahydro-3,5-ethanobenzo[*h*]cyclopenta[*d*][1,2,7]thiadiazonin-1-(4*H*)-one 6,6-dioxide (8c): Obtained in 67% yield as a white solid. mp 212–213 °C. ^{1}H NMR: δ 7.68 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.34 (ddd, *J* = 8.6, 6.9, 1.6 Hz, 1H), 7.08 (d, *J* = 8.6 Hz, 1H), 6.90 (dd, *J* = 8.0, 6.9 Hz, 1H), 5.56–5.48 (m, 1H), 5.02 (dd, *J* = 15.2, 2.1 Hz, 1H), 4.42 (dd, *J* = 16.5, 11.0 Hz, 1H), 3.86–3.79 (comp, 2H), 3.74 (d, *J* = 15.1 Hz, 1H), 2.93 (dd, *J* = 15.1, 12.4 Hz, 1H), 2.40 (dd, *J* = 19.3, 6.2 Hz, 1H), 2.24 (dd, *J* = 10.3, 6.2 Hz, 1H), 1.61 (d, *J* = 18.6 Hz, 1H), 0.78 (d, *J* = 6.9 Hz, 3H), 0.28–0.18 (m, 1H). ^{13}C NMR: δ 206.5, 168.6, 147.0, 138.7, 134.4, 131.4, 128.7, 123.9, 121.8, 52.7, 46.4, 45.8, 42.4, 39.6, 39.1, 17.5. IR (neat): 3399, 2968, 2950, 2888, 1698, 1650, 1595, 1460, 1328, 1130 cm^{-1}. CIMS *m/z*: $[M + H]^+$ calcd for $C_{16}H_{19}N_2O_3S$, 319.1116; found, 319.1138.

(3*R/S*,14*S/R*,*E*)-14-Methyl-2,3,11,12-tetrahydro-3,5-ethanobenzo[*h*]cyclopenta[*d*][1,2,7]thiadiazonin-1-(4*H*)-one 6,6-dioxide (8d): Obtained in 7% yield from **7c** as a white solid. mp 215–216 °C. ^{1}H NMR: δ 7.73 (dd, *J* = 8.5, 1.4 Hz, 1H), 7.35 (ddd, *J* = 8.0, 7.3, 1.4 Hz, 1H), 7.19 (d, *J* = 8.0 Hz, 1H), 6.89 (dd, *J* = 8.5, 7.3 Hz, 1H), 5.26–5.19 (m, 1H), 5.13 (d, *J* =14.4 Hz, 1H), 4.50 (dd, *J* =16.5, 11.0 Hz, 1H), 3.90 (d, *J* = 17.2 Hz, 1H), 3.76 (d, *J* = 14.4 Hz, 1H), 3.52–3.44 (comp, 2H), 3.04 (dd, *J* = 6.9, 6.9 Hz, 1H), 2.31–2.22 (comp, 2H), 1.98 (d, *J* =18.6 Hz, 1H), -0.17 (d, *J* = 7.6 Hz, 3H). ^{13}C NMR: δ 206.9, 167.1, 146.6, 138.5, 134.3, 131.8, 130.4, 122.9, 121.2, 52.3, 46.9, 41.8, 40.2, 37.6, 36.1, 12.4. IR (neat): 3399, 2968, 2888, 1699, 1651, 1460, 1328, 1143 cm^{-1}. CIMS *m/z*: $[M + H]^+$ calcd for $C_{16}H_{19}N_2O_3S$, 319.1116; found, 319.1122.

(4*R/S*,4a*R/S*)-2-(2-Aminophenylsulfonyl)-7-[(*tert*-butyldimethylsilyloxy)methyl]-4-methyl-1,2,3,4,4a,5-hexahydro-6*H*-cyclopenta[*c*]pyridin-6-one (9): Cobalt complex **6c** (134 mg, 0.189 mmol) was dissolved in $ClCH_2CH_2Cl$ (38 mL) and stirred at 80 °C for 30 min. The reaction mixture was filtered through a Celite pad with $CHCl_3$ and the filtrate was evaporated under reduced pressure. The residue was purified by silica gel column chromatography by eluting with hexane:EtOAc (2:1 to 1:1) to give

cyclopentenone **9** (57 mg) in 67% yield as a white solid. mp 150–151 °C. ^{1}H NMR: δ 7.58 (d, *J* = 8.0 Hz, 1H), 7.29 (dd, *J* = 8.3, 7.1 Hz, 1H), 6.74 (dd, *J* = 8.0, 7.1 Hz, 1H), 6.71 (d, *J* = 8.3 Hz, 1H), 5.29 (d, *J* = 14.4 Hz, 1H), 5.03 (s, 2H), 4.43 (d, *J* = 14.4 Hz, 1H), 4.36 (d, *J* = 14.4 Hz, 1H), 3.86–3.81 (m, 1H), 3.33 (d, *J* = 14.4 Hz, 1H), 2.54 (dd, *J* = 18.6, 6.2 Hz, 1H), 2.40 (dd, *J* = 11.0, 11.0 Hz, 1H), 2.20–2.13 (m, 1H), 1.97 (dd, *J* = 18.6, 2.8 Hz, 1H), 1.58–1.48 (m, 1H), 0.96 (d, *J* = 6.2 Hz, 3H), 0.91 (s, 9H), 0.12 (s, 3H), 0.07 (s, 3H). ^{13}C NMR: δ 206.0, 166.6, 146.3, 138.2, 134.5, 130.4, 118.3, 117.8, 117.4, 56.9, 51.9, 45.41, 45.40, 39.5, 37.8, 26.0 (3C), 18.4, 17.7, -5.4, -5.5. IR (neat): 3483, 3376, 2928, 2859, 1697, 1663, 1633, 1484, 1454, 1289, 1131 cm^{-1}. CIMS *m/z*: [M + H]+ calcd for $C_{22}H_{35}N_2O_4SiS$, 451.2087; found, 451.2074.

One-pot procedure for the synthesis of 8a from 6a

To a stirred solution of **6a** (100 mg, 0.14 mmol) in DCE (29 mL) was added $BF_3{\cdot}Et_2O$ (44 μL, 0.35 mmol) at 0 °C. After stirring for 30 min, saturated aqueous $NaHCO_3$ was added to the mixture and stirred for 1 h at room temperature. The reaction mixture was then heated to 60 °C for 3 h. The organic layer and aqueous layer were separated and the organic layer was dried with $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography by eluting with $CHCl_3$ to afford **8a** (38 mg) in 87% yield.

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REFERENCES (AND NOTES)

1. (a) I. Omae, *Appl. Organometal. Chem.*, 2007, **21**, 318; (b) J. Pérez-Castells, 'Cascade Reactions Involving Pauson-Khand and Related Processes', In Metal Catalyzed Cascade Reactions, Springer Berlin Heidelberg. 2006, pp. 207–257.
2. (a) N. Kann, *Curr. Org. Chem.*, 2012, **16**, 322; (b) B. J. Teobald, *Tetrahedron*, 2002, **58**, 4133; (c) J. R. Green, *Curr. Org. Chem.*, 2001, **5**, 809.
3. (a) 'The Pauson-Khand Reaction Scope, Variation and Applications', ed. by R. R. Torres, John Wiley & Sons Ltd: UK, 2012, pp. 1–305; (b) H. W. Lee and F. Y. Kwong, *Eur. J. Org. Chem.*, 2010, **5**, 789; (c) B. E. Moulton, 'The Pauson-Khand Reaction', In Organometallic Chemistry, ed. by I. Fairlamb and J. Lynam, RCS, London, 2010; Vol. 36, pp. 93–120.
4. (a) R. Ni, N. Mitsuda, T. Kashiwagi, K. Igawa, and K. Tomooka, *Angew. Chem. Int. Ed.*, 2015, **54**,

1190; (b) J. Huang, L. Fang, J. Gong, C. Li, and Z. Yang, *Tetrahedron*, 2015, **71**, 3720; (c) J. R. López, N. Ortega, V. S. Martin, and T. Martin, *Chem. Commun.*, 2014, **50**, 3685; (d) S. J. McKerrall, L. Jørgensen, C. A. Kuttruff, F. Ungeheuer, and P. S. Baran, *J. Am. Chem. Soc.*, 2014, **136**, 5799.

5. (a) K. D. Closser, M. M. Quintal, and K. M. Shea, *J. Org. Chem.*, 2009, **74**, 3680; (b) D. G. J. Young, J. A. Burlison, and U. Peters, *J. Org. Chem.*, 2003, **68**. 3494; (c) T. F. Jamison, S. Shambayati, W. E. Crowe, and S. L. Schreiber, *J. Am. Chem. Soc.*, 1997, **119**, 4353; (d) N. Jeong, S. Yoo, S. J. Lee, S. H. Lee, and Y. K. Chung. *Tetrahedron Lett.*, 1991, **32**, 2137.
6. T. Asamizu, R. Naruse, G. Yongxue, and K. Kaneda, *Tetrahedron Lett.*, 2015, **56**, 4674.
7. (a) J. K. Loh, N. Asad, T. B. Samarakoon, and P. R. Hanson, *J. Org. Chem.*, 2015, **80**, 9926; (b) B. Niu, P. Xie, M. Wing, Y. Wang, W. Zhao, C. U. Pittman, Jr., and A. Zhou, *Mol. Divers.*, 2015, **19**, 447; (c) B. Gerard, J. R. Duvall, J. T. Lowe, T. Murillo, J. Wei, L. B. Akella, and L. A. Marcaurelle, *ACS Comb. Sci.*, 2011, **13**, 365.
8. (a) K. Hagiya, N. Muramoto, T. Misaki, and T. Sugimura, *Tetrahedron*, 2009, **65**, 6109; (b) T. Sugimura and K. Hagiya, *Chem. Lett.*, 2007, **36**, 566.
9. (a) O. Mitsunobu, *Synthesis*, 1981, **1**, 1; (b) K. C. K. Swamy, N. N. B. Kumar, E. Balaraman, and K. V. P. Kumar, *Chem. Rev.*, 2009, **109**, 2551.
10. (a) T. Kan and T. Fukuyama, *Chem. Commun.*, 2004, 353; (b) T. Fukuyama, M. Cheung, and T. Kan, *Synlett*, 1999, 1301.
11. (a) K. Ramadas and N. Srinivasan, *Synth. Commun.*, 1992, **22**, 3189; (b) Z.-P. Xiao, Y.-C. Wnag, G.-Y. Du, J. Wu, T. Luo, and S.-F. Yi, *Synth. Commun.*, 2010, **40**, 661.
12. K. Kaneda and T. Honda, *Tetrahedron*, 2008, **64**, 11589.
13. Deposition number CCDC-1433846 for **8b** and 1433878 for **8c**. (http://www.ccdc.cam.ac.uk/conts/retrieving.html)