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Tetrahedron
Tetrahedron 63 (2007) 12015–12025

Tandem furo[3,4-*b*]pyridine formation—Diels–Alder reaction: an approach to the synthesis of nitrogen containing heterocyclic analogues of 1-arylnaphthalene lignans

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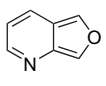
Received 19 April 2007; revised 22 August 2007; accepted 6 September 2007
Available online 11 September 2007

Abstract—The coupling of Fischer carbene complexes with 2-alkynyl-3-pyridine carbonyl derivatives has been examined. The reaction affords furo[3,4-*b*]pyridine as transient intermediates; the latter undergo [4+2] cycloaddition with an electron-deficient dienophile. Acid/base-induced ring opening of the *exo*-cycloadducts followed by aromatization give substituted quinolines related to heterocyclic analogues of 1-arylnaphthalene lignans. An intramolecular variant of this protocol is also feasible with use of unactivated alkenyl tethers; however, the bridged cycloadducts are unisolable as they undergo spontaneous ring opening to yield alcohol. This method is also useful for the in situ generation of the furo[3,4-*b*]quinoline intermediate for the first time, which can be trapped with dienophiles.

1. Introduction

While the *o*-quinoid 10π-electron isobenzofuran system has remained the subject of intense theoretical, structural and reactivity studies,[1,2] little, if any, work has been done with the analogous furo[3,4-*b*]pyridines.[3] Parent furo[3,4-*b*]pyridine (**1**) and furo[3,4-*b*]quinoline (**2**) are unknown, with the only method so far available in the literature being the in situ generation of substituted furo[3,4-*b*]pyridine intermediates from treatment of 2-(α-acetoxy-3,4-dimethoxybenzyl)-2-pyridine-3-carboxaldehyde (**3**) with acid.[4]



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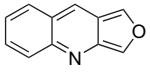

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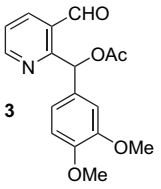

3

One of the efficient and interesting methods for the generation of isobenzofurans involves the coupling of Fischer carbene complexes with *o*-alkynylbenzoyl derivatives.[2] These isobenzofurans are unstable, but readily undergo inter- and intramolecular Diels–Alder reactions when suitable dienophiles are present. So far, this methodology has not been utilized for the generation of heteroaromatic isobenzofurans. In this paper, we wish to report the one step generation of furo[3,4-*b*]pyridine intermediates[3] through the coupling of *o*-alkynylpyridine carbonyl derivatives **4** with a Fischer carbene complex **5**. Although, furo[3,4-*b*]pyridines are unstable, they have been proven to be useful[4] for the synthesis of heterocyclic analogues of 1-arylnaphthalene lignans of biological significance.[5] Our synthetic plan towards arylquinoline lignan derivative **9** is outlined in Scheme 1. This involves the generation of substituted furo[3,4-*b*]pyridine intermediate **6** by coupling of 2-alkynyl-3-pyridine carbonyl derivatives **4** with Fischer carbene complex **5** followed by Diels–Alder reaction with an added dienophile to give cycloadduct **8**, which is readily convertible to heterolignans **9** by treatment with acid or base. The possible alternative pathway is formation of pyrone derivative **7**, which could also lead to **9** via intermolecular Diels–Alder reaction followed by CO_2 extrusion.[6]

2. Results and discussion

Our studies began with the 2-bromo-3-pyridine carboxaldehyde (**10**), which was prepared by the regioselective *ortho*-lithiation of 2-bromopyridine with LDA at −78 °C followed by quenching with DMF according to the procedure described by Sakamoto et al.[7] The Sonogashira coupling of **10** with trimethylsilylacetylene afforded alkyne aldehyde **11** in 85% yield. Conversion of **11** to the corresponding alkyne carbonyl derivatives **12** was then accomplished by

Keywords: Carbene complexes; Chromium; Azaisobenzofuran; Diels–Alder reaction; Heterolignan.
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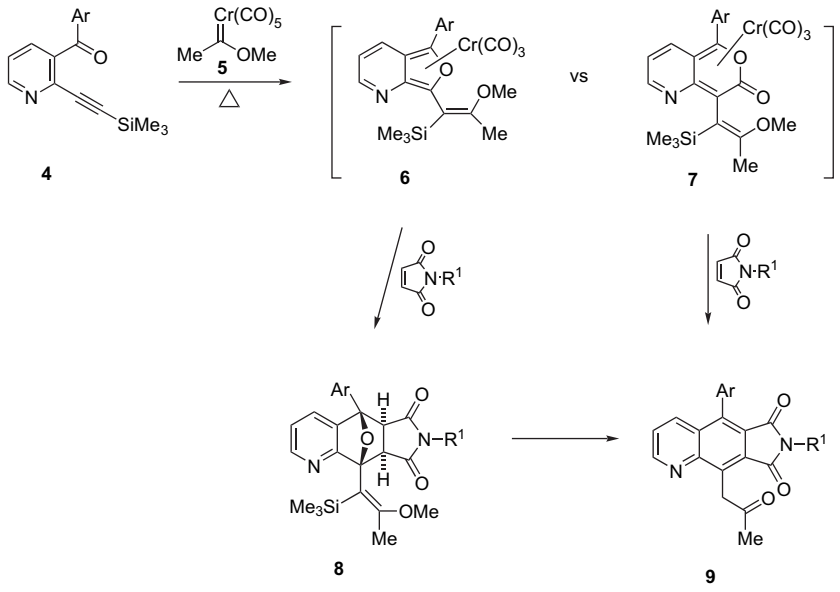
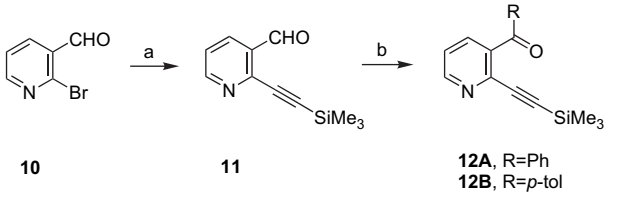
0040–4020/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2007.09.007

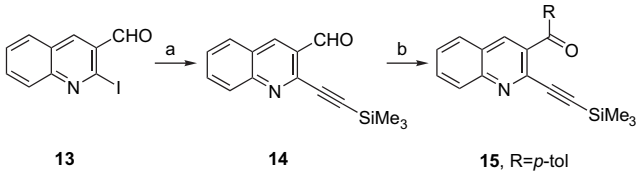


Scheme 1. Our strategy towards arylquinoline lignan derivative.

treatment with an aryl-Grignard reagent in diethyl ether and subsequent oxidation with PDC as depicted in Scheme 2. The corresponding benzo analogue **14** was prepared by the palladium-catalyzed Sonogashira reaction of 3-formyl-2-iodoquinoline (**13**),[8] which on exposure to an aryl-Grignard reagent in diethyl ether followed by PDC oxidation resulted alkyne carbonyl derivative **15** (Scheme 3).



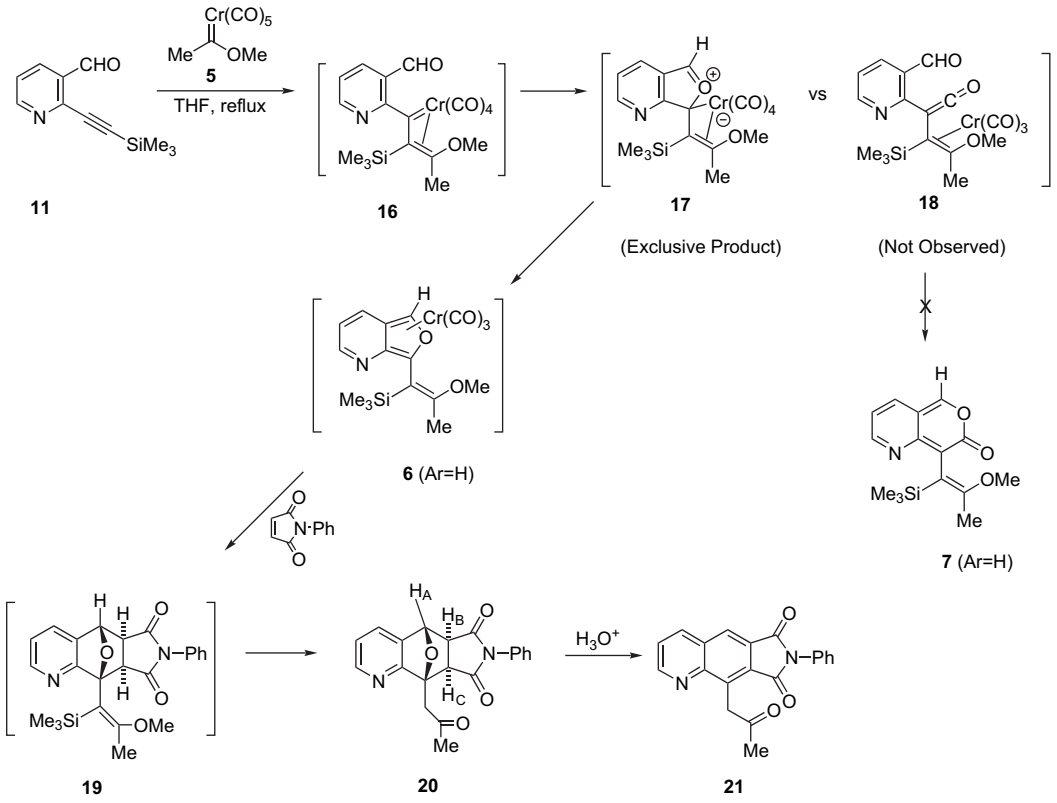
Scheme 2. Reagents and conditions: (a) trimethylsilylacetylene, $(Ph_3P)_2PdCl_2$, CuI, THF, Et_3N, rt, 85%; (b) (i) RMgBr; (ii) CrO_3, 2Py, **12A** (88%), **12B** (68%).



Scheme 3. Reagents and conditions: (a) trimethylsilylacetylene, $(Ph_3P)_2PdCl_2$, CuI, THF, Et_3N, rt, 86%; (b) (i) RMgBr; (ii) CrO_3, 2Py, 69%.

Coupling of pyridine carboxaldehyde **11**, carbene complex **5** and *N*-phenylmaleimide (~1:1:1 ratio) in refluxing tetrahydrofuran for 12 h followed by acidic hydrolysis afforded a mixture of the oxa-bridged adduct **20** and quinoline derivative **21** (Scheme 4). In this reaction, coupling of the carbene complex with the alkyne initially provides intermediate alkyne carbene complex **16**, which is then captured by the oxygen to form the carbonyl ylide derivative **17**. Loss of metal from the carbonyl ylide leads to the isobenzofuran derivative **6**, which then undergoes Diels–Alder reaction with *N*-phenylmaleimide. In this reaction, quinoline derivative **21** was the major product of the reaction. The stereochemistry of the oxa-bridged adduct **20** was assigned as *exo* based on the 0 Hz coupling of H_A and H_B, and the chemical shifts of H_B and H_C (<4 ppm).[2a,9] The absence of coupling between H_A and H_B suggests that the dihedral angle between these hydrogen is about 90° (Karplus curve). A free azaisobenzofuran is unlikely in the reaction of **11** based on the high *exo* selectivity, coupled with the substantial lifetime of the intermediate at 70 °C. The observed azaisobenzofurans could be stabilized by complexation with chromium,[10] and thus the adducts could result from an oxidative insertion–reductive elimination sequence.[11] The reaction process was also carried out without the acid treatment. After filtration through Celite and purification by column chromatography (silica gel) a mixture of ketone **20** and quinoline derivative **21** was obtained. Attempt to isolate enol ether **19** was unsuccessful, as it readily converted to the corresponding ketone **20** and quinoline derivative **21** during column chromatography on silica gel. Here the [4+2] oxa-bridged adduct **20** underwent spontaneous ring cleavage followed by dehydration upon treatment with aqueous hydrochloric acid to give stable quinoline derivative **21**. The possibility of a pyrone derivative **7** from this reaction was initially expected based on the formation of pyrone derivatives from the coupling of carbene complexes with heteroaromatic alkyne aldehydes.[6] In this reaction, formation of pyrone derivative **7** was not detected, which could result from the insertion of CO with the intermediate alkyne carbene complex **16**. Although, pyrone derivative **7** can also lead to the product quinoline derivative **21** via intermolecular Diels–Alder reaction followed by CO_2 extrusion. In these examples, capture of the intermediate vinylcarbene complex **16** by the oxygen might precede any CO insertion processes and hence pyridinopyrone derivative **7** formation is not observed.[6] The formation of azaisobenzofuran intermediate **6** in these studies might be attributed to the lowered ring strain involved, compared to furan and thiophene systems.

The furo[3,4-*b*]pyridine intermediate forming reaction was tested for different heteroaromatic alkynyl carbonyl

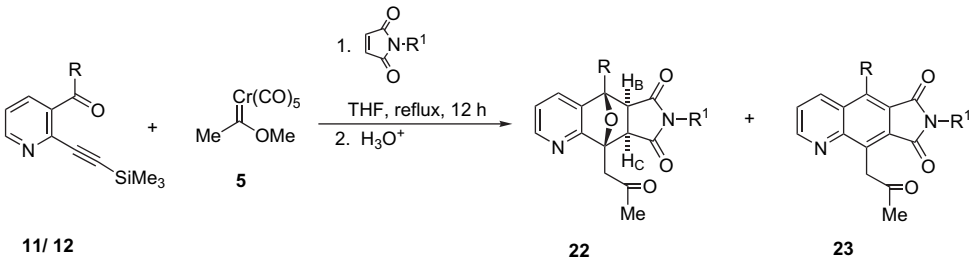


Scheme 4.

derivatives; the results are presented in Table 1. This reaction process was found to be general and afforded a mixture of oxa-bridged compound **22** and quinoline **23** derivatives. Since the azaisobenzofurans derived from the benzophenone analogues appeared to be fairly stable, a two-step process (sequential azaisobenzofuran synthesis—Diels–Alder coupling) was attempted. The reaction of alkyne carbonyl compounds **12** with carbene complex **5** for 0.5 h was followed by addition of *N*-phenylmaleimide/*N*-methylmaleimide as a dienophile and the crude product was treated with aqueous hydrochloric acid to result in a mixture of *exo* Diels–Alder adduct **22** and quinoline derivative **23** (entries **B**–**D**). In these cases with *N*-phenylmaleimide, the oxa-bridged compounds are the major products (entries **B**, **D**), although the ratio was reversed when *N*-methylmaleimide was used (entry **C**).

The reaction process was also carried out with dimethyl maleate as dienophile. The reaction of pyridine carbonyl compound **12A** and carbene complex **5** with dimethyl maleate afforded the mixture of enol ether **24** and the corresponding ketone **25** with no acid treatment at the end of the reactions. However, the enol ether **24** is not stable in chloroform and it readily converted to the corresponding ketone **25**. The isolated yield of **25** from **12A** was 35%. The oxa-bridged compound **25** was converted to the quinoline derivative **26** on treatment with aqueous hydrochloric

Table 1. Generation and trapping of furo[3,4-*b*]pyridine with maleimides formed by the coupling reaction of Fischer carbene complexes **5** with alkynyl pyridinoyl derivatives **11** or **12**



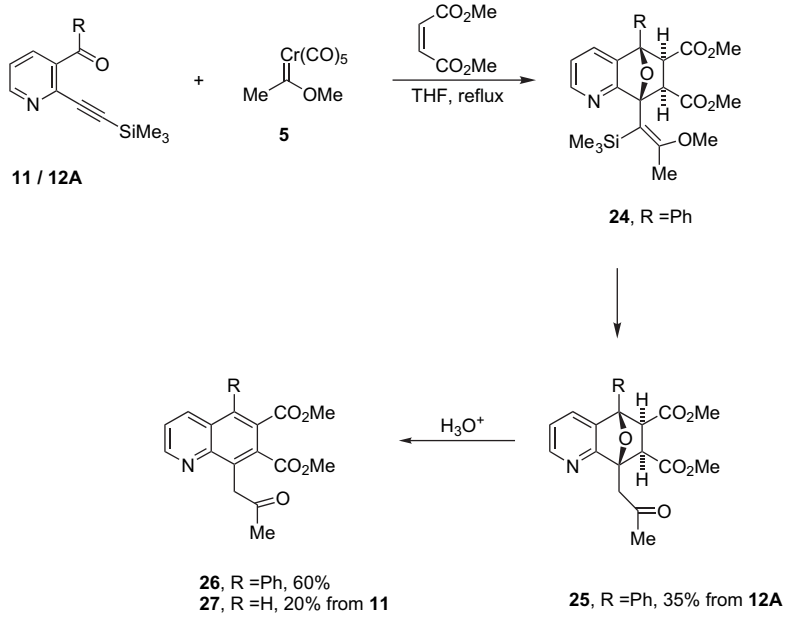
Entry	R	R^1	Yield[a] of **22**	Yield[a] of **23**
A	H	Ph	5	35
B	Ph	Ph	43	11
C	Ph	Me	10	42
D	*p*-Tol	Ph	30	18

[a] Isolated yield in %.

acid. Although the reaction was incomplete, the yield of **26** with respect to recovered starting material **25** is 60%. The quinoline derivative **27** was obtained in 20% yield from the three-component coupling of pyridine carboxaldehyde **11**, carbene complex **5** and dimethyl maleate, followed by treatment of the crude reaction mixtures with aqueous hydrochloric acid (Scheme 5).

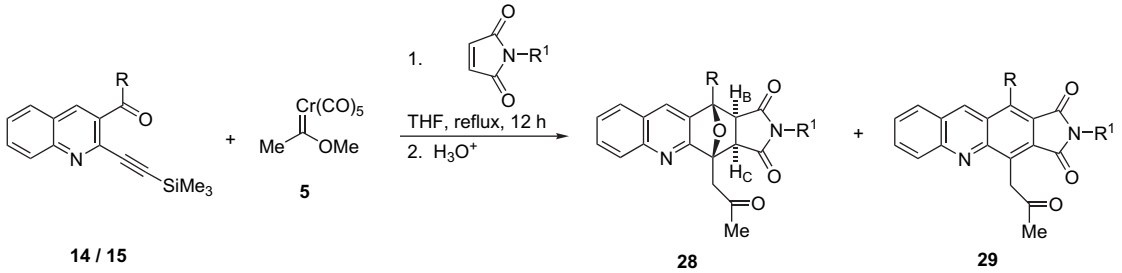
The three-component coupling of benzopyridine alkynyl aldehyde **14**/benzopyridine alkynyl carbonyl derivative **15**, carbene complex **5** and *N*-methylmaleimide/*N*-phenylmaleimide were also examined, which led to the mixture of [4+2] oxa-bridged adduct **28** and benzoquinoline derivative **29**, through the in situ generation of the hitherto unknown system, furo[3,4-*b*]quinoline (Table 2). As in the previous case, the stereochemistry of the oxa-bridge adduct **28** is assigned as *exo* based on the lack of a coupling between H_A and H_B, the chemical shifts of H_B and H_C (<4 ppm) and N-*Me* signal in the proton NMR at δ ~3.0, where applicable.[2a,9]

The oxa-bridge in the initially formed cycloadducts **22**/**28** from the three-component coupling of alkynyl carbonyl derivatives, carbene complex and dienophile, could be readily cleaved leading to the substituted quinolines **23**/substituted benzoquinolines **29** using DBU in refluxing toluene (Scheme 6).[5a,b] However, this process is not efficient as the average yield of this process 40–50%. Although, oxa-bridged compounds **20**, **22C**, **25** and **28B** were readily converted to the quinoline derivatives **21**, **23C**, **26** and **29B** on treatment with aqueous hydrochloric acid, but partial conversion of **22B**, **22D** and **28A** to the corresponding quinoline derivatives **23B**, **23D** and **29A** took place under the same conditions. Compounds **23** (R=Ph or *p*-tol), **26** (R=Ph)



Scheme 5.

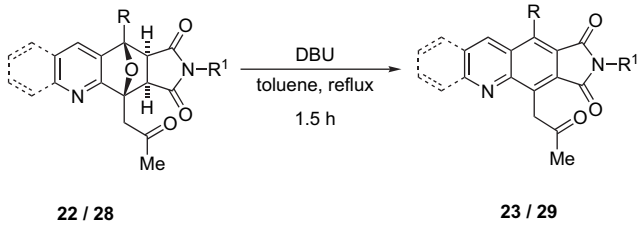
Table 2. Generation and trapping of furo[3,4-*b*]quinolines with maleimides formed by the coupling reaction of Fischer carbene complex **5** with alkynyl pyridinoyl derivatives **14** or **15**



Entry	R	R^1	Yield[a] of **28**	Yield[a] of **29**
A	H	Ph	40	10
B	H	Me	6[b]	36
C	*p*-Tol	Me	—	48

[a] Isolated yield in %.
[b] Obtained as a mixture of **28B** and **29B**, as in this case oxa-bridged compound readily converted to the corresponding benzoquinoline derivative in chloroform at room temperature.

and **29** (R=*p*-tol) may be viewed as heterocyclic analogues of potentially bioactive 1-arylnaphthalene lignans.[5]



22 / 28 **23 / 29**

Scheme 6.

The coupling of alkynyl carbonyl compounds with carbene complexes for the generation and trapping of α-phenylsubstituted furo[3,4-*b*]pyridines can also be extended to intramolecular cases (Scheme 7). Towards this γ,δ-unsaturated Fischer carbene complex **30** was prepared from carbene complex **5** via deprotonation using *n*-BuLi at −78 °C followed by addition of an excess allylic bromide as reported by Herndon et al.[2j] Thus the coupling of carbene complex **30** with alkynyl carbonyl derivative **12A** under the same conditions as previously described undergoes an *exo*-selective intramolecular Diels–Alder reaction[12] through the generation of azaisobenzofuran intermediate **31** leading to a pyridine fused to the hydronaphthalene derivative **33** in one pot and in good yield. The initial Diels–Alder adduct **32**, resulting from **31**, appears to be unstable with respect to ring opening processes.[1] The high-yielding intramolecular [4+2] cycloaddition reaction of **31** is obviously related to entropic factors, which place the tethered double bond in close proximity to the diene system.

Various attempts to isolate the heteroaromatic isobenzofurans **6** were unsuccessful owing to their extreme instability. The reaction of alkyne carbonyl compound **12A** with carbene complex in refluxing THF for 4 h in absence of dienophile followed by exposure to silica gel gave a crystalline dicarbonyl compound **34**, which may result from the insertion of oxygen into the intermediate alkenylcarbene complex **16** (Scheme 8).

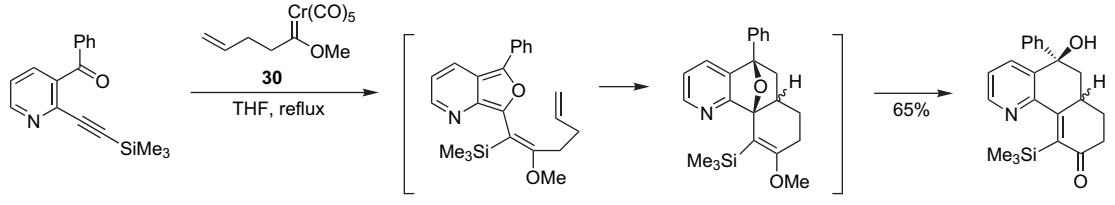
3. Conclusion

In conclusion, we have demonstrated a new route to the generation of furo[3,4-*b*]pyridines/furo[3,4-*b*]quinolines from the coupling of alkynyl carbonyl derivative with Fischer carbene complexes. In fact this is the first report of in situ generation of furo[3,4-*b*]quinoline intermediates. The intermediates can be trapped through Diels–Alder reaction with dienophiles leading to the synthesis of nitrogen containing heterocyclic analogues of 1-arylnaphthalene lignans in a single step. Our results clearly indicate that this methodology provides rapid entry into heteroaromatic *o*-quinodimethanes. Further work utilizing azaisobenzofuran intermediates is currently underway in our laboratory.

4. Experimental

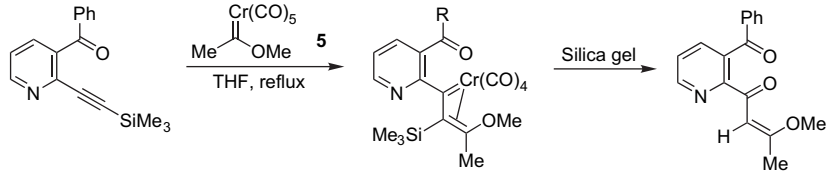
4.1. General

All melting points are uncorrected. 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_2O_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 eluent unless specified otherwise.



12A **31** **32** **33**

Scheme 7.



12A **16** (R=Ph) **34**

Scheme 8.

4.2. General procedure 1—for synthesis of alkynyl pyridine/quinoline carboxaldehyde 11, 14

A mixture of aldehyde (1 mmol), $Pd(PPh_3)_2Cl_2$ (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) was added. The reaction was stirred for 12–16 h at room temperature, and the solvent was removed on a rotary evaporator. The residue was treated with dichloromethane and filtered through Celite. The filtrate was concentrated and the residue was purified by chromatography (silica gel, ethyl acetate/petroleum ether 1:9).

4.2.1. 2-Trimethylsilylethynylpyridine-3-carboxaldehyde (11).[7] General procedure 1 was followed using 2-bromo-3-pyridine carboxaldehyde (**10**)[7] (0.74 g, 3.99 mmol), $Pd(PPh_3)_2Cl_2$ (0.14 g, 0.2 mmol), PPh_3 (26 mg, 0.1 mmol), trimethylsilylacetylene (0.59 g, 6.0 mmol) and triethylamine (0.60 g, 6 mmol) in THF (20 mL), followed by CuI (7 mg, 0.04 mmol). After column chromatography a single fraction was isolated and assigned as compound **11** (0.689 g, 85%). IR (KBr, cm^{-1}): 2850, 2745, 2158, 1700; ^1H NMR (400 MHz, $CDCl_3$): δ 10.55 (s, 1H), 8.77 (dd, 1H, J=5.0, 1.8 Hz), 8.17 (dd, 1H, J=8.0, 1.8 Hz), 7.39 (dd, 1H, J=8.0, 5.0 Hz), 0.30 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 191.3, 154.8, 146.1, 134.9, 132.5, 123.9, 103.3, 99.7, 0.0 (3C).

4.2.2. 2-Trimethylsilylethynylquinoline-3-carboxaldehyde (14). General procedure 1 was followed using 3-formyl-2-iodoquinoline (**13**)[8] (1.13 g, 3.99 mmol), $Pd(PPh_3)_2Cl_2$ (0.14 g, 0.2 mmol), PPh_3 (26 mg, 0.1 mmol) and trimethylsilylacetylene (0.59 g, 6.0 mmol) and triethylamine (0.60 g, 6.0 mmol) in THF (20 mL), followed by CuI (7 mg, 0.04 mmol). After column chromatography a single fraction was isolated as a white needle and assigned as compound **14** (0.87 g, 86%). Mp 88–89 °C; R_f (10% EtOAc/petroleum ether) 0.73; IR (KBr, cm^{-1}): 2849, 2729, 2165, 1697; ^1H NMR (400 MHz, $CDCl_3$): δ 10.68 (s, 1H), 8.69 (s, 1H), 8.12 (d, 1H, J=8.3 Hz), 7.92 (d, 1H, J=8.3 Hz), 7.83 (t, 1H, J=7.6 Hz), 7.60 (t, 1H, J=7.6 Hz), 0.32 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 191.3, 150.4, 144.0, 137.1, 133.3, 130.0, 129.8, 129.2, 128.7, 126.9, 102.7, 100.4, 0.01 (3C); MS: *m/e* (relative intensity): 254 (MH^+, 100). Anal. Calcd for $C_{15}H_{15}NOSi$: C, 71.11; H, 5.97; N, 5.53. Found: C, 70.92; H, 6.12; N, 5.42.

4.3. General procedure 2—synthesis of alkynyl pyridine/quinoline carbonyl derivatives 12, 15

To a stirred solution of aldehyde (2 mmol) in dry diethyl ether (10 mL) was added dropwise a solution of arylmagnesium bromide (2.2 mmol) in dry diethyl ether [prepared from arylbromide (3 mmol) and magnesium (4 mmol) in 10 mL dry diethyl ether] over a period of 20 min at 0 °C. After 3 h stirring the mixture was allowed to come at room temperature and then quenched with saturated aqueous NH_4Cl (5 mL). The organic layer was separated and the aqueous layer was extracted with diethyl ether (3×10 mL). The combined organic layer was washed with brine (5 mL) and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure and the crude alcohol was used in the next step. A solution of crude alcohol in dry CH_2Cl_2 (2 mL) was added to a red solution of $CrO_3 \cdot 2Py$ [prepared from vigorously stirred suspension of CrO_3 (6 mmol) and pyridine (12 mmol) in dry CH_2Cl_2 (12 mL) for 1.5 h at room temperature] and stirred at room temperature for 4 h. The mixture was then diluted with Et_2O (10 mL) and passed through a bed of silica gel (5 g). The solution was then concentrated under reduced pressure and purified by column chromatography (silica gel, ethyl acetate/petroleum ether 2:8).

4.3.1. Phenyl-(2-trimethylsilylethynylpyridine-3-yl)methanone (12A). Starting from aldehyde **11** (406 mg, 2 mmol) and phenylmagnesium bromide (0.5 M, 4.4 mL, 2.2 mmol), following the general procedure 2, the product was obtained as a white needle **12A** (0.49 g, 88%). Mp 58–59 °C; R_f (20% EtOAc/petroleum ether) 0.65; IR (KBr, cm^{-1}): 2168, 1668; ^1H NMR (500 MHz, $CDCl_3$): δ 8.77 (dd, 1H, J=4.8, 1.7 Hz), 7.90–7.84 (m, 3H), 7.66 (m, 1H), 7.54–7.49 (m, 2H), 7.44 (dd, 1H, J=7.5, 4.8 Hz), 0.0 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 196.2, 152.0, 141.2, 139.0, 137.5, 137.0, 134.4, 130.9 (2C), 129.3 (2C), 123.7, 102.8, 102.3, 0.0 (3C); MS: *m/e* (relative intensity): 281 (MH^++1, 26), 280 (MH^+, 100), 206 (3). Anal. Calcd for $C_{17}H_{17}NOSi$: C, 73.08; H, 6.13; N, 5.01. Found: C, 72.93; H, 6.27; N, 4.86.

4.3.2. *p*-Tolyl-(2-trimethylsilylethynylpyridine-3-yl)methanone (12B). Starting from aldehyde **11** (406 mg, 2 mmol) and *p*-tolylmagnesium bromide (0.5 M, 4.4 mL, 2.2 mmol), following the general procedure 2, the product **12B** was obtained (0.40 g, 68%) as a colourless thick liquid. R_f (20% EtOAc/petroleum ether) 0.62; IR (KBr, cm^{-1}): 2166, 1655; ^1H NMR (400 MHz, $CDCl_3$): δ 8.60 (dd, 1H, J=4.8, 1.4 Hz), 7.71 (dd, 1H, J=7.8, 1.4 Hz), 7.62 (d, 2H, J=8.0 Hz), 7.28 (dd, 1H, J=7.8, 4.8 Hz), 7.17 (d, 2H, J=8.0 Hz), 2.33 (s, 3H), −0.10 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 194.7, 150.8, 144.4, 140.0, 138.2, 135.9, 133.9, 130.0 (2C), 128.9 (2C), 122.6, 101.4, 101.3, 21.4, −0.8 (3C); MS: *m/e* (relative intensity): 294 (MH^+, 100). Anal. Calcd for $C_{18}H_{19}NOSi$: C, 73.68; H, 6.53; N, 4.77. Found: C, 73.49; H, 6.39; N, 4.91.

4.3.3. *p*-Tolyl-(2-trimethylsilylethynylquinoline-3-yl)methanone (15). Starting from aldehyde **14** (506 mg, 2 mmol) and *p*-tolylmagnesium bromide (0.5 M, 4.4 mL, 2.2 mmol), following the general procedure 2, the product **15** was obtained as a thick brown liquid (0.47 g, 69%). R_f (20% EtOAc/petroleum ether) 0.72; IR (KBr, cm^{-1}): 2164, 1662; ^1H NMR (500 MHz, $CDCl_3$): δ 8.29 (s, 1H), 8.17 (dd, 1H, J=8.0, 1.0 Hz), 7.87 (dd, 1H, J=8.0, 1.0 Hz), 7.81 (ddd, 1H, J=8.0, 7.0, 1.0 Hz), 7.75 (d, 2H, J=8.0 Hz), 7.61 (ddd, 1H, J=8.0, 7.0, 1.0 Hz), 7.27 (d, 2H, J=8.0 Hz), 2.44 (s, 3H), 0.0 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 195.7, 149.1, 145.4, 141.0, 137.2, 136.5, 135.4, 132.1, 131.2 (2C), 130.1, 129.9 (2C), 128.9, 128.8, 127.1, 103.0, 102.4, 22.5, 0.0 (3C). Anal. Calcd for $C_{22}H_{21}NOSi$: C, 76.93; H, 6.16; N, 4.08. Found: C, 76.78; H, 6.35; N, 3.87.

4.4. General procedure 3—coupling of carbene complex with alkynyl pyridine/quinoline carboxaldehyde and maleimides/dimethyl maleate

To a refluxing solution of alkynyl aldehyde **11** or **14** (1 mmol) and maleimide/dimethyl maleate (1 mmol) in THF (5 mL) was added a solution of carbene complex **5**

(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 was filtered through Celite (1.0 g). The solvent was removed on a rotary evaporator, and the crude products were 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 was stirred for 6 h at room temperature. The organic layer was separated. The aqueous layer was neutralized with saturated $NaHCO_3$ solution (3 mL) and extracted with ethyl acetate (3×10 mL). The combined organic layer (diethyl ether layer and ethyl acetate layer) was washed with water (3 mL) and brine (3 mL), and dried over anhydrous Na_2SO_4. Evaporation of solvent and purification by chromatography gave the pure products.

4.4.1. Coupling of carbene complex 5 with 2-trimethylsilylethynylpyridine-3-carboxaldehyde (11) and *N*-phenylmaleimide (Table 1, entry A). General procedure 3 was followed using carbene complex **5** (275 mg, 1.1 mmol), alkynyl aldehyde **11** (203 mg, 1 mmol) and *N*-phenylmaleimide (173 mg, 1 mmol). The crude product was purified using column chromatography (silica gel, ethyl acetate/petroleum ether 1:3) to yield the quinoline derivative **21** (115 mg, 35%) and the oxa-bridged compound **20** (17 mg, 5%) as white solids. *Compound* **21**: mp 232 °C (decomposed); R_f (25% EtOAc/petroleum ether) 0.48; IR (KBr, cm^{-1}): 1716; ^1H NMR (300 MHz, $CDCl_3$): δ 8.99 (d, 1H, J=3.6 Hz), 8.32 (s, 1H), 8.31 (d, 1H, J=6.0 Hz), 7.55 (dd, 1H, J=8.1, 4.1 Hz), 7.50–7.32 (m, 5H), 4.97 (s, 2H), 2.40 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 205.1, 167.5, 166.4, 152.5, 149.8, 138.4, 136.5, 131.8, 131.0, 129.4, 129.3, 128.9, 128.6, 128.0, 126.8 (2C), 124.3, 123.8, 40.9, 30.8; MS (FAB): *m/e* (relative intensity): 331 (42, MH^+), 176 (15), 154 (100), 136 (99), 107 (58). Anal. Calcd for $C_{20}H_{14}N_2O_3$: C, 72.72; H, 4.27; N, 8.48. Found: C, 72.56; H, 4.43; N, 8.27. *Compound* **20**: mp>250 °C; R_f (25% EtOAc/petroleum ether) 0.20; IR (KBr, cm^{-1}): 1711; ^1H NMR (300 MHz, $CDCl_3$): δ 8.47 (br s, 1H), 7.72 (br s, 1H), 7.27–7.60 (m, 6H), 5.82 (s, 1H), 3.38–3.75 (m, 4H), 2.35 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 203.2, 175.4, 174.4, 165.9, 149.3, 138.3, 132.2, 130.0 (2C), 129.7, 128.8, 127.3 (2C), 123.4, 87.9, 80.6, 52.2, 50.0, 42.8, 31.7; MS (FAB): *m/e* (relative intensity): 371 (100, M^++Na), 349 (46, MH^+), 198 (56), 176 (56). Anal. Calcd for $C_{20}H_{16}N_2O_4$: C, 68.96; H, 4.63; N, 8.04. Found: C, 68.79; H, 4.84; N, 7.85.

4.4.2. Coupling of carbene complex 5 with 2-trimethylsilylethynylpyridine-3-carboxaldehyde (11) and *N*-phenylmaleimide. General procedure 3 was followed using carbene complex **5** (192 mg, 0.77 mmol), alkynyl aldehyde **11** (142 mg, 0.7 mmol) and *N*-phenylmaleimide (121 mg, 0.7 mmol) with the exception that acid hydrolysis was not employed as the last step. The crude product was purified using column chromatography (silica gel, ethyl acetate/petroleum ether 1:3) to yield the oxa-bridged compound **20** (37 mg, 15%) and quinoline derivative **21** (65 mg, 28%).

4.4.3. Dimethyl 8-(2-oxopropyl)quinoline-6,7-dicarboxylate (27). General procedure 3 was followed using carbene complex **5** (138 mg, 0.55 mmol), alkynyl aldehyde **11** (101 mg, 0.5 mmol) and dimethyl maleate (77 mg, 0.5 mmol). The crude product was purified using column chromatography (silica gel, ethyl acetate/petroleum ether 2:3) to yield the white needle quinoline derivative **27** (30 mg, 20%). Mp 115 °C; R_f (40% EtOAc/petroleum ether) 0.68; IR (KBr, cm^{-1}): 1733, 1717; ^1H NMR (300 MHz, $CDCl_3$): δ 9.01 (d, 1H, J=3.3 Hz), 8.47 (s, 1H), 8.25 (d, 1H, J=7.6 Hz), 7.52 (dd, 1H, J=8.2, 4.2 Hz), 4.44 (s, 2H), 3.96 (s, 6H), 2.23 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 205.2, 169.0, 166.0, 152.4, 147.9, 135.6, 134.3, 133.5, 130.9, 127.4, 126.1, 122.8, 52.8 (2C), 43.2, 29.7; MS (FAB): *m/e* (relative intensity): 302 (62, MH^+), 270 (100), 105 (42). Anal. Calcd for $C_{16}H_{15}NO_5$: C, 63.78; H, 5.02; N, 4.65. Found: C, 63.69; H, 5.18; N, 4.87.

4.4.4. Coupling of carbene complex 5 with 2-trimethylsilylethynylquinoline-3-carboxaldehyde (14) and *N*-phenylmaleimide (Table 2, entry A). General procedure 3 was followed using carbene complex **5** (138 mg, 0.55 mmol), alkynyl aldehyde **14** (127 mg, 0.50 mmol) and *N*-phenylmaleimide (87 mg, 0.50 mmol). The crude product was purified using column chromatography (silica gel, ethyl acetate/petroleum ether 1: 3) to yield benzoquinoline derivative **29A** (19 mg, 10%) and oxa-bridged compound **28A** (80 mg, 40%) as white solids. *Compound* **29A**: mp 137–138 °C; R_f (25% EtOAc/petroleum ether) 0.71; IR (KBr, cm^{-1}): 1764, 1714; ^1H NMR (500 MHz, $CDCl_3$): δ 8.90 (s, 1H), 8.49 (s, 1H), 8.24 (d, 1H, J=8.5 Hz), 8.03 (d, 1H, J=8.5 Hz), 7.87 (t, 1H, J=7.5 Hz), 7.64 (t, 1H, J=7.5 Hz), 7.57–7.46 (m, 4H), 7.43 (t, 1H, J=7.0 Hz), 5.15 (s, 2H), 2.54 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 205.1, 167.1, 166.1, 149.7, 148.9, 139.0, 137.0, 131.9, 131.7, 130.2, 129.1 (2C), 128.3, 128.2, 127.7, 127.44, 127.4, 127.3, 126.6 (2C), 126.1, 125.2, 40.9, 30.7; MS: *m/e* (relative intensity): 381 (MH^+, 67), 254 (100), 186 (24), 153 (27). Anal. Calcd for $C_{24}H_{16}N_2O_3$: C, 75.78; H, 4.24; N, 7.36. Found: C, 75.92; H, 4.21; N, 7.28. *Compound* **28A**: mp 163–165 °C; R_f (25% EtOAc/petroleum ether) 0.47; IR (KBr, cm^{-1}): 1712; ^1H NMR (400 MHz, $CDCl_3$): δ 8.13 (d, 1H, J=8.0 Hz), 8.04 (s, 1H), 7.85 (d, 1H, J=8.0 Hz), 7.73 (t, 1H, J=7.2 Hz), 7.59 (t, 1H, J=7.2 Hz), 7.50 (t, 2H, J=7.2 Hz), 7.42 (t, 1H, J=7.2 Hz), 7.32 (d, 2H, J=7.2 Hz), 5.95 (s, 1H), 3.79 (d, 1H, J=17.7 Hz), 3.59 (d, 1H, J=6.8 Hz), 3.55 (d, 1H, J=17.7 Hz), 3.33 (d, 1H, J=6.8 Hz), 2.36 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 202.7, 174.7, 173.6, 164.7, 147.2, 134.0, 131.6, 129.7, 129.7, 129.2 (2C), 128.8, 128.2, 127.2, 127.0, 126.5 (2C), 126.4, 87.2, 79.8, 51.3, 48.4, 41.7, 31.1; MS (FAB): *m/e* (relative intensity): 399 (100, MH^+), 381 (5), 367 (18), 226 (25), 182 (35). Anal. Calcd for $C_{24}H_{18}N_2O_4$: C, 72.35; H, 4.55; N, 7.03. Found: C, 72.14; H, 4.73; N, 6.86.

4.4.5. Coupling of carbene complex 5 with 2-trimethylsilylethynylquinoline-3-carboxaldehyde (14) and *N*-methylmaleimide (Table 2, entry B). General procedure 3 was followed using carbene complex **5** (217 mg, 0.87 mmol), alkynyl aldehyde **14** (200 mg, 0.79 mmol) and *N*-methylmaleimide (88 mg, 0.79 mmol). The crude product was purified using column chromatography (silica gel, ethyl acetate/petroleum ether 25:75) to yield benzoquinoline derivative **29B** (90 mg, 36%) as a thick brown liquid and oxa-bridged compound **28B** (16 mg, 6%). However, the oxa-bridged

compound **28B** in chloroform is slowly converted to the **29B**. *Compound* **29B**: R_f (25% EtOAc/petroleum ether) 0.66; IR (KBr, cm^{-1}): 1762, 1703, 1602; ^1H NMR (400 MHz, $CDCl_3$): δ 8.92 (s, 1H), 8.44 (s, 1H), 8.23 (d, 1H, J=8.4 Hz), 8.04 (d, 1H, J=8.4 Hz), 7.86 (t, 1H, J=7.6 Hz), 7.65 (t, 1H, J=7.6 Hz), 5.08 (s, 2H), 3.25 (s, 3H), 2.53 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 205.7, 168.7, 167.7, 150.1, 149.3, 139.5, 136.7, 132.2, 130.7, 130.6, 128.6, 128.4, 128.3, 128.1, 127.1, 124.9, 41.3, 31.2, 24.8; MS: *m/e* (relative intensity): 319 (MH^+, 100), 292 (40), 138 (21), 125 (43). Anal. Calcd for $C_{19}H_{14}N_2O_3$: C, 71.69; H, 4.43; N, 8.80. Found: C, 71.63; H, 4.56; N, 8.96. *Compound* **28B** (contaminated with 11% **29B**): R_f (25% EtOAc/petroleum ether) 0.20; IR (KBr, cm^{-1}): 1762, 1706, 1602; ^1H NMR (400 MHz, $CDCl_3$): δ 8.05 (d, 1H, J=8.0 Hz), 7.96 (s, 1H), 7.80 (d, 1H, J=8.0 Hz), 7.70 (t, 1H, J=8.0 Hz), 7.56 (t, 1H, J=7.6 Hz), 5.80 (s, 1H), 3.67 (d, 1H, J=17.6 Hz), 3.48 (d, 1H, J=17.6 Hz), 3.42 (d, 1H, J=6.8 Hz), 3.16 (d, 1H, J=6.8 Hz), 3.04 (s, 3H), 2.33 (s, 3H); MS: *m/e* (relative intensity): 337 (MH^+, 100), 319 (30), 295 (61), 286 (18), 277 (10).

4.5. General procedure 4—coupling of carbene complex with alkynyl pyridine/quinoline carbonyl derivatives and maleimides/dimethyl maleate

To a refluxing solution of alkynyl carbonyl derivatives **12** or **15** (1 mmol) in THF (2 mL) was added a solution of carbene complex **5** (1.1 mmol) in THF (10 mL) over a period of 0.5 h. After the addition was complete, the mixture was heated to reflux for 0.5 h. The dienophile (1 mmol) in THF (3 mL) was then added to the solution at reflux. The mixture was heated at reflux for an additional 12 h and then 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 crude products were 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 was stirred for 6 h at room temperature. The organic layer was separated. The aqueous layer was neutralized with saturated $NaHCO_3$ solution (3 mL) and extracted with ethyl acetate (3×10 mL). The combined organic layer (diethyl ether layer and ethyl acetate layer) was washed with water (3 mL) and brine (3 mL), and dried over anhydrous Na_2SO_4. Evaporation of solvent and purification by chromatography gave the pure products.

4.5.1. Coupling of carbene complex 5 with phenyl-(2-trimethylsilylethynylpyridine-3-yl)methanone (12A) and *N*-phenylmaleimide (Table 1, entry B). General procedure 4 was followed using carbene complex **5** (110 mg, 0.44 mmol), alkynyl carbonyl derivatives **12A** (110 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 1:3) to yield the quinoline derivative **23B** (18 mg, 11%) and the oxa-bridged compound **22B** (71 mg, 43%) as white solids. *Compound* **23B**: mp 212–215 °C; R_f (25% EtOAc/petroleum ether) 0.63; IR (KBr, cm^{-1}): 1723; ^1H NMR (400 MHz, $CDCl_3$): δ 9.03 (dd, 1H, J=4.4, 1.6 Hz), 8.14 (dd, 1H, J=8.0, 1.6 Hz), 7.57–7.32 (m, 11H), 5.01 (s, 2H) 2.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 205.3, 167.0, 165.6, 151.7, 149.3, 139.7, 136.5, 135.3, 133.2, 131.4, 130.9, 129.8 (2C), 128.8 (2C), 128.7, 128.2 (2C), 128.1, 127.4, 126.6 (2C), 123.4, 123.2, 40.6, 29.6; MS: *m/e* (relative intensity): 407 (MH^+, 100), 325 (5), 309 (8); Anal. Calcd for $C_{26}H_{18}N_2O_3$: C, 76.83; H, 4.46; N, 6.89. Found: C, 76.59; H, 4.62; N, 6.68. *Compound* **22B**: mp 186–188 °C; R_f (25% EtOAc/petroleum ether) 0.21; IR (KBr, cm^{-1}): 1713; ^1H NMR (400 MHz, $CDCl_3$): δ 8.44 (d, 1H, J=4.4 Hz), 7.61 (d, 2H, J=7.2 Hz), 7.49 (t, 3H, J=7.2 Hz), 7.45–7.36 (m, 3H), 7.32 (m, 1H), 7.13 (d, 3H, J=7.2 Hz), 3.89 (d, 1H, J=4.0 Hz), 3.70 (d, 1H, J=17.8 Hz), 3.60 (d, 1H, J=17.8 Hz), 3.56 (d, 1H, J=4.0 Hz), 2.38 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 203.1, 173.3, 171.9, 164.8, 148.0, 140.6, 133.0, 131.6, 129.0 (2C), 128.6 (2C), 128.5 (2C), 127.3, 126.3 (2C), 125.7 (2C), 122.3, 90.2, 86.3, 52.9, 50.3, 42.4, 30.8; MS (FAB): *m/e* (relative intensity): 425 (MH^+, 38), 252 (35), 219 (50), 191 (70), 159 (67), 147 (92), 105 (100). Anal. Calcd for $C_{26}H_{20}N_2O_4$: C, 73.57; H, 4.75; N, 6.60. Found: C, 73.35; H, 4.95; N, 6.41.

4.5.2. Coupling of carbene complex 5 with phenyl-(2-trimethylsilylethynylpyridine-3-yl)methanone (12A) and *N*-methylmaleimide (Table 1, entry C). General procedure 4 was followed using carbene complex **5** (175 mg, 0.7 mmol), alkynyl carbonyl derivatives **12A** (177 mg, 0.63 mmol) and *N*-methylmaleimide (70 mg, 0.63 mmol). The crude product was purified using column chromatography (silica gel, ethyl acetate/petroleum ether 1:3) to yield the quinoline derivative **23C** (91 mg, 42%) and the oxa-bridged compound **22C** (23 mg, 10%) as white solids. *Compound* **23C**: mp 160–163 °C; R_f (25% EtOAc/petroleum ether) 0.62; IR (KBr, cm^{-1}): 1762, 1711, 1611; ^1H NMR (400 MHz, $CDCl_3$): δ 8.99 (dd, 1H, J=4.0, 1.6 Hz), 8.09 (dd, 1H, J=8.4, 1.6 Hz), 7.58–7.50 (m, 3H), 7.46 (dd, 1H, J=8.4, 4.0 Hz), 7.39–7.33 (m, 2H), 5.03 (s, 2H), 3.13 (s, 3H), 2.49 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 205.7, 168.7, 167.3, 152.0, 149.4, 137.0, 136.4, 135.2, 133.9, 131.2, 130.3 (2C), 129.6, 129.2, 128.9, 128.7 (2C), 123.6, 41.3, 31.0, 24.5; MS: *m/e* (relative intensity): 345 (MH^+, 100), 282 (51), 250 (61). Anal. Calcd for $C_{21}H_{16}N_2O_3$: C, 73.24; H, 4.68; N, 8.13. Found: C, 73.11; H, 4.85; N, 7.98. *Compound* **22C**: mp 171 °C; R_f (25% EtOAc/petroleum ether) 0.20; IR (KBr, cm^{-1}): 1769, 1725, 1700; ^1H NMR (400 MHz, $CDCl_3$): δ 8.40 (dd, 1H, J=5.2, 1.2 Hz), 7.58–7.54 (m, 2H), 7.51–7.46 (m, 2H), 7.44–7.41 (m, 1H), 7.39 (dd, 1H, J=7.6, 1.2 Hz), 7.08 (dd, 1H, J=7.6, 5.2 Hz), 3.69 (d, 1H, J=6.8 Hz), 3.62 (d, 1H, J=17.6 Hz), 3.54 (d, 1H, J=17.6 Hz), 3.43 (d, 1H, J=6.8 Hz), 2.90 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.1, 174.1, 172.9, 164.6, 147.9, 140.3, 132.9, 128.4, 128.3 (2C), 127.1, 125.7 (2C), 122.1, 89.6, 85.7, 52.6, 50.3, 42.2, 30.8, 25.0; MS: *m/e* (relative intensity: 363 (MH^+, 100), 321 (25), 288 (8), 252 (90), 210 (68), 153 (27). Anal. Calcd for $C_{21}H_{18}N_2O_4$: C, 69.60; H, 5.01; N, 7.73. Found: C, 69.89; H, 4.70; N, 7.93.

4.5.3. Coupling of carbene complex 5 with *p*-tolyl-(2-trimethylsilylethynylpyridine-3-yl)methanone (12B) and *N*-phenylmaleimide (Table 1, entry D). General procedure 4 was followed using carbene complex **5** (170 mg, 0.68 mmol), alkynyl carbonyl derivatives **12B** (180 mg, 0.61 mmol) and *N*-phenylmaleimide (107 mg, 0.62 mmol). The crude product was purified using column chromatography (silica gel, ethyl acetate/petroleum ether 1:3) to yield the quinoline

derivative **23D** (46 mg, 18%) and the oxa-bridged compound **22D** (80 mg, 30%) as white solids. *Compound* **23D**: mp 158–159 °C; R_f (25% EtOAc/petroleum ether) 0.67; IR (KBr, cm^{-1}): 1711; ^1H NMR (300 MHz, $CDCl_3$): δ 9.04 (d, 1H, J=3.0 Hz), 8.20 (d, 1H, J=8.4 Hz), 7.51 (d, 1H, J=8.4, 3.9 Hz), 7.48–7.29 (m, 9H), 5.11 (s, 2H), 2.50 (s, 3H), 2.47 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 205.3, 167.0, 165.6, 151.7, 149.3, 140.0, 138.5, 136.5, 135.1, 131.4, 131.0, 130.1, 129.7 (2C), 128.9 (2C), 128.7 (2C), 128.0, 127.4, 126.5 (2C), 123.3, 123.1, 40.6, 30.4, 21.3; MS: *m/e* (relative intensity): 421 (100, MH^+), 403 (5), 266 (4), 153 (54). Anal. Calcd for $C_{27}H_{20}N_2O_3$: C, 77.13; H, 4.79; N, 6.66. Found: C, 76.94; H, 4.95; N, 6.78. *Compound* **22D**: mp 181 °C; R_f (25% EtOAc/petroleum ether) 0.21; IR (KBr, cm^{-1}): 1779, 1725, 1713; ^1H NMR (300 MHz, $CDCl_3$): δ 8.42 (d, 1H, J=4.5 Hz), 7.55–7.26 (m, 9H), 7.23–7.08 (m, 2H), 3.89 (d, 1H, J=6.7 Hz), 3.68 (d, 1H, J=17.8 Hz), 3.59 (d, 1H, J=17.6 Hz), 3.53 (d, 1H, J=6.8 Hz), 2.39 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.2, 173.4, 171.9, 164.7, 147.9, 140.5, 138.1, 131.4, 129.9, 129.1 (2C), 128.8 (2C), 128.4, 127.0, 126.2 (2C), 125.4 (2C), 122.1, 90.0, 86.0, 52.7, 50.1, 42.3, 30.7, 21.6. MS (FAB) *m/e* (relative intensity): 439 (MH^+, 56), 421 (MH^+-H_2O, 10), 349 (20), 322 (26), 266 (62), 222 (47), 136 (100). Anal. Calcd for $C_{27}H_{22}N_2O_4$: C, 73.96; H, 5.06; N, 6.39. Found: C, 73.71; H, 4.96; N, 6.61.

4.5.4. Coupling of carbene complex 5 with phenyl-(2-trimethylsilylethynylpyridine-3-yl)methanone (12A) and dimethyl maleate (Scheme 5). General procedure 4 was followed using carbene complex **5** (112 mg, 0.45 mmol), alkynyl carbonyl derivatives **12A** (100 mg, 0.36 mmol) and dimethyl maleate (52 mg, 0.36 mmol), with the exception that acid hydrolysis was not employed at the last step. The crude product was purified using column chromatography (silica gel, ethyl acetate/petroleum ether 1:4) to yield a mixture of the oxa-bridged enol ether **24** as a brownish thick liquid and the oxa-bridged ketone **25** (R=Ph) as a white solid. However, the enol ether **24** is not stable enough in chloroform and it readily converted to the stable **25** (50 mg, 35% from **12A**). *Compound* **24**: R_f (20% EtOAc/petroleum ether) 0.41; IR (KBr, cm^{-1}): 1736, 1609; ^1H NMR (300 MHz, $CDCl_3$): δ 8.47 (d, 1H, J=4.9 Hz), 7.68 (d, 2H, J=7.5 Hz), 7.37–7.55 (m, 4H), 7.08 (dd, 1H, J=7.4, 5.1 Hz), 3.84 (d, 1H, J=5.1 Hz), 3.73 (d, 1H, J=5.1 Hz), 3.72 (s, 3H), 3.70 (s, 3H), 3.60 (s, 3H), 2.19 (s, 3H), 0.13 (s, 9H); MS (FAB) *m/e* (relative intensity): 482 (MH^+, 30), 337 (100), 306 (50). *Compound* **25**: mp 113–115 °C; R_f (25% EtOAc/petroleum ether) 0.29; IR (KBr, cm^{-1}): 1734, 1712; ^1H NMR (500 MHz, $CDCl_3$): δ 8.42 (d, 1H, J=5.0 Hz), 7.68 (d, 2H, J=5.0 Hz), 7.50–7.40 (m, 4H), 7.13 (dd, 1H, J=7.5, 5.0 Hz), 4.17 (d, 1H, J=5.0 Hz), 3.79 (s, 3H), 3.72 (d, 1H, J=17.0 Hz), 3.52 (s, 3H), 3.33 (d, 1H, J=5.0 Hz), 3.26 (d, 1H, J=17.0 Hz), 2.23 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 203.6, 171.6, 170.6, 165.5, 148.0, 138.5, 135.1, 129.9, 129.1, 128.6 (2C), 127.5 (2C), 121.9, 89.5, 86.4, 54.2, 53.7, 52.5, 52.2, 42.5, 31.1; MS: *m/e* (relative intensity): 396 (MH^+, 57), 378 (MH^+-H_2O, 2), 346 (15), 252 (100), 210 (29). Anal. Calcd for $C_{22}H_{21}NO_6$: C, 66.83; H, 5.35; N, 3.54. Found: C, 67.11; H, 5.04; N, 3.75.

4.5.5. Coupling of carbene complex 5 with *p*-tolyl-(2-trimethylsilylethynylquinoline-3-yl)methanone (15) and *N*-methylmaleimide (Table 2, entry C). General procedure 4 was followed using carbene complex **5** (200 mg, 0.80 mmol), alkynyl carbonyl derivatives **15** (250 mg, 0.73 mmol) and *N*-methylmaleimide (81 mg, 0.73 mmol). The crude product was purified using column chromatography (silica gel, ethyl acetate/petroleum ether 3:7) to yield the benzoquinoline derivative **29C** (143 mg, 48%) as a yellow solid. Mp>250 °C; R_f (30% EtOAc/petroleum ether) 0.71; IR (KBr, cm^{-1}): 1758, 1699, 1646; ^1H NMR (500 MHz, $CDCl_3$): δ 8.73 (s, 1H), 8.32 (d, 1H, J=8.0 Hz), 7.90 (d, 1H, J=8.0 Hz), 7.87 (t, 1H, J=7.3 Hz), 7.59 (t, 1H, J=7.3 Hz), 7.42 (d, 2H, J=7.5 Hz), 7.36 (d, 2H, J=7.5 Hz), 5.21 (s, 2H), 3.17 (s, 3H), 2.58 (s, 3H) 2.54 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 206.1, 168.6, 167.2, 149.6, 149.2, 140.7, 139.2, 138.5, 135.7, 132.3, 131.1, 130.4 (2C), 130.3, 129.6 (2C), 129.0, 128.7, 128.4, 127.8, 127.5, 122.7, 41.4, 31.7, 24.6, 22.0; MS: *m/e* (relative intensity): 409 (MH^+, 100), 309 (10), 288 (5). Anal. Calcd for $C_{26}H_{20}N_2O_3$: C, 76.45; H, 4.94; N, 6.86. Found: C, 76.24; H, 5.13; N, 6.68.

4.6. Dimethyl 8-(2-oxopropyl)-5-phenylquinoline-6,7-dicarboxylate (26)

To a solution of the oxa-bridged compound **25** (R=Ph) (40 mg, 0.1 mmol) in ether (10 mL) was added aqueous HCl (1:1) (0.1 mL) and the mixture was stirred for 6 h at room temperature. The organic layer was separated. The aqueous layer was neutralized with saturated $NaHCO_3$ solution (1.0 mL) and extracted with ethyl acetate (3×5 mL). The combined organic layer (diethyl ether layer and ethyl acetate layer) was washed with water (1 mL) and brine (1 mL), and dried over anhydrous Na_2SO_4. Evaporation of solvent and purification by chromatography (silica gel, ethyl acetate/petroleum ether 2:8) to yield the quinoline derivative **26** (17 mg) as a yellow solid. In this reaction, starting material **25** (10 mg) was recovered. The yield of **26** with respect to recovered starting material is 60%. Mp 107–109 °C; R_f (20% EtOAc/petroleum ether) 0.48; IR (KBr, cm^{-1}): 1734, 1716; ^1H NMR (500 MHz, $CDCl_3$): δ 8.96 (s, 1H), 7.93 (d, 1H, J=8.0 Hz), 7.52–7.42 (m, 3H), 7.40 (dd, 1H, J=8.0, 3.5 Hz), 7.35–7.28 (m, 2H), 4.71 (s, 2H), 3.89 (s, 3H), 3.51 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 205.3, 168.4, 167.9, 151.0, 146.6, 138.8, 136.3, 135.6, 134.7, 131.2, 130.1, 129.9 (2C), 128.2 (4C), 122.7, 52.7, 52.1, 43.1, 30.0; MS: *m/e* (relative intensity): 378 (MH^+, 57), 346 (100), 314 (12), 286 (7), 242 (5). Anal. Calcd for $C_{22}H_{19}NO_5$: C, 70.02; H, 5.07; N, 3.71. Found: C, 69.98; H, 5.19; N, 3.87.

4.7. General procedure 5—the aromatization of the oxa-bridged compounds 22 and 28 using DBU

To a stirred solution of oxa-bridged compounds (1 mmol) in toluene (5 mL) was added dropwise DBU (10 mmol) at room temperature. The mixture was heated at reflux for 1.5 h giving a reddish brown solution, cooled to room temperature, washed with 10% aqueous HCl, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The crude products were purified by column chromatography using ethyl acetate/petroleum ether as eluent.

4.7.1. 9-(2-Oxopropyl)-5,7-diphenylpyrrolo[3,4-*g*]quinoline-6,8-dione (23B). General procedure 5 was followed

using oxa-bridged compound **22B** (40 mg, 0.09 mmol) and DBU (0.14 mL, 0.94 mmol). The crude product was purified by using column chromatography (silica gel, ethyl acetate/petroleum ether 1:4) to yield **23B** (19 mg, 50%).

4.7.2. 9-(2-Oxopropyl)-7-phenyl-5-*p*-tolylpyrrolo[3,4-*g*]-quinoline-6,8-dione (23D). General procedure 5 was followed using oxa-bridged compound **22D** (122 mg, 0.28 mmol) and DBU (0.42 mL, 2.78 mmol). The crude product was purified by using column chromatography (silica gel, ethyl acetate/petroleum ether 1:4) to yield **23D** (56 mg, 48%).

4.7.3. 4-(2-Oxopropyl)-2-phenylpyrrolo[3,4-*b*]acridine-1,3-dione (29A). General procedure 5 was followed using oxa-bridged compound **28A** (30 mg, 0.07 mmol) and DBU (0.11 mL, 0.75 mmol). The crude product was purified by using column chromatography (silica gel, ethyl acetate/petroleum ether 1:4) to yield **29A** (11 mg, 40%).

4.8. 5-Hydroxy-5-phenyl-10-trimethylsilyl-6,6a,7,8-tetrahydro-5*H*-benzo[*h*]quinoline-9-one (33)

To a solution of alkynyl ketone **12A** (200 mg, 0.71 mmol) in THF (3 mL) at reflux was added a solution of γ,δ-unsaturated carbene complex **30**[2j] (250 mg, 0.86 mmol) in THF (10 mL) over a period of 1 h. After the addition was complete, the mixture was heated at reflux for 18 h. The reaction mixture was cooled to room temperature. The THF was removed under reduced pressure, ethyl acetate (10 mL) was added and the residue was filtered through Celite (1.0 g). The solvent was removed on a rotary evaporator, and the crude products were 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 was stirred for 4 h at room temperature. The organic layer was separated. The aqueous layer was neutralized with saturated $NaHCO_3$ solution (3 mL) and extracted with ethyl acetate (3×10 mL). The combined organic layer (diethyl ether layer and ethyl acetate layer) was washed with water (3 mL) and brine (3 mL), and dried over anhydrous Na_2SO_4. Evaporation of solvent and purified by column chromatography (silica gel, ethyl acetate/petroleum ether 3:7) afforded a white solid alcohol **33** (168 mg, 65%). Mp 160 °C; R_f (30% EtOAc/petroleum ether) 0.57; IR (KBr, cm^{-1}): 3444, 1639; ^1H NMR (400 MHz, $CDCl_3$): δ 8.60 (dd, 1H, J=4.4, 1.6 Hz), 7.79 (dd, 1H, J=8.0, 1.6 Hz), 7. 34 (dd, 1H, J=8.0, 4.4 Hz), 7.32–7.26 (m, 3H), 7.13–7.06 (m, 2 H), 2.50 (s, 1H exchangeable with D_2O), 2.50–2.36 (m, 3H), 2.25 (ddd, 1H, J=18.0, 14.4, 5.2 Hz), 2.14 (t, 1H, J=12.4 Hz), 1.87 (m, 1H), 1.75 (m, 1H), 0.18 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 203.6 (s), 162.7 (s), 151.03 (s), 147.7 (d),146.0 (s) 142.8 (s), 139.9 (s) 136.0 (d), 128.3 (d, 2C), 127.8 (d), 126.7 (d, 2C), 124.9 (d), 75.1 (s), 48.3 (t), 37.5 (t), 35.8 (d), 28.9 (t), 2.8 (q, 3C); MS: *m/e* (relative intensity): 364 (100, MH^+), 348 (MH^+-H_2O, 10), 314, 153. Anal. Calcd for $C_{22}H_{25}NO_2Si$: C, 72.69; H, 6.93; N, 3.85. Found: C, 72.58; H, 7.05; N, 3.71.

4.9. 1-(3-Benzoyl-pyridine-2-yl)-3-methoxy-but-2-ene-1-one (34)

To a refluxing solution of alkynyl carbonyl derivative **12A** (120 mg, 0.43 mmol) in THF (5 mL) was added a solution of carbene complex **5** (118 mg, 0.47 mmol) in THF (5 mL) over a period of 1 h. After the addition was complete, the mixture was heated at reflux for a period of 4 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, the crude product was dissolved in chloroform (20 mL) and stirred with silica gel for 6 h. The solvent was removed and the residue purified by chromatography (silica gel, ethyl acetate/petroleum ether 2:8), which gave a white needles **34** (38 mg, 31%). Mp 152 °C; R_f (20% EtOAc/petroleum ether) 0.62; IR (KBr, cm^{-1}): 1670, 1580; ^1H NMR (500 MHz, $CDCl_3$): δ 8.75 (dd, 1H, J=3.6, 1.0 Hz), 7.76–7.70 (m, 3H), 7.60–7.50 (m, 2H), 7.42 (t, 2H, J=6.0 Hz), 6.88 (s, 1H), 3.82 (s, 3H), 2.23 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 195.8, 188.1, 176.8, 154.5, 149.0, 137.0, 136.5, 135.9, 132.9, 129.1 (2C), 128.4 (2C), 125.2, 95.1, 55.9, 20.3; MS: *m/e* (relative intensity): 282 (MH^+, 100), 210 (75). Anal. Calcd for $C_{17}H_{15}NO_3$: C, 72.58; H, 5.37; N, 4.98. Found: C, 72.61; H, 5.32; N, 4.91.

Acknowledgements

Financial support from CSIR [No. 01 (1874)/03-EMR-II] and UGC [No. F. 12-24/2004(SR)], Government of India is gratefully acknowledged. We thank Soumita Mukherjee for experimental assistance. We thank Professor J. W. Herndon, Department of Chemistry and Biochemistry, New Mexico State University, Las Cruces, New Mexico, USA for help.

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