Supporting Information

for

One-pot three-component synthesis of quinoxaline and phenazine ring systems using Fischer carbene complexes

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General procedure for the preparation of o-alkynyl carbonyl derivatives 1 and quinoxaline and phenazine derivatives and spectral data for selected compounds.
General details:

All melting points are uncorrected. IR spectra were recorded on a Jasco FT/IR-460 plus instrument (KBr or neat). The $^1$H NMR and $^{13}$C NMR spectra were recorded at Bruker-AV500 (500 MHz). Splitting patterns of $^1$H NMR spectra are designated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. LCMS spectra were recorded on a Agilent 6120 mass spectrometer. Unless otherwise noted, all reactions were carried out under an inert atmosphere in flame dried flasks. Solvents and reagents were dried and purified by distillation before use as follows: tetrahydrofuran, toluene, hexane, diethyl ether from sodium benzophenone ketyl; dichloromethane and chloroform from P$_2$O$_5$; DMF and diisopropylamine from CaH$_2$; triethylamine and pyridine from solid KOH. After drying, organic extracts were evaporated under reduced pressure and the residue was column chromatographed on silica gel (Spectrochem, particle size 100-200 mesh), using an ethyl acetate-petroleum ether (60–80 °C) mixture as eluant unless specified otherwise.

1. General procedure I – synthesis of $o$-alkynyl carbonyl derivatives 1

A mixture of carbonyl derivative (1 mmol), Pd(PPh$_3$)$_2$Cl$_2$ (0.05 mmol), PPh$_3$ (0.025 mmol), trimethylsilylacetylene (1.5 mmol) and triethylamine (1.5 mmol) in THF (5 mL) was stirred for 20 min at room temperature, and then CuI (0.01 mmol) added. The reaction was stirred for 12–16 h at room temperature, and the solvent removed on a rotary evaporator. The residue was treated with dichloromethane and filtered through celite. The filtrate was concentrated and the residue purified by chromatography (silica gel/ethyl acetate: petroleum ether, 1:9).
1.1. Phenyl-(3-trimethylsilanylethynyl-2-pyrazinyl)methanone (1A):

![Chemical Structure Image]

General procedure I was followed using (3-iodo-2-pyrazinyl)phenylmethanone (6A) (0.70 g, 2.26 mmol), Pd(PPh$_3$)$_2$Cl$_2$ (0.08 g, 0.11 mmol), PPh$_3$ (0.02 g, 0.06 mmol), trimethylsilylacetylene (0.33 g, 3.38 mmol) and triethylamine (0.34 g, 3.38 mmol) in THF (20 mL), followed by CuI (5 mg, 0.03 mmol). After column chromatography, a brown oil (0.537 g, 85%) identified as compound 1A was obtained. IR (KBr, cm$^{-1}$): 2173, 1677; $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 8.67 (d, 1H, $J$=2.5 Hz), 8.57 (d, 1H, $J$=2.5 Hz), 7.88-7.81 (m, 2H), 7.62 (m, 1H), 7.54-7.44 (m, 2H), 0.06 (s, 9H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 192.2, 154.3, 145.0, 141.9, 137.4, 135.3, 134.0, 130.2 (2C), 128.6 (2C), 105.0, 99.3, -0.8 (3C); MS: m/e (relative intensity): 281 (MH$^+$, 100), 233 (30), 209 (26); Anal. Calcd for C$_{16}$H$_{16}$N$_2$OSi: C, 68.54; H, 5.75; N, 9.99. Found: C, 68.48; H, 5.84; N, 9.91.

1.2. 3-Trimethylsilanylethynylquinoxaline-2-carboxaldehyde (1C):

![Chemical Structure Image]

General procedure I was followed using 3-chloroquinoxaline-2-carboxaldehyde (6C) [1] (0.37 g, 1.90 mmol), Pd(PPh$_3$)$_2$Cl$_2$ (0.07 g, 0.09 mmol), PPh$_3$ (.01 g, 0.04 mmol), trimethylsilylacetylene (0.28 g, 2.85 mmol) and triethylamine (0.29 g, 2.85 mmol) in THF (15 mL), followed by CuI (4 mg, 0.02 mmol). After column chromatography a single fraction was obtained which gave a white solid assigned as compound 1A (0.386 g, 80%). Mp 100-101 °C, IR (KBr, cm$^{-1}$): 2172, 1709; $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 10.55 (s, 1H), 8.25 (dd, 1H, $J$=8.5, 1.0 Hz), 8.16 (dd, 1H,
$J=8.5, 1.0 \text{ Hz}$, 7.93 (td, 1H, $J=8.5, 1.0 \text{ Hz}$), 7.87 (td, 1H, $J=8.5, 1.0 \text{ Hz}$), 0.37 (s, 9H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 189.9, 146.0, 142.9, 140.5, 137.7, 133.3, 131.6, 130.4, 129.0, 105.1, 99.6, -0.5 (3C); MS: m/e (relative intensity): 256 (MH$^+$+1, 23), 255 (MH$^+$, 100), 241 (25), 227 (10), 183 (17); Anal. Calcd for C$_{14}$H$_{14}$N$_2$OSi: C, 66.11; H, 5.55; N, 11.01. Found: C, 66.02; H, 5.69; N, 10.93.

1.3. Phenyl-(3-trimethylsilanylethynyl-2-quinoxalinyl)methanone (1B):

General procedure I was followed using (3-chloro-2-quinoxalinyl)phenylmethanone (6B) (0.61 g, 2.26 mmol), Pd(PPh$_3$)$_2$Cl$_2$ (0.08 g, 0.11 mmol), PPh$_3$ (.02 g, 0.06 mmol), trimethylsilylacetylene (0.33 g, 3.38 mmol) and triethylamine (0.34 g, 3.38 mmol) in THF (20 mL), followed by CuI (5 mg, 0.03 mmol). After column chromatography a single fraction was isolated as yellow thick liquid and assigned as compound 1B (0.56 g, 75%). IR (KBr, cm$^{-1}$): 2157, 1677; $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 8.18-8.12 (m, 2H), 7.97 (d, 1H, $J=7.5 \text{ Hz}$), 7.91 (d, 1H, $J=7.5 \text{ Hz}$), 7.90-7.82 (m, 2H), 7.65 (m, 1H), 7.51-7.47 (m, 2H), 0.09 (s, 9H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 192.6, 153.6, 141.9, 139.6, 136.5, 135.4, 134.1, 131.6, 131.3, 130.3 (2C), 129.6, 129.2, 128.6 (2C), 140.7, 100.3, -0.8 (3C); MS: m/e (relative intensity): 331 (MH$^+$, 100), 311 (5), 259 (5); Anal. Calcd for C$_{20}$H$_{18}$N$_2$OSi: C, 72.69; H, 5.49; N, 8.48. Found: C, 72.57; H, 5.59; N, 8.42.
2. General procedure II – coupling of carbene complex with alkynyl pyrazine/quinoxaline carbonyl derivatives and maleimides/dimethyl maleate

To a refluxing solution of alkynyl carbonyl derivative 1A or 1C (1 mmol) and maleimide/dimethylmaleate (1 mmol) in THF (5 mL), was added a solution of carbene complex 2 (1.1 mmol) in THF (10 mL) over a period of 1 h. After the addition was complete, the mixture was heated to reflux for a period of 12 h. The mixture was allowed to cool to room temperature and concentrated on a rotary evaporator. EtOAc (20 mL) was added and the residue filtered through celite (1.0 g). The solvent was removed on a rotary evaporator, and the crude products dissolved in ether (20 mL). To this solution of crude product in ether was added aqueous HCl (1:1) (0.5 mL) and the mixture stirred for 6 h at room temperature. The organic layer was separated. The aqueous layer was neutralized with saturated NaHCO₃ solution (3 mL) and extracted with ethyl acetate (3×10 mL). The combined organic layers (diethyl ether layer and ethyl acetate layer) was washed with water (3 mL) and brine (3 mL), and dried over anhydrous Na₂SO₄. Evaporation of solvent and purification by chromatography gave the pure products.

2.1. Coupling of carbene complex 2 with phenyl-(3-trimethylsilanylethynyl-2-pyrazinyl)methanone (1A) and N-phenylmaleimide (Table 1, entry 1).

General procedure II was followed using carbene complex 2 (98 mg, 0.39 mmol), alkynyl carbonyl derivative 1A (100 mg, 0.35 mmol) and N-phenylmaleimide (62 mg, 0.35 mmol). The
crude product was purified using column chromatography (silica gel/ethyl acetate: petroleum ether 1:5) to yield the quinoxaline derivative 5a (44 mg, 30%) and the oxa-bridged compound 7a (64 mg, 42%) as yellow solids. **Compound 7a**: Mp: 170 °C (decomposed); Rf (40% EtOAc/hexane) 0.53; IR (KBr, cm⁻¹): 1713, 1635; ¹H NMR (400 MHz, CDCl₃): δ 8.37 (d, 1H, J=2.8 Hz), 8.33 (d, 1H, J=2.8 Hz), 7.77 (d, 2H, J=7.6 Hz), 7.50 (t, 2H, J=7.6 Hz), 7.45-7.38 (m, 3H), 7.34 (m, 1H), 7.17 (d, 2H, J=7.6 Hz), 3.95 (d, 1H, J=6.9 Hz), 3.68 (d, 1H, J=18.0 Hz), 3.59 (d, 1H, J=18.0 Hz), 3.56 (d, 1H, J=6.9 Hz), 2.40 (s, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 202.9, 172.9, 171.2, 160.0, 159.1, 142.5, 142.3, 131.5, 131.3, 129.1 (2C), 128.9, 128.8, 128.3 (2C), 126.2 (2C), 126.1 (2C), 89.4, 85.3, 52.4, 50.3, 42.6, 30.6; MS: m/e (relative intensity): 426 (MH⁺, 15), 408 (MH⁺-H₂O, 40), 366 (50), 289 (45), 279 (40), 253 (100), 211 (18); Anal. Calcd for C₂₅H₁₉N₃O₄: C, 70.58; H, 4.50; N, 9.88. Found: C, 70.39; H, 4.65; N, 9.69. **Compound 5a**: Mp: 160 °C (decomposed); Rf (40% EtOAc/hexane) 0.76; IR (KBr, cm⁻¹): 1714, 1634; ¹H NMR (500 MHz, CDCl₃): δ 8.99 (d, 1H, J=1.5 Hz), 8.95 (d, 1H, J=1.5 Hz), 7.58-7.48 (m, 5H), 7.46 (d, 2H, J=7.2 Hz), 7.44-7.36 (m, 3H), 5.08 (s, 3H), 2.50 (s, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 204.8, 166.6, 165.2, 146.5, 145.6, 144.8, 144.7, 141.1, 135.6, 132.1, 131.3, 130.7 (2C), 129.0 (2C), 128.9, 128.4, 128.1, 127.7 (2C), 126.6 (2C), 126.5, 40.3, 30.5; MS: m/e (relative intensity): 409 (MH⁺+1, 39), 408 (MH⁺, 100), 380 (68), 335 (64); HRMS calcd for C₂₅H₂₀N₃O₄ (MH⁺): 407.1270; found: 407.1270.
2.2. Coupling of carbene complex 2 with 3-trimethylsilylphenylethynylquinoxaline-2-carboxaldehyde (1C) and N-phenylmaleimide (Table 1, entry 3).

General procedure II was followed using carbene complex 2 (108 mg, 0.43 mmol), alkynyl aldehyde 1C (100 mg, 0.39 mmol) and N-phenylmaleimide (68 mg, 0.39 mmol). The crude product was purified using column chromatography (silica gel/ethyl acetate: petroleum ether 1:5) to yield the oxa-bridged compound 7c (16 mg, 10%) and the phenazine derivative 5c (78 mg, 52%) as white solids. In this case compound 7c was readily converted to phenazine derivative 5c. Compound 7c: Rf (40% EtOAc/hexane) 0.76; IR (KBr, cm⁻¹): 1713, 1635; ¹H NMR (400 MHz, CDCl₃): δ 8.10 (d, 1H, J=4.8 Hz), 8.08 (d, 1H, J=4.8 Hz), 7.83-7.74 (m, 2H), 7.52-7.37 (m, 2H), 7.32 (d, 2H, J=7.6 Hz), 7.22 (d, 1H, J=8.0 Hz), 5.87 (s, 1H), 3.76 (d, 1H, J=7.0 Hz), 3.62 (d, 1H, J=18.0 Hz), 3.55 (d, 1H, J=18.0 Hz), 3.46 (d, 1H, J=7.0 Hz), 2.38 (s, 3H); ¹³C NMR (150 MHz, CDCl₃): δ 202.3, 173.9, 173.1, 158.1, 157.4, 141.1, 140.8, 130.3, 130.1, 129.8, 129.3 (2C), 129.1, 128.9, 126.44, 126.4, 126.0, 86.9, 80.2, 49.2, 48.0, 42.2, 40.0; MS: m/e (relative intensity): 401 (MH⁺+1, 25), 400 (MH⁺, 92), 383 (40), 382 (100, 340 (60); Compound 5c (partial from the mixture of 7c and 5c): ¹H NMR (400 MHz, CDCl₃): δ 8.77 (s, 1H), 8.35-8.23 (m, 2H), 7.96 (d, 1H, J=4.0 Hz), 7.95 (d, 1H, J=4.0 Hz), 7.59-7.39 (m,
5H), 5.15 (s, 2H), 2.53 (s, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 204.5, 166.6, 165.6, 144.7, 144.3, 144.1, 143.5, 137.5, 132.4, 132.2, 131.4, 130.5, 130.1, 129.8, 129.2 (2C), 128.6, 127.2, 126.6 (2C), 126.3, 40.6, 30.7; MS: m/e (relative intensity): 383 (MH$^+$+1, 30), 382 (MH$^+$, 100), 340 (47); Anal. Calcd for C$_{23}$H$_{15}$N$_3$O$_3$: C, 72.43; H, 3.96; N, 11.02. Found: C, 72.19; H, 4.15; N, 10.89.

2.3. Coupling of carbene complex 2 with phenyl-(3-trimethylsilanylethynyl-2-pyrazinyl)methanone (1A) and dimethyl maleate (Scheme 3).

![Scheme 3](image)

General procedure II was followed using carbene complex 2 (98 mg, 0.39 mmol), alkynyl carbonyl derivatives 1A (100 mg, 0.35 mmol) and dimethyl maleate (50 mg, 0.35 mmol). The crude product was purified using column chromatography (silica gel/ethyl acetate: petroleum ether 1:5) to yield the oxa-bridged ketone 9A (57 mg, 40%) as a thick yellow liquid.$R_f$ (40% EtOAc/hexane) 0.42; IR (KBr, cm$^{-1}$): 1735, 1710; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.33 (bs, 2H), 7.94-7.87 (m, 2H), 7.52-7.39 (m, 3H), 3.95 (d, 1H, $J$=4.8 Hz), 3.78 (s, 3H), 3.71 (d, 1H, $J$=17.4 Hz), 3.51 (s, 3H), 3.46 (d, 1H, $J$=4.8 Hz), 3.33 (d, 1H, $J$= 17.4 Hz), 2.27 (s, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 203.0, 171.2, 169.9, 159.6, 158.1, 142.2, 141.9, 133.9, 129.0, 128.4 (2C), 126.9 (2C), 88.2, 85.3, 56.1, 53.0, 52.5, 52.3, 42.5, 30.9; MS: m/e (relative intensity): 379 (MH$^+$, 5), 347 (48), 335 (20), 252 (68), 211 (40); Anal. Calcd for C$_{21}$H$_{20}$N$_2$O$_6$: C, 63.63; H, 5.09; N, 7.07. Found: C, 63.85; H, 4.81; N, 7.25.

To a refluxing solution of alkynyl carbonyl derivative 1A or 1B (1 mmol) in THF (10 mL) was added a solution of γ,δ-unsaturated carbene complex 10 (1.1 mmol) in THF (10 mL) over a period of 1 h. After the addition was complete, the mixture was heated to reflux for a period of 24 h. The mixture was allowed to cool to room temperature and concentrated on a rotary evaporator. EtOAc (20 mL) was added and the residue was filtered through celite (1.0 g). The solvent was removed on a rotary evaporator, and the residue stirred in silica gel/chloroform in the air for a further 2 h period and then filtered through a thin layer of celite. The solvent was removed on a rotary evaporator. Final purification was achieved by column chromatography on silica gel using ethylacetate/petroleum ether as eluent.

3.1. Coupling of carbene complex 10 with phenyl-(3-trimethylsilaneylethynyl-2-pyrazinyl)methanone (1A) (Scheme 4).

General procedure III was followed using carbene complex 10 (124 mg, 0.43 mmol) and alkynyl aldehyde 1A (100 mg, 0.39 mmol). The crude product was purified using column chromatography (silica gel/ethyl acetate: petroleum ether 1:10) to yield alcohol 13A (97 mg, 75%) as a white solid. Mp: 140 °C; Rf (40% EtOAc/hexane) 0.61; IR (KBr, cm\(^{-1}\)): 3417, 1649; \(^1\)H NMR (500 MHz, CDCl\(_3\)): δ 8.61 (d, 1H, \(J=2.2\) Hz), 8.58 (d, 1H, \(J=2.2\) Hz), 7.33-7.27 (m, 3H), 7.05-7.00 (m, 2H), 4.15 (s, 1H), 2.58-2.47 (m, 2H), 2.43 (dd, 1H, \(J=12.8, 3.7\) Hz), 2.38-2.20
(m, 2H), 1.93 (m, 1H), 1.82 (m, 1H), 0.20 (s, 9H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 203.7, 160.1, 157.2, 147.3, 146.6, 146.2, 145.2, 143.1, 128.8 (2C), 128.3, 127.0 (2C), 75.4, 45.7, 38.0, 35.3, 29.5, 2.9 (3C); MS: m/e (relative intensity): 365 (MH$^+$, 7), 350 (25), 349 (100), 279 (6); Anal. Calcd for C$_{21}$H$_{24}$N$_2$O$_2$: C, 69.19; H, 6.64; N, 7.69. Found: C, 69.01; H, 6.86; N, 7.76.

3.2. Coupling of carbene complex 10 with phenyl-(3-trimethylsilanylethynyl-2-quinoxalinylmethanone (1B) (Scheme 4).

General procedure III was followed using carbene complex 10 (97 mg, 0.33 mmol) and alkynyl aldehyde 1B (100 mg, 0.30 mmol). The crude product was purified using column chromatography (silica gel/ethyl acetate: petroleum ether 1:10) to yield alcohol 13B (88 mg, 70%) as a white solid. Mp: 140 °C; R$_f$ (20% EtOAc/hexane) 0.46; IR (KBr, cm$^{-1}$): 3417, 1657; $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 8.90 (dd, 1H, $J=3.5$, 1.5 Hz), 8.04 (dd, 1H, $J=3.5$, 1.5 Hz), 7.86-7.79 (m, 2H), 7.29-7.24 (m, 3H), 7.02-6.98 (m, 2H), 4.61 (s, 1H), 2.61 (m, 1H), 2.59-2.52 (m, 2H), 2.41-2.31 (m, 2H), 2.01 (m, 1H), 1.88 (m, 1H), 0.26 (s, 9H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 203.3, 160.1, 157.1, 147.2, 146.8, 146.6, 141.8, 141.3, 131.2, 130.9, 129.1, 129.0, 128.3 (2C), 127.7, 126.7 (2C), 75.2, 45.2, 37.7, 35.2, 29.3, 2.6 (3C); MS: m/e (relative intensity): 415 (MH$^+$, 29), 399 (100), 337 (62), 279 (79), 205 (37); Anal. Calcd for C$_{25}$H$_{36}$N$_2$O$_2$: C, 72.43; H, 6.32; N, 6.76. Found: C, 72.21; H, 6.51; N, 6.61.

References