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# Silver versus Gold Catalysis in Tandem Reactions of Carbonyl Functions onto Alkynes: A Versatile Access to Furoquinoline and Pyranoquinoline Cores

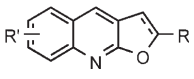
**Thomas Godet,[a] Carine Vaxelaire,[a] Carine Michel,[b] Anne Milet,[b] and Philippe Belmont*[a]**

**Abstract:** An efficient and versatile tandem process of acetalization and cycloisomerization reactions has been developed for the reactions of 1-alkynyl-2-carbonylquinoline substrates. The reaction occurs thanks to $Au^I$ and $Ag^I$ catalysis. Silver(I) catalysis has been extensively studied (11 different silver species) on a broad range of quinoline derivatives (variation of alkyne substituent, of carbonyl function and of nucleophiles), leading to a variety of furoquinoline and pyranoquinoline moieties. An insight is given for the presumed mechanism along with DFT-B3LYP/6–31G** calculations to address the 6-*endo* and 5-*exo* regioselectivities observed.

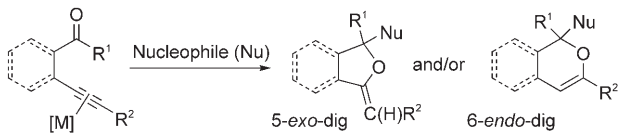
**Keywords:** acetalization · cycloisomerization · gold · quinolines · silver · tandem reactions

## Introduction

Furoquinoline (furo[2,3-*b*]quinoline, shown here) and pyranoquinoline derivatives are alkaloids isolated mainly from rutaceous plants.[1] Many efforts are still being made in order to isolate new family members due to their broad biological properties, which include antiplatelet aggregation, antifungal, insecticide, antibacterial, antimicrobial, analgesic, antipyretic and also cytotoxic properties.[1] We recently developed a base-catalyzed reaction that allowed the formation of 1,3-dihydro-furo[3,4-*b*]quinoline derivatives through a 5-*exo*-dig cyclization process.[2]




Due to limitations of this methodology we searched for an original method with an extended scope. Electrophilic activation (with organic or metallic species) of related alkynyl-derived structures (Scheme 1) has been extensively studied with various activating species such as $IPy_2BF_4$,[3] $I_2$,[4] ICl,[4] NBS,[4] PhSeBr,[4] $p$-$NO_2C_6H_4SCl$,[4] $Pd^{II}$,[5] $Cu^{II}$ or $Cu^I$,[6a]




Scheme 1. Carbonyl groups addition on alkynes.

$Pd^{II}/Cu^{II}$,[6b] $Au^I$ or $Au^{III}$,[7] and various other metallic salts (W, Pt, Ru).[5c] Upon activation of the alkyne group, oxygenated functions, among others, have been studied for their ability to target activated alkynes.[8] Carbonyl groups are of particular interest, since tandem reactions with nucleophiles can occur at this function, broadening the structural panel of the products formed (Scheme 1).[3–7] Although recent developments in gold chemistry include activation of alkynes,[7–9] to the best of our knowledge this tandem reaction (Scheme 1) has received little interest under the aspect of gold catalysis.[10] A publication from Li[11a] reported a cascade alkynylation/cyclization catalyzed with a phosphane–$Au^I$ complex, and related work on a α,β-unsaturated ketone[11b] and on carboxylated species have been reported.[11c]

Therefore, we have studied the gold-catalyzed tandem acetalization/cycloisomerization reactions of quinoline substrates. However, the main interest of this paper is to inves-

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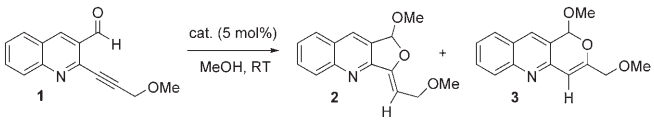
tigate and empower the novel use of silver catalysts in such reactions in order to reach furoquinoline and pyranoquinoline cores.

## Results and Discussion

We first investigated $Au^{I}$ and $Au^{III}$ tandem acetalization/cycloisomerization catalysis on quinoline derivative **1** (Table 1),[12] easily amenable in one step from commercially available 2-chloro-3-quinoline carboxaldehyde.[12b]

Table 1. [Au]-catalyzed tandem acetalization/cycloisomerization.[a]




| | Catalyst (5 mol %) | Product | Conv.[%][c] |
|---|---|---|---|
| 1 | $AuCl_3$ | **1**[d] | – |
| 2 | $[AuCl(PPh_3)]$ | **3** | 25 |
| 3 | $[AuCl(PPh_3)]/AgSbF_6$[b] | **3** | >95 |
| 4 | $AgSbF_6$ | **3** | >95 |

[a] 0.05 M reaction mixture in MeOH. [b] $[AuCl(PPh_3)]$ (5 mol %) and $AgSbF_6$ (5 mol %) mixed in situ prior to addition of **1**. [c] Conversion calculated by $^1$H NMR analysis. [d] Contaminated with undetermined compounds.

It appeared that chloride salts $AuCl_3$ (Table 1, entry 1), with methanol as nucleophile and solvent, did not catalyzed the formation of furoquinolines **2** or pyranoquinolines **3** (Table 1) and only poor conversion (25 %) was observed with $[AuCl(PPh_3)]$ (Table 1, entry 2). The lack of conversion was circumvented with the use of a more reactive gold complex such as $[Au(PPh_3)]SbF_6$ ($[AuCl(PPh_3)]/AgSbF_6$),[7j,q,v] providing pyranoquinoline **3** with a high conversion rate (Table 1, entry 3).

Interestingly, a control experiment with $AgSbF_6$ gave results comparable to the activated gold catalyst (Table 1, entry 4 vs. entry 3). It should be noted that in most of the literature reports on gold studies, control experiments are performed with the requisite silver salts used for preparation of the activated gold catalyst. Usually, the comparative results are poor[7n] or nonexistent[7p,q] with the silver species, but in some cases when noticeable yields are observed, the reaction may be much slower,[7j,u] or even faster[7e] than in the gold-catalyzed reaction. Also, control experiments may pinpoint a different reaction product.[7o]

Silver catalysis has received less attention and in recent work mostly C–C and C–N bond formation have been reported,[13] and no mention has been made for such direct tandem acetalization/cycloisomerization reactions with carbonyl species. The sole example is one side product reported by Yamamoto.[14]

Therefore we studied this new reactivity by using a range of silver catalysts with quinoline derivative **1** as a model substrate (Table 2). The results can be divided in three categories. First of all, $AgSbF_6$, $AgPF_6$, AgOTf, and $AgNO_3$

Table 2. Diversity in silver catalysis.[a]

| | [Ag] complex | Reaction time [h] | 5-*exo*-dig product **2**[b] | 6-*endo*-dig product **3**[b] | p$K_a$[c] |
|---|---|---|---|---|---|
| 1 | $AgSbF_6$ | 2 | | 100 | <0 |
| 2 | $AgPF_6$ | 2 | | 100 | <0 |
| 3 | AgOTf | 4 | | 100 | <0 |
| 4 | $AgNO_3$ | 0.75 | | 100 | <0 |
| 5 | $Ag_2SO_4$ | 3 | 5 | 95 | 2 |
| 6 | AgF | 1 | 5 | 95 | 3.2 |
| 7 | AgOCN | 2 | 40 | 60 | 3.7 |
| 8 | AgOAc | 12 | 48 | 52 | 4.8 |
| 9 | $Ag_2CO_3$ | 2 | 100 | | 10.3 |
| 10 | $Ag_2O$ | 0.16 | 100 | | 15.7 |
| 11 | AgO | 0.5 | 100 | | 15.7 |

[a] 0.05 M reaction mixture in MeOH and [Ag] 5 mol %. [b] Ratio between **2** and **3**, estimated by $^1$H NMR analysis. [c] p$K_a$ values of silver counterion.[18]

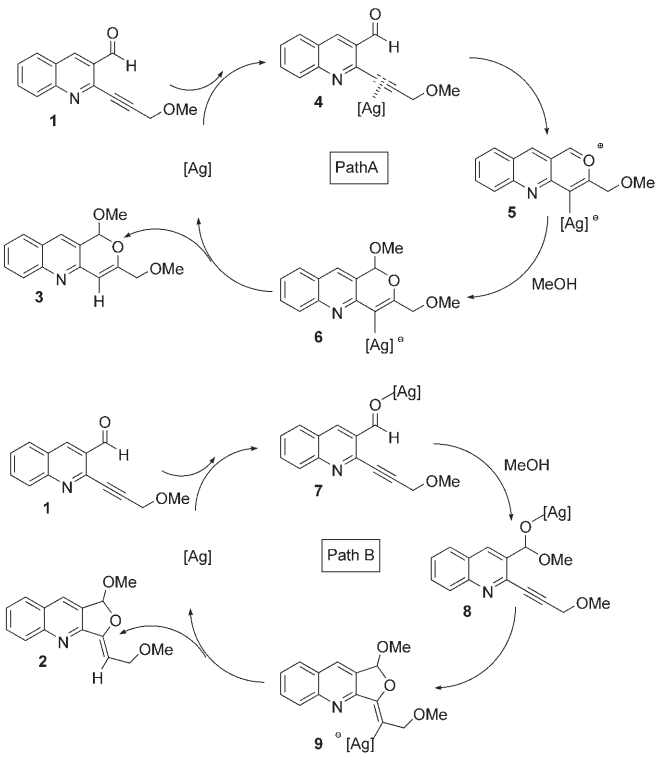
(Table 2, entry 1–4) allow an efficient transformation of quinoline derivative **1** to the 6-*endo*-dig product **3**. With $Ag_2SO_4$ and AgF (Table 2, entry 5 and 6) a 95:5 ratio between cyclized derivative **3**:**2** was observed. A second group, AgOCN and AgOAc (Table 2, entry 7 and 8), led to poor or no selectivity between products **2** and **3** (ratio 40:60 and 48:52, respectively). Finally, for the last group of silver salts, $Ag_2CO_3$, $Ag_2O$, and AgO (Table 2, entry 9–11), the selectivity was reversed from that of the first group, since the only compound detected was the 5-*exo*-dig product **2**.

The first group of silver salts ($AgSbF_6$, $AgPF_6$, AgOTf, and $AgNO_3$) is known for forming π complexes with alkynes,[13,15] thus acting as a transition-metal catalyst[16] and we can assume that the same reactivity occurs with AgF and $Ag_2SO_4$, since they give the same regioselectivity upon reaction with quinoline **1** (Scheme 2, path A). The last group of silver catalysts group ($Ag_2CO_3$, $Ag_2O$, and AgO) are mainly characterized through their oxidizing properties of oxygenated functions.[17] Therefore, they should interact mainly with compound **1** by activation of the aldehyde function (Scheme 2, path B); this may explain the different regioselectivity observed (5-*exo* versus 6-*endo*). The second group of silver salts, AgOCN and AgOAc (Table 2, entry 7 and 8) may exhibit hybrid activation from the two other groups which may account for the poor regioselectivity.

Also, it is worth noting that the p$K_a$ value[18] of the silver counterion fits fairly well with the regioselectivity observed. Overall, the nature of the silver salts (lewis acidity, oxidizing agent, transition-metal properties, type of counter anion) seems to be determinant for the regioselectivity, so we presume that the reaction mechanism may be different, and we propose two reaction pathways (Scheme 2, path A and B) depending on the silver coordination site.,[5d,6a,7y,11b,13d]

The path A (Scheme 2) accounts for the first silver salts group (Table 2, entry 1–6), for which upon coordination of the triple-bond of **1** (intermediate **4**) the enhancement of electrophilicity of the alkyne gives rise to subsequent nucleophilic attack of the carbonyl oxygen atom on the electron-deficient alkyne to yield the intermediate silver ate complex **5**.[7w,z] The solvent/nucleophile MeOH can then attack inter-




Scheme 2. Proposed cyclization mechanisms: Paths A and B.

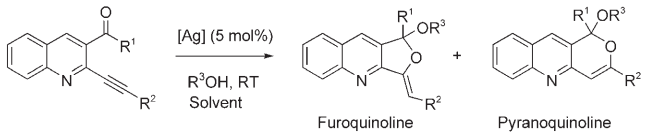
mediate **5**, to give intermediate **6**, and lead to catalyst recycling and liberation of the 6-*endo*-dig product **3**.

Path B (Scheme 2) can account for reactivity of the last group of silver catalysts (Table 2, entry 9–11), the oxidative properties of which direct coordination to the oxygen atom of the aldehyde function. Thus, intermediate **7** (Scheme 2, path B) can then lead in turn to the acetal derivative **8**, which cyclizes to give complex **9** and, after catalyst recycling, yields the 5-*exo*-dig product **2**.

AgOTf, $Ag_2O$, and AgOAc catalysts were used to expand the structural diversity of furo- and pyranoquinolines (Table 3).[12]

Quinoline derivative **1** was treated under AgOTf catalysis with various alcohol substrates such as methanol, diol (ethylene glycol); poor nucleophiles (trifluoromethanol, hexafluoroisopropanol); and benzylic or hindered secondary and tertiary alcohols (entries 1–8, Table 3). In all cases, 6-*endo*-dig products (**3**, **10**--**12**, **14**--**16**, **18**) were obtained efficiently (88%–quantitative yields). On the other hand, $Ag_2O$ catalysis with methanol, benzylic, and tertiary alcohols (entries 1, 5, 8) gave exclusively 5-*exo*-dig products (**2**, **13**, **17**) in high yields (94%–quantitative). Modification of the quinoline ring (entry 9 and 10) or the presence of functionalized or hindered alkyl-alkynes (entries 11–14) made no difference in the reactivity. Thus, 6-*endo*-dig products (**20**, **22**, **25**, **28**, **30**, **32**) were obtained with AgOTf catalysis, whereas $Ag_2O$ catalysis led to 5-*exo*-dig products (**24**, **27**), always in high yield (85%–quantitative). Interestingly, the reaction conducted with simple or substituted phenylalkynes (entries 15–18) gave reversed selectivity compared with previous data

Table 3. Furoquinolines and pyranoquinolines synthesis.[a]



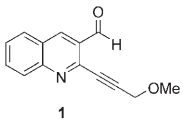
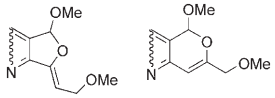
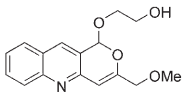
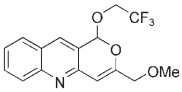
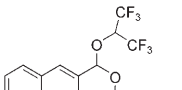
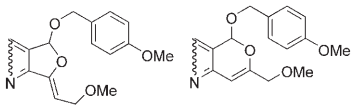
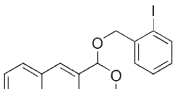
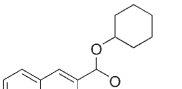
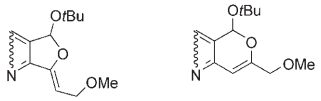
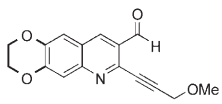
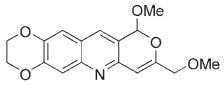
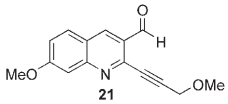
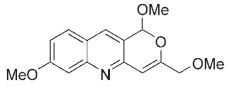
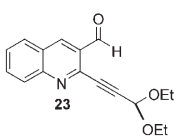
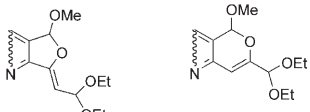
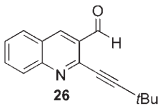
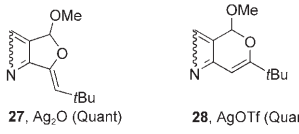
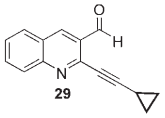
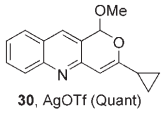
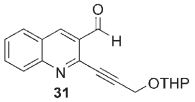
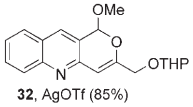
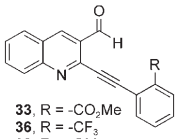
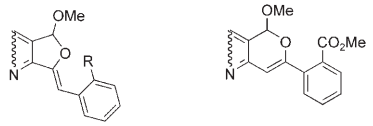
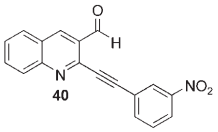
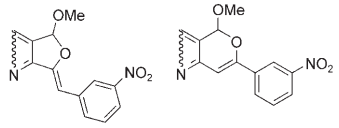
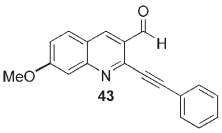
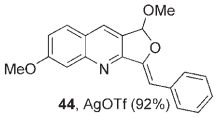
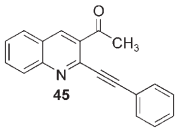
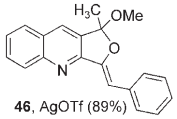
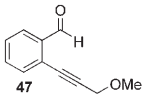
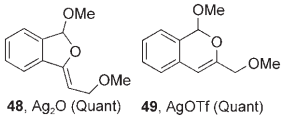
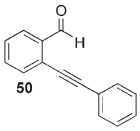
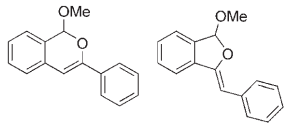

| | Starting material | Product[b], [Ag] (yield %[c]) |
|---|---|---|
| 1 |  **1** |  **2**, $Ag_2O$ (Quant) **3**, AgOTf (Quant) ratio **2**:**3**, 1:1, AgOAc |
| 2 | **1** |  **10**, AgOTf (Quant) |
| 3 | **1** |  **11**, AgOTf (Quant) |
| 4 | **1** |  **12**, AgOTf (Quant) |
| 5 | **1** |  **13**, $Ag_2O$ (94%) **14**, AgOTf (93%) ratio **13**:**14**, 3.2:1, AgOAc |
| 6 | **1** |  **15**, AgOTf (92%) |
| 7 | **1** |  **16**, AgOTf (88%) |
| 8 | **1** |  **17**, $Ag_2O$ (Quant) **18**, AgOTf (Quant) ratio **17**:**18**, 1:3.1, AgOAc |
| 9 |  **19** |  **20**, AgOTf (Quant) |
| 10 |  **21** |  **22**, AgOTf (Quant) |
| 11 |  **23** |  **24**, $Ag_2O$ (93%) **25**, AgOTf (95%) ratio **24**:**25**, 2:1, AgOAc |

Table 3. (Continued)

| | Starting material | Product[b], [Ag] (yield %[c]) |
|---|---|---|
| 12 |  **26** |  **27**, $Ag_2O$ (Quant) **28**, AgOTf (Quant) ratio **27**:**28**, 1:1.3, AgOAc |
| 13 |  **29** |  **30**, AgOTf (Quant) |
| 14 |  **31** |  **32**, AgOTf (85%) |
| 15 |  **33**, R = -$CO_2$Me<br>**36**, R = -$CF_3$<br>**38**, R = -OMe |  **34**, R = -$CO_2$Me, AgOTf (95%) **35**, $Ag_2O$ (96%) ratio **34**:**35**, 1:7, AgOAc<br>**37**, R = -$CF_3$, AgOTf (89%)<br>**39**, R = -OMe, AgOTf (94%) |
| 16 |  **40** |  **41**, AgOTf (90%) **42**, $Ag_2O$ (93%) ratio **41**:**42**, 1:6, AgOAc |
| 17 |  **43** |  **44**, AgOTf (92%) |
| 18 |  **45** |  **46**, AgOTf (89%) |
| 19 |  **47** |  **48**, $Ag_2O$ (Quant) **49**, AgOTf (Quant) ratio **48**:**49**, 1.5:1, AgOAc |
| 20 |  **50** |  **51**, $Ag_2O$ (96%) **52**, AgOTf (96%) ratio **51**:**52**, 5.1:1, AgOAc |

[a] [Ag] (5 mol %) in a 0.05 M reaction mixture. [b] $R^3$-OH (1.2 equiv) in $Cl(CH_2)_2Cl$ or as solvent.[12b] [c] Isolated yield. Quant = quantitative.

(entries 1–14). Indeed 5-*exo*-dig products (**34**, **37**, **39**, **41**, **44**, **46**) were produced under AgOTf catalysis, whereas catalysis with $Ag_2O$ gave only 6-*endo*-dig products (**35**, **42**). Again, the tandem reactions occurred in high yields (89–96%). Also, the presence of an electron-withdrawing or electron-donating group on the phenyl substituent made no difference on the selectivity, which seems to be driven by the nature of the silver salt. Moreover, experiments performed with model compounds **47** and **50** (entries 19–20) attested that the presence of the nitrogen on the quinoline ring had no impact on the reaction course. Finally, the reactions tested with AgOAc gave as expected mixture of compounds, in various ratios.[19]

The 5-*exo* versus 6-*endo* cycloaddition is a long-standing observation[20] and we tried to rationalize our results through DFT-B3LYP/6–31G** calculations[21] using Gaussian 03 software.[22] If we consider the reactive complex formed between $Ag^I$ (AgF) and a phenyl-substituted triple bond (Figure 1), a slight elongation of the triple bond and deformation from the linearity is observed. We note that the coordination of the silver atom is *trans* to the attacking oxygen atom, in accordance with the final stereochemistry of the double bond formed in the 5-*exo* product. The reactive LUMO clearly shows a difference of orbital coefficients between the two acetylenic carbon atoms in agreement with the reactivity obtained. However, when the $CH_2OMe$ substituent is used, no such difference is observed and only the natural charge population analysis can explain the reaction with a difference of 0.1 e between the two acetylenic carbon atoms, the more electrophilic carbon atom leading to the formation of the *6-endo* product.

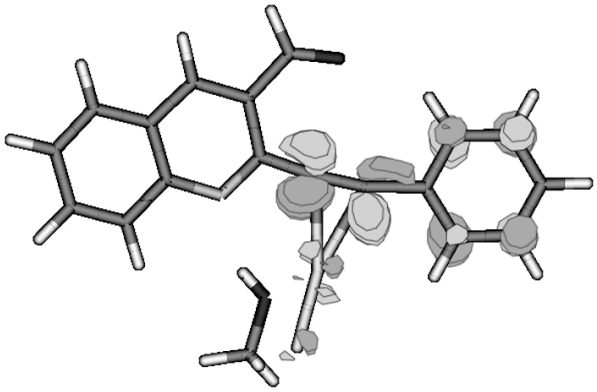


Figure 1. Reactive LUMO of modeled compounds with AgF complex.

## Conclusion

We have described a versatile and efficient method with silver catalysts producing a broad range of functionalized furoquinolines and pyranoquinolines, under smooth reaction conditions, allowing acetalization/cycloisomerization reactions even with poor and/or hindered nucleophiles. Moreover the methodology is handy, since we can control the regiochemistry depending on the type of silver catalyst used. Besides, the nature of the alkynyl substituent is an important factor in the regiochemistry observed. Also, we disclosed here an original study to rationalize the regiochemistry showing that the coordination of the silver complex to the triple bond modifies its properties both from an orbital

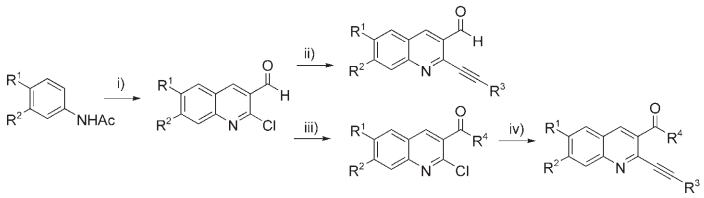
  

and charge point of view and can explain the difference in reactivity.

## Experimental Section

**General information**: Unless otherwise noted, all commercial materials were used without further purification. Methanol and 1,2-dichloroethane are ACS reagents grade, and were used as received unless otherwise noted. Silver salts were obtained from Acros and Strem chemicals companies. TLC analysis of reaction mixtures was performed on Merck silica gel 60 $F_{254}$ TLC plates. Flash chromatography was carried out on Merck 60 silica gel (32–63 mm). $^1$H and $^{13}$C NMR spectra were recorded with Bruker ALS-300 and DRX-300 spectrometers and referenced to $CDCl_3$ unless otherwise noted. Low- and high-resolution mass spectra ($m/z$) were measured on a Thermo-Finnigan Mat 95XL spectrometer by the Mass facility operated by the Université Claude Bernard Lyon 1 (UMR CNRS-UCBL 5246, Lyon), and also by the CNRS Service Central d'Analyse (USR CNRS 59, Lyon) on a LCT Waters, electrospray/TOF.

Starting materials were synthesized according to published procedures[23] and following Scheme 3.




Scheme 3. Starting materials were synthesized according to published procedures: i) Villsmeyer–Haack[23a]; ii) Sonogashira[23b–d]; iii) 1. Grignard[23c,d], 2. oxidation[23c,d]; iv) Sonogashira.[23b–d]

**General procedure for the Sonogashira reaction**: CuI (0.025 mmol, 4.5 mg), $Pd(PPh_3)_2Cl_2$ (0.05 mmol, 35 mg), $Et_3N$ (0.6 mL) and the alkyne (1.2 mmol) were added under argon to a stirred solution of quinoline (1 mmol) in anhydrous DMF (1 mL). The mixture was stirred at room temperature and monitored by TLC. After evaporation under vacuum, the crude mixture was purified by column chromatography on silica gel.

**Compound 1**: This compound was isolated as a brown-reddish solid (quantitative). $^1$H NMR (300 MHz, [D]$CHCl_3$, 25 °C): $\delta$ = 10.66 (s, 1H), 8.71 (s, 1H), 8.12 (d, $^3J$(H,H) = 8.7 Hz, 1H), 7.94 (dd, $^4J$(H,H) = 1.1 Hz, $^3J$(H,H) = 8.3 Hz, 1H), 7.85 (ddd, $^4J$(H,H) = 1.5 Hz, $^3J$(H,H) = 6.8 Hz, $^3J$(H,H) = 8.3 Hz, 1H), 7.62 (ddd, $^4J$(H,H) = 1.1 Hz, $^3J$(H,H) = 6.8 Hz, $^3J$(H,H) = 7.9 Hz, 1H), 4.47 (s, 2H), 3.51 ppm (s, 3H); $^{13}$C NMR (75 MHz, [D]$CHCl_3$, 25 °C): $\delta$ = 190.5, 149.9, 143.1, 137.1, 133.0, 129.6, 129.3, 128.7, 128.3, 126.5, 91.5, 82.5, 60.2, 58.2 ppm; TOF MS ES+: $m/z$ (%): 226 (100) $[M+H]^+$; HRMS (ESI+): $m/z$ calcd for $[C_{14}H_{12}NO_2]^+$: 226.0868; found: 226.0876.

**Compound 19**: This compound was isolated as a yellow solid (98%). $^1$H NMR (300 MHz, [D]$CHCl_3$, 25 °C): $\delta$ = 10.59 (s, 1H), 8.49 (s, 1H), 7.52 (s, 1H), 7.30 (s, 1H), 4.45 (s, 2H), 4.39 (m, 4H), 3.50 ppm (s, 3H); $^{13}$C NMR (75 MHz, [D]$CHCl_3$, 25 °C): $\delta$ = 191.0, 150.5, 147.3, 146.3, 142.1, 135.6, 127.9, 123.1, 114.5, 114.0, 91.1, 83.2, 65.0, 64.6, 60.7, 58.6 ppm; MS (TOF ES+): $m/z$ (%): 284 (100) $[M+H]^+$; HRMS (TOF ES+): $m/z$ calcd for $[C_{16}H_{14}NO_4]^+$: 284.0923; found: 284.0921.

**Compound 21**: This compound was isolated as an orange solid (quantitative). $^1$H NMR (300 MHz, [D]$CHCl_3$, 25 °C): $\delta$ = 10.64 (s, 1H), 8.64 (s, 1H), 7.83 (d, $^3J$(H,H) = 9.0 Hz, 1H), 7.45 (d, $^4J$(H,H) = 2.3 Hz, 1H), 7.27 (dd, $^4J$(H,H) = 2.6 Hz, $^3J$(H,H) = 9.0 Hz, 1H), 4.49 (s, 2H), 3.99 (s, 3H), 3.54 ppm (s, 3H); $^{13}$C NMR (75 MHz, [D]$CHCl_3$, 25 °C): $\delta$ = 190.4, 163.7, 152.2, 143.8, 136.4, 130.7, 127.2, 122.0, 121.9, 107.0, 91.3, 82.6, 60.3, 58.2, 55.8 ppm; MS (TOF ES+): $m/z$ (%): 256 (100) $[M+H]^+$; HRMS (TOF ES+): $m/z$ calcd for $[C_{15}H_{14}NO_3]^+$: 256.0974; found: 256.0982.

**Compound 23**: This compound was isolated as an brown solid (quantitative). $^1$H NMR (300 MHz, [D]$CHCl_3$, 25 °C): $\delta$ = 10.65 (s, 1H), 8.71 (s, 1H), 8.12 (d, $^3J$(H,H) = 8.7 Hz, 1H), 7.94 (d, $^3J$(H,H) = 8.3 Hz, 1H), 7.85 (ddd, $^4J$(H,H) = 1.5 Hz, $^3J$(H,H) = 6.8 Hz, $^3J$(H,H) = 8.3 Hz, 1H), 7.63 (ddd, $^4J$(H,H) = 1.1 Hz, $^3J$(H,H) = 6.8 Hz, $^3J$(H,H) = 7.9 Hz, 1H), 5.60 (s, 1H), 3.91–3.66 (m, 4H), 1.28 ppm (t, $^3J$(H,H) = 7.2 Hz, 6H); $^{13}$C NMR (75 MHz, [D]$CHCl_3$, 25 °C): $\delta$ = 190.3, 149.9, 142.6, 137.0, 133.0, 129.6, 129.3, 128.8, 128.5, 128.4, 126.9, 91.6, 80.9, 61.4, 15.0 ppm; MS ESI+: $m/z$ (%): 284 (100) $[M+H]^+$; HRMS (ESI+): $m/z$ calcd for $[C_{17}H_{18}NO_3]^+$: 284.1287; found: 284.1287.

**Compound 26**: This compound was isolated as a pale yellow solid (95%). $^1$H NMR (300 MHz, [D]$CHCl_3$, 25 °C): $\delta$ = 10.67 (s, 1H), 8.67 (s, 1H), 8.12 (dd, $^4J$(H,H) = 0.8 Hz, $^3J$(H,H) = 8.7 Hz, 1H), 7.91 (dd, $^4J$(H,H) = 1.5 Hz, $^3J$(H,H) = 8.3 Hz, 1H), 7.82 (ddd, $^4J$(H,H) = 1.5 Hz, $^3J$(H,H) = 6.8 Hz, $^3J$(H,H) = 8.3 Hz, 1H), 7.58 (ddd, $^4J$(H,H) = 1.1 Hz, $^3J$(H,H) = 6.8 Hz, $^3J$(H,H) = 8.3 Hz, 1H), 1.42 ppm (s, 9H); $^{13}$C NMR (75 MHz, [D]$CHCl_3$, 25 °C): $\delta$ = 191.3, 150.0, 144.5, 136.8, 132.8, 129.6, 129.1, 128.7, 127.9, 126.2, 105.9, 76.0, 30.5, 28.4 ppm; MS ESI+: $m/z$ (%): 238 (100) $[M+H]^+$; HRMS (ESI+): $m/z$ calcd $[C_{16}H_{16}NO]^+$: 238.1232; found: 238.1230.

**Compound 29**: This compound was isolated as a yellow solid (98%). $^1$H NMR (300 MHz, [D]$CHCl_3$, 25 °C): $\delta$ = 10.63 (s, 1H), 8.65 (s, 1H), 8.08 (d, $^3J$(H,H) = 8.3 Hz, 1H), 7.90 (d, $^3J$(H,H) = 7.9 Hz, 1H), 7.81 (ddd, $^4J$(H,H) = 1.5 Hz, $^3J$(H,H) = 7.2 Hz, $^3J$(H,H) = 8.7 Hz, 1H), 7.57 (ddd, $^4J$(H,H) = 1.1 Hz, $^3J$(H,H) = 7.2 Hz, $^3J$(H,H) = 8.3 Hz, 1H), 1.61 (m, 1H), 1.00 ppm (d, $^3J$(H,H) = 6.8 Hz, 4H); $^{13}$C NMR (75 MHz, [D]$CHCl_3$, 25 °C): $\delta$ = 191.2, 150.0, 144.4, 136.8, 132.8, 129.5, 129.1, 128.8, 127.8, 126.1, 101.4, 72.8, 30.1, 9.2, 0.3 ppm; MS ES+: $m/z$ (%): 222 (100) $[M+H]^+$; HRMS (TOF ES+): $m/z$ calcd for $[C_{15}H_{12}NO]^+$: 222.0919; found: 222.0927.

**Compound 31**: This compound was isolated as a brown solid (94%). M.p 77 °C; $^1$H NMR (300 MHz, [D]$CHCl_3$, 25 °C): $\delta$ = 10.6 (s, 1H), 8.69 (s, 1H), 8.10 (d, $^3J$(H,H) = 8.1 Hz, 1H), 7.92 (d, $^3J$(H,H) = 7.8 Hz, 1H), 7.83 (ddd, $^4J$(H,H) = 1.5 Hz, $^3J$(H,H) = 6.6 Hz, $^3J$(H,H) = 8.1 Hz, 1H), 7.60 (ddd, $^4J$(H,H) = 1.2 Hz, $^3J$(H,H) = 6.9 Hz, $^3J$(H,H) = 8.1 Hz, 1H), 4.92 (t, $^4J$(H,H) = 3.3 Hz, 1H), 4.70–4.55 ( m, 2H), 3.94–3.81(m, 1H), 3.62–3.50 (m, 1H), 1.92–1.44 ppm (m, 6H); further characterization was consistent with published data.[23d]

**Compound 33**: This compound was isolated as a yellowish solid (92%). $^1$H NMR (300 MHz, [D]$CHCl_3$, 25 °C): $\delta$ = 10.9 (s, 1H), 8.70 (s, 1H), 8.12 (d, $^3J$(H,H) = 8.3 Hz, 1H), 8.01 (d, $^3J$(H,H) = 7.5 Hz, 1H), 7.90 (d, $^3J$(H,H) = 8.3 Hz, 1H), 7.85–7.78 (m, 2H), 7.59–7.50 (m, 2H), 7.44 (t, $^3J$(H,H) = 7.5 Hz, 1H), 3.93 ppm (s, 3H); $^{13}$C NMR (75 MHz, [D]$CHCl_3$, 25 °C): $\delta$ = 192.2, 166.0, 150.2, 144.1, 136.6, 135.0, 132.9, 132.1, 132.0, 130.7, 129.7, 129.4, 129.4, 128.2, 126.5, 122.1, 93.7, 52.6 ppm; MS (TOF ES+): $m/z$ (%): 316 (100) $[M+H]^+$; HRMS (TOF ES+): $m/z$ calcd for $[C_{20}H_{14}NO_3]^+$: 316.0974; found: 316.0985.

**Compound 36**: This compound was isolated as a yellow solid (91%). $^1$H NMR (300 MHz, [D]$CHCl_3$, 25 °C): $\delta$ = 10.6 (s, 1H), 8.58 (s, 1H), 8.03 (d, $^3J$(H,H) = 8.7 Hz, 1H), 7.83–7.70 (m, 3H), 7.64 (d, $^3J$(H,H) = 7.2 Hz, 1H), 7.53–7.40 ppm (m, 3H); $^{13}$C NMR (75 MHz, [D]$CHCl_3$, 25 °C): $\delta$ = 191.1, 150.5, 143.7, 137.2, 135.4, 133.4, 132.1 (q, $^1J$(C,F) = 4.9 Hz), 132.0, 130.1, 130.0, 129.8, 129.7, 128.9, 127.0, 126.5 (q, $^2J$(C,F) = 1.1 Hz), 90.9, 90.7 ppm; MS (TOF ES+): $m/z$ (%): 326 (100) $[M+H]^+$; HRMS (TOF ES+): $m/z$ calcd for $[C_{19}H_{11}NOF_3]^+$: 326.0793; found: 326.0801.

**Compound 38**: This compound was isolated as a yellow solid (89%). $^1$H NMR (300 MHz, [D]$CHCl_3$, 25 °C): $\delta$ = 10.9 (s, 1H), 8.65 (s, 1H), 8.11 (d, $^3J$(H,H) = 8.7 Hz, 1H), 7.87 (d, $^3J$(H,H) = 8.3 Hz, 1H), 7.78 (ddd, $^4J$(H,H) = 1.5 Hz, $^3J$(H,H) = 7.2 Hz, $^3J$(H,H) = 8.7 Hz, 1H), 7.62 (dd, $^4J$(H,H) = 1.9 Hz, $^3J$(H,H) = 7.9 Hz, 1H), 7.54 (ddd, $^4J$(H,H) = 0.8 Hz, $^3J$(H,H) = 7.9 Hz, $^3J$(H,H) = 8.7 Hz, 1H), 7.35 (ddd, $^4J$(H,H) = 1.9 Hz, $^3J$(H,H) = 7.5 Hz, $^3J$(H,H) = 8.3 Hz, 1H), 6.92 (td, $^4J$(H,H) = 0.8 Hz, $^3J$(H,H) = 7.5 Hz, 1H), 6.86 (d, $^3J$(H,H) = 8.7 Hz, 1H), 3.91 ppm (s, 3H); $^{13}$C NMR (75 MHz, [D]$CHCl_3$, 25 °C): $\delta$ = 192.5, 161.6, 150.6, 144.9, 137.0, 134.2, 133.2, 131.9, 130.1, 129.7, 129.4, 128.4, 126.8, 121.0, 111.1, 93.2,

90.2, 56.2 ppm; MS (TOF ES+): *m/z* (%): 288 (100) $[M+H]^+$; HRMS (TOF ES+): *m/z* calcd for $[C_{19}H_{14}NO_2]^+$: 288.1025; found: 288.1044.

**Compound 40**: This compound was isolated as a yellow solid (95%). $^1$H NMR (300 MHz, [D]$CHCl_3$, 25°C): $\delta$=10.7 (s, 1H), 8.77 (s, 1H), 8.54 (s, 1H), 8.28 (d, $^3J$(H,H)=4.9 Hz, 1H), 8.18 (d, $^3J$(H,H)=6.0 Hz, 1H), 7.99–7.90 (m, 3H), 7.67–7.61 ppm (m, 2H); $^{13}$C NMR (75 MHz, [D]$CHCl_3$, 25°C): $\delta$=190.0, 150.1, 148.2, 142.6, 137.8, 137.7, 133.3, 129.7, 129.6, 129.4, 128.9, 128.7, 127.0, 126.6, 124.4, 123.2, 91.9, 87.6 ppm; MS (TOF ES+): *m/z* (%): 303 (100) $[M+H]^+$; HRMS (TOF ES+): *m/z* calcd for $[C_{18}H_{11}N_2O_3]^+$: 303.0770; found: 303.0785.

**Compound 43**: This compound was isolated as an orange solid (96%). $^1$H NMR (300 MHz, [D]$CHCl_3$, 25°C): $\delta$=10.71 (s, 1H), 8.60 (s, 1H), 7.78 (d, $^3J$(H,H)=9.0 Hz, 1H), 7.67 (m, 2H), 7.41 (m, 4H), 7.22 (dd, $^4J$(H,H)=2.6 Hz, $^3J$(H,H)=9.0 Hz, 1H), 3.95 ppm (s, 3H); $^{13}$C NMR (75 MHz, [D]$CHCl_3$, 25°C): $\delta$=190.5, 149.9, 163.6, 152.3, 144.4, 136.3, 132.2, 130.7, 130.6, 129.7, 128.7, 128.5, 127.2, 121.8, 121.7, 121.4, 107.0, 95.2, 85.5, 55.8 ppm; IR (neat): $\tilde{\nu}$=3362, 2927, 1614, 1505, 1451, 1264, 1160, 1023, 737 cm$^{-1}$; MS ES+: *m/z* (%): 288 (100) $[M+H]^+$; HRMS (TOF ES+): *m/z* calcd for $[C_{19}H_{14}NO_2]^+$: 288.1025; found: 288.1043.

**Compound 45**: This compound was isolated as a dark oil. $^1$H NMR (300 MHz, [D]$CHCl_3$, 25°C): $\delta$=8.39 (s, 1H), 8.03 (d, $^3J$(H,H)=8.3 Hz, 1H), 7.73 (d, $^3J$(H,H)=8.3 Hz, 1H), 7.67 (ddd, $^4J$(H,H)=1.5 Hz, $^3J$(H,H)=7.2 Hz, $^3J$(H,H)=8.7 Hz, 1H), 7.60 (m, 2H), 7.44 (ddd, $^4J$(H,H)=1.1 Hz, $^3J$(H,H)=6.8 Hz, $^3J$(H,H)=7.9 Hz, 1H), 7.28 (m, 3H), 2.78 ppm (s, 3H); $^{13}$C NMR (75 MHz, [D]$CHCl_3$, 25°C): $\delta$=192.5, 161.6, 150.6, 144.9, 137.0, 134.2, 133.2, 131.9, 130.1, 129.7, 129.4, 128.4, 126.8, 121.0, 111.1, 93.2, 90.2, 56.2 ppm; MS EI+: *m/z* (%): 271 (100) $[M]^+$, 256 (64) $[M-CH_3]^+$, 228 (40) $[M-CH_3-CO]^+$.

**Compound 47**: This compound was isolated as a yellow oil (86%). $^1$H NMR (300 MHz, [D]$CHCl_3$, 25°C): $\delta$=10.4 (s, 1H), 7.81 (d, $^3J$(H,H)=7.5 Hz, 1H), 7.48–7.46 (m, 2H), 7.36–7.35 (m, 1H), 4.30 (s, 2H), 3.39 ppm (s, 3H); $^{13}$C NMR (75 MHz, [D]$CHCl_3$, 25°C): $\delta$=191.5, 136.2, 133.9, 133.7, 129.0, 127.4, 126.2, 92.5, 82.2, 60.5, 58.0 ppm; MS ES+: *m/z* (%): 175 (100) $[M+H]^+$; HRMS (TOF ES+): *m/z* calcd for $[C_{11}H_{11}O_2]^+$: 175.0759; found: 175.0766.

**Compound 50**: This compound was isolated as an orange oil (89%). $^1$H NMR (300 MHz, [D]$CHCl_3$, 25°C): $\delta$=10.6 (s, 1H), 7.93 (dd, $^4J$(H,H)=1.1 Hz, $^3J$(H,H)=7.5 Hz, 1H), 7.61–7.52 (m, 4H), 7.42–7.33 ppm (m, 4H); $^{13}$C NMR (75 MHz, [D]$CHCl_3$, 25°C): $\delta$=191.7, 136.1, 134.0, 133.5, 129.3, 128.8, 128.8, 127.5, 122.6, 96.6, 85.2 ppm; MS ES+: *m/z* (%): 207 (100) $[M+H]^+$; HRMS (TOF ES+): *m/z* calcd for $[C_{15}H_{11}O]^+$: 207.0810; found: 207.0821.

**General procedures for the silver(I) catalyzed O-cyclization**

*Method A*: The silver catalyst (5 mol%) was added to a flask charged with quinoline (0.1 mmol) dissolved in the corresponding alcohol (0.05 M solution in MeOH, *t*BuOH, ethylene glycol, trifluoroethanol). The flask was rubber capped and stirred at room temperature (25°C) until the reaction was judged complete by TLC analysis. The crude reaction mixture was dissolved in dichloromethane and washed three times with a saturated aqueous solution of $NaHCO_3$. The organic phase was dried over $Na_2SO_4$ and filtered, and the solvents removed under vacuum. If needed, the residue was loaded on a silica gel column and elution with the appropriate mixture of cyclohexane/ethyl acetate yielded the pure cyclized products.

*Method B*: The corresponding alcohol (1.2 equivalents) and then the silver catalyst (5 mol%) were added to a flask charged with quinoline (0.1 mmol) dissolved in 1,2-dichloroethane (0.05 M solution). The flask was rubber capped and stirred at room temperature (25°C) until the reaction was judged complete by TLC analysis. The crude reaction mixture was dissolved in dichloromethane and washed three times with a saturated aqueous solution of $NaHCO_3$. The organic phase was dried over $Na_2SO_4$ and filtered, and the solvents removed under vacuum. The residue was loaded on a silica gel column and elution with the appropriate mixture of cyclohexane/ethyl acetate yielded the pure cyclized products.

**Compound 2**: This compound was prepared by method A. It was isolated as a light yellow solid (quantitative). $^1$H NMR (300 MHz, [D]$CHCl_3$, 25°C): $\delta$=8.21 (s, 1H), 8.16 (d, $^3J$(H,H)=8.7 Hz, 1H), 7.85 (dd, $^4J$(H,H)=1.1 Hz, $^3J$(H,H)=8.3 Hz, 1H), 7.75 (ddd, $^4J$(H,H)=1.5 Hz, $^3J$(H,H)=6.8 Hz, $^3J$(H,H)=8.3 Hz, 1H), 7.55 (ddd, $^4J$(H,H)=0.8 Hz, $^3J$(H,H)=7.2 Hz, $^3J$(H,H)=7.9 Hz, 1H), 6.47 (s, 1H), 6.01 (t, $^3J$(H,H)=7.2 Hz, 1H), 4.32 (m, 2H), 3.53 (s, 3H), 3.38 ppm (s, 3H); $^{13}$C NMR (75 MHz, [D]$CHCl_3$, 25°C): $\delta$=153.3, 152.9, 149.9, 131.5, 130.6, 129.6, 129.0, 128.5, 127.7, 126.9, 104.4, 97.4, 66.2, 57.8, 55.0 ppm; MS ESI+: *m/z* (%): 258 (100) $[M+H]^+$; HRMS (CI): *m/z* calcd for $[C_{15}H_{16}NO_3]^+$: 258.1130; found: 258.1130.

**Compound 3**: This compound was prepared by method A. It was isolated as a yellow solid (quantitative). $^1$H NMR (300 MHz, [D]$CHCl_3$, 25°C): $\delta$=8.10 (s, 1H), 8.07 (d, $^3J$(H,H)=8.3 Hz, 1H), 7.80 (dd, $^4J$(H,H)=1.5 Hz, $^3J$(H,H)=8.3 Hz, 1H), 7.68 (ddd, $^4J$(H,H)=1.5 Hz, $^3J$(H,H)=7.1 Hz, $^3J$(H,H)=8.7 Hz, 1H), 7.47 (ddd, $^4J$(H,H)=1.1 Hz, $^3J$(H,H)=7.2 Hz, $^3J$(H,H)=8.3 Hz, 1H), 6.50 (s, 1H), 6.21 (s, 1H), 4.17 (ddd, $^4J$(H,H)=0.8 Hz, $^2J$(H,H)=13.9 Hz, $^2J$(H,H)=28.6 Hz, 1H), 3.61 (s, 3H), 3.40 ppm (s, 3H); to confirm that the signal at 4.17 ppm was not a quadruplet, the spectrum was also performed in [D6]acetone: $^1$H NMR (300 MHz, [D6]acetone, 25°C): $\delta$=8.11 (s, 1H), 7.87 (d, $^3J$(H,H)=8.7 Hz, 1H), 7.75 (app. d, $^3J$(H,H)=7.9 Hz, 1H), 7.51 (ddd, $^4J$(H,H)=1.5 Hz, $^3J$(H,H)=7.2 Hz, $^3J$(H,H)=8.3 Hz, 1H), 7.32 (ddd, $^4J$(H,H)=0.8 Hz, $^3J$(H,H)=6.8 Hz, $^3J$(H,H)=7.9 Hz, 1H), 6.26 (s, 1H), 6.13 (s, 1H), 3.86 (dd, $^2J$(H,H)=14.9 Hz, $^2J$(H,H)=36.2 Hz, 1H), 3.35 (s, 3H), 3.11 ppm (s, 3H); $^{13}$C NMR (75 MHz, [D]$CHCl_3$, 25°C): $\delta$=158.4, 149.1, 147.3, 135.0, 131.0, 128.2, 127.9, 127.2, 126.2, 122.6, 103.6, 99.8, 71.5, 58.5, 55.9 ppm; IR (neat): $\tilde{\nu}$=2918, 2849, 1739, 1618, 1500, 1252, 1139, 1076, 990, 635 cm$^{-1}$; TOF MS ES+: *m/z* (%): 258 (100) $[M+H]^+$; HRMS (TOF ES+): *m/z* calcd for $[C_{15}H_{16}NO_3]^+$: 258.1130; found: 258.1146.

**Compound 10**: This compound was prepared by method A. It was isolated as a pale oil (quantitative). $^1$H NMR (300 MHz, [D]$CHCl_3$, 25°C): $\delta$=8.01 (d, $^3J$(H,H)=8.7 Hz, 1H), 7.97 (s, 1H), 7.73 (d, $^3J$(H,H)=7.9 Hz, 1H), 7.67 (td, $^3J$(H,H)=6.8 Hz, $^4J$(H,H)=1.5 Hz, 1H), 7.44 (d, $^3J$(H,H)=8.3 Hz, $^4J$(H,H)=1.1 Hz, 1H), 6.41 (s, 1H), 6.30 (s, 1H), 4.21 (m, 1H), 4.16 (d, $^2J$(H,H)=13.9 Hz, 1H), 4.05 (d, $^2J$(H,H)=13.9 Hz, 1H), 4.05 (m, 1H), 3.95 (m, 1H), 3.78 (m, 2H), 3.44 ppm (s, 3H); $^{13}$C NMR (75 MHz, [D]$CHCl_3$, 25°C): $\delta$=156.4, 149.1, 149.0, 134.0, 130.8, 129.0, 128.3, 127.5, 126.3, 122.8, 105.4, 99.9, 72.3, 71.5, 62.2, 59.0 ppm; IR (neat): $\tilde{\nu}$=3200, 2919, 2850, 1735, 1461, 1376, 1260, 1079, 635 cm$^{-1}$; MS ES+: *m/z* (%): 288 (100) $[M+H]^+$; HRMS (TOF ES+): *m/z* calcd for $[C_{16}H_{18}NO_4]^+$: 288.1236; found: 288.1242.

**Compound 11**: This compound was prepared by method A. It was isolated as a yellow solid (quantitative). $^1$H NMR (300 MHz, [D]$CHCl_3$, 25°C): $\delta$=8.08 (d, $^3J$(H,H)=7.9 Hz, 1H), 8.07 (s, 1H), 7.83 (d, $^3J$(H,H)=8.3 Hz, 1H), 7.74 (t, $^3J$(H,H)=7.2 Hz, 1H), 7.52 (t, $^3J$(H,H)=7.9 Hz, 1H), 6.52 (s, 1H), 6.42 (s, 1H), 4.23 (d, $^2J$(H,H)=13.6 Hz, 1H), 4.23 (m, 2H), 4.10 (d, $^2J$(H,H)=13.6 Hz, 1H), 3.47 ppm (s, 3H); $^{13}$C NMR (75 MHz, [D]$CHCl_3$, 25°C): $\delta$=155.5, 148.2, 134.3, 130.7, 128.7, 128.0, 127.0, 126.1, 121.0, 105.4, 98.7, 71.7, 65.1, 64.6, 64.2, 63.7, 58.4 ppm; IR (neat): $\tilde{\nu}$=2920, 2851, 1660, 1621, 1498, 1432, 1269, 1178, 1161, 1082, 1035, 771 cm$^{-1}$; MS (TOF ES+): *m/z* (%): 326 (100) $[M+H]^+$; HRMS (TOF ES+): *m/z* calcd for $[C_{16}H_{15}F_3NO_3]^+$: 326.1004; found: 326.10117.

**Compound 12**: This compound was prepared by method B. It was isolated as a pale yellow solid (quantitative). $^1$H NMR (300 MHz, [D]$CHCl_3$, 25°C): $\delta$=8.09 (d, $^3J$(H,H)=7.2 Hz, 1H), 8.08 (s, 1H), 7.87 (dd, $^4J$(H,H)=1.1 Hz, $^3J$(H,H)=7.9 Hz, 1H), 7.78 (ddd, $^4J$(H,H)=1.1 Hz, $^3J$(H,H)=6.8 Hz, $^3J$(H,H)=8.3 Hz, 1H), 7.55 (ddd, $^4J$(H,H)=1.1 Hz, $^3J$(H,H)=7.2 Hz, $^3J$(H,H)=8.3 Hz, 1H), 6.58 (s, 1H), 4.93 (hept, $^3J$(H,F)=6.0 Hz, 1H), 4.17 (dd, $^2J$(H,H)=14.3 Hz, $^2J$(H,H)=17.7 Hz, 2H), 3.48 ppm (s, 3H); $^{13}$C NMR (75 MHz, [D]$CHCl_3$, 25°C): $\delta$=155.0, 149.3, 134.5, 129.0, 128.1, 127.0, 126.3, 119.7, 105.3, 99.0, 71.2, 58.8, 29.7, 26.9, 14.1 ppm; MS ESI+: *m/z* (%): 394 (100) $[M+H]^+$; HRMS (ESI+): *m/z* calcd for $[C_{17}H_{14}F_6NO_3]^+$: 394.0878; found: 394.0884.

**Compound 13**: This compound was prepared by method B. It was isolated as a yellow solid (94%). $^1$H NMR (300 MHz, [D]$CHCl_3$, 25°C): $\delta$=8.16 (s, 1H), 8.14 (d, $^3J$(H,H)=9.4 Hz, 1H), 7.84 (dd, $^4J$(H,H)=1.1 Hz, $^3J$(H,H)=8.3 Hz, 1H), 7.75 (ddd, $^4J$(H,H)=1.5 Hz, $^3J$(H,H)=6.8 Hz, $^3J$(H,H)=8.3 Hz, 1H), 7.55 (ddd, $^4J$(H,H)=1.1 Hz, $^3J$(H,H)=7.9 Hz, $^3J$(H,H)=8.3 Hz, 1H), 7.34 (d, $^3J$(H,H)=8.3 Hz, 2H), 7.30 (d, $^3J$(H,H)=

8.7 Hz, 2H), 6.63 (s, 1H), 5.96 (t, $^3J$(H,H) = 7.5 Hz, 1H), 4.78 (q, $^2J$(H,H) = 11.3 Hz, 2H), 4.44–4.29 (m, 2H), 3.81 (s, 3H), 3.44 ppm (s, 3H).

**Compound 14**: This compound was prepared by method B. It was isolated as a yellow solid (93%). $^1$H NMR (300 MHz, [D]CHCl$_3$, 25°C): $\delta$ = 8.01 (dd, $^4J$(H,H) = 1.1 Hz, $^3J$(H,H) = 7.9 Hz, 1H), 7.89 (s, 1H), 7.76 (dd, $^4J$(H,H) = 1.1 Hz, $^3J$(H,H) = 7.9 Hz, 1H), 7.68 (ddd, $^4J$(H,H) = 1.5 Hz, $^3J$(H,H) = 6.8 Hz, $^3J$(H,H) = 7.2 Hz, 1H), 7.45 (ddd, $^4J$(H,H) = 1.1 Hz, $^3J$(H,H) = 6.8 Hz, $^4J$(H,H) = 7.2 Hz, 1H), 7.32 (d, $^3J$(H,H) = 8.7 Hz, 2H), 7.90 (d, $^3J$(H,H) = 9.0 Hz, 2H), 6.44 (d, $^4J$(H,H) = 0.8 Hz, 1H), 6.32 (s, 1H), 4.85 (dd, $^2J$(H,H) = 11.7 Hz, $^2J$(H,H) = 23.7 Hz, 2H), 4.11 (ddd, $^4J$(H,H) = 0.8 Hz, $^3J$(H,H) = 13.6 Hz, $^2J$(H,H) = 27.5 Hz, 2H), 3.81 (s, 3H), 3.47 ppm (s, 3H); $^{13}$C NMR (75 MHz, [D]CHCl$_3$, 25°C): $\delta$ = 159.5, 156.3, 149.1, 148.8, 133.3, 130.1, 129.8, 129.0, 128.8, 127.9, 127.2, 125.6, 122.7, 113.9, 104.9, 97.4, 71.8, 69.4, 58.4, 55.3 ppm; IR (neat): $\tilde{\nu}$ = 2923, 2852, 1720, 1618, 1560, 1500, 1432, 1259, 1199, 1086, 1015, 972, 906, 801, 638 cm$^{-1}$; MS (TOF ES+): *m*/*z* (%): 364 (100) [*M*+H]$^+$; HRMS (TOF ES+): *m*/*z* calcd for [C$_{22}$H$_{22}$NO$_4$]$^+$: 364.1549; found: 364.1539.

**Compound 15**: This compound was prepared by method B. It was isolated as an orange powder (92%). $^1$H NMR (300 MHz, [D]CHCl$_3$, 25°C): $\delta$ = 8.06 (s, 1H), 8.03 (d, $^3J$(H,H) = 8.7 Hz, 1H), 7.85 (dd, $^4J$(H,H) = 1.1 Hz, $^3J$(H,H) = 7.9 Hz, 1H), 7.80 (dd, $^4J$(H,H) = 1.1 Hz, $^3J$(H,H) = 8.3 Hz, 1H), 7.70 (ddd, $^4J$(H,H) = 1.5 Hz, $^3J$(H,H) = 7.2 Hz, $^3J$(H,H) = 8.7 Hz, 1H), 7.68 (ddd, $^4J$(H,H) = 1.1 Hz, $^3J$(H,H) = 6.8 Hz, $^3J$(H,H) = 7.9 Hz, 1H), 7.39 (dd, $^4J$(H,H) = 1.9 Hz, $^3J$(H,H) = 7.5 Hz, 1H), 7.33 (qd, $^4J$(H,H) = 1.1 Hz, $^3J$(H,H) = 7.5 Hz, 1H), 7.00 (td, $^4J$(H,H) = 1.5 Hz, $^3J$(H,H) = 7.5 Hz, 2H), 6.46 (s, 2H), 4.88 (dd, $^3J$(H,H) = 12.4 Hz, $^2J$(H,H) = 38.0 Hz, 2H), 4.85 (ddd, $^4J$(H,H) = 0.8 Hz, $^3J$(H,H) = 13.6 Hz, $^2J$(H,H) = 23.7 Hz, 2H), 3.46 ppm (s, 3H); $^{13}$C NMR (75 MHz, [D]CHCl$_3$, 25°C): $\delta$ = 156.3, 149.0, 139.4, 139.2, 133.7, 130.3, 129.6, 129.5, 128.8, 128.4, 128.3, 128.0, 127.2, 125.7, 122.3, 104.9, 98.7, 98.3, 74.0, 71.8, 58.5 ppm; IR (neat): $\tilde{\nu}$ = 2922, 2849, 1722, 1619, 1562, 1497, 1432, 1364, 1229, 1196, 1074, 976, 906, 797, 647 cm$^{-1}$; MS ESI+: *m*/*z* (%): 460.0 (100) [*M*+H]$^+$; HRMS (TOF ES+): *m*/*z* calcd for [C$_{21}$H$_{19}$INO$_3$]$^+$: 460.0410; found: 460.0434.

**Compound 16**: This compound was prepared by method B. It was isolated as a pale oil (88%). $^1$H NMR (300 MHz, [D]CHCl$_3$, 25°C): $\delta$ = 8.01 (d, $^3J$(H,H) = 8.3 Hz, 1H), 7.93 (s, 1H), 7.77 (dd, $^4J$(H,H) = 1.1 Hz, $^3J$(H,H) = 8.3 Hz, 1H), 7.67 (ddd, $^4J$(H,H) = 1.5 Hz, $^3J$(H,H) = 7.2 Hz, $^3J$(H,H) = 8.7 Hz, 1H), 7.45 (ddd, $^4J$(H,H) = 1.1 Hz, $^3J$(H,H) = 7.2 Hz, $^3J$(H,H) = 8.3 Hz, 1H), 6.41 (s, 1H), 6.40 (s, 1H), 4.13 (dd, $^2J$(H,H) = 19.6 Hz, $^2J$(H,H) = 13.6 Hz, 2H), 4.06–3.95 (m, 1H), 3.45 (s, 3H), 2.13–2.03 (m, 1H), 1.99–1.90 (m, 1H), 1.83–1.70 (m, 2H), 1.61–1.51 (m, 1H), 1.45–1.33 (m, 2H), 1.32–1.20 (m, 2H), 0.92–0.80 ppm (m, 1H); $^{13}$C NMR (75 MHz, [D]CHCl$_3$, 25°C): $\delta$ = 156.5, 149.3, 133.0, 130.0, 128.7, 127.8, 127.2, 125.5, 123.2, 104.5, 97.2, 77.2, 71.9, 58.4, 33.6, 31.8, 29.7, 25.5, 24.2, 24.0 ppm; MS ESI+: *m*/*z* (%): 326 (100) [*M*+H]$^+$; HRMS (TOF ES+): *m*/*z* calcd for [C$_{20}$H$_{24}$NO$_3$]$^+$: 326.1756; found: 326.1744.

**Compound 18**: This compound was prepared by method A. It was isolated as a pale solid (quantitative). $^1$H NMR (300 MHz, [D]CHCl$_3$, 25°C): $\delta$ = 8.01 (d, $^3J$(H,H) = 8.3 Hz, 1H), 7.86 (s, 1H), 7.77 (dd, $^4J$(H,H) = 1.3 Hz, $^3J$(H,H) = 7.9 Hz, 1H), 7.66 (ddd, $^4J$(H,H) = 1.5 Hz, $^3J$(H,H) = 7.2 Hz, $^3J$(H,H) = 8.7 Hz, 1H), 7.44 (ddd, $^4J$(H,H) = 1.1 Hz, $^3J$(H,H) = 7.2 Hz, $^3J$(H,H) = 8.3 Hz, 1H), 6.51 (s, 1H), 6.37 (d, $^4J$(H,H) = 0.8 Hz, 1H), 4.11 (ddd, $^4J$(H,H) = 0.8 Hz, $^2J$(H,H) = 20.7 Hz, $^2J$(H,H) = 13.6 Hz, 2H), 3.45 (s, 3H), 1.41 ppm (s, 9H); $^{13}$C NMR (75 MHz, [D]CHCl$_3$, 25°C): $\delta$ = 156.9, 149.5, 132.2, 129.7, 128.5, 127.6, 127.1, 125.2, 123.8, 103.9, 94.2, 76.4, 71.7, 58.2, 28.7 ppm; IR (neat): $\nu$ = 2960, 2907, 1632, 1622, 1498, 1433, 1261, 1063, 977, 913, 779, 620 cm$^{-1}$; MS ESI+: *m*/*z* (%): 300 (100) [*M*+H]$^+$; HRMS (ESI+): *m*/*z* calcd for [C$_{18}$H$_{22}$NO$_3$]$^+$ 300.1599; found: 326.1597.

**Compound 20**: This compound was prepared by method A. It was isolated as an orange solid (quantitative). $^1$H NMR (300 MHz, [D]CHCl$_3$, 25°C): $\delta$ = 7.77 (s, 1H), 7.45 (s, 1H), 7.17 (s, 1H), 6.35 (s, 1H), 6.13 (s, 1H), 4.36 (m, 4H), 4.18 (d, $^2J$(H,H) = 13 Hz, 1H), 4.13 (d, $^2J$(H,H) = 13 Hz, 1H), 3.59 (s, 3H), 3.44 ppm (s, 3H); $^{13}$C NMR (75 MHz, [D]CHCl$_3$, 25°C): $\delta$ = 155.2, 147.4, 147.4, 145.2, 143.8, 131.9, 123.0, 120.9, 113.5, 112.1, 105.0, 100.1, 71.9, 64.4, 64.3, 58.3, 55.5 ppm; IR (neat): $\tilde{\nu}$ = 2920, 2850, 1655, 1499, 1285, 1246, 1233, 1066, 639 cm$^{-1}$; MS (TOF ES+): *m*/*z* (%): 316 (100) [*M*+H]$^+$; HRMS (TOF ES+): *m*/*z* calcd for [C$_{17}$H$_{18}$NO$_5$]$^+$: 316.1185; found: 316.1193.

**Compound 22**: This compound was prepared by method A. It was isolated as a light yellow solid (quantitative). $^1$H NMR (300 MHz, [D]CHCl$_3$, 25°C): $\delta$ = 7.91 (s, 1H), 7.65 (d, $^3J$(H,H) = 9.0 Hz, 1H), 7.35 (d, $^4J$(H,H) = 2.6 Hz, 1H), 7.10 (dd, $^3J$(H,H) = 9.0 Hz, $^4J$(H,H) = 2.6 Hz, 1H), 6.38 (s, 1H), 6.17 (s, 1H), 4.20 (d, $^2J$(H,H) = 12.8 Hz, 1H), 4.10 (d, $^2J$(H,H) = 12.8 Hz, 1H), 3.93 (s, 3H), 3.60 (s, 3H), 3.46 ppm (s, 3H); $^{13}$C NMR (75 MHz, [D]CHCl$_3$, 25°C): $\delta$ = 161.4, 156.1, 150.5, 149.0, 133.2, 128.8, 122.2, 119.0, 106.7, 104.7, 100.1, 71.8, 58.4, 55.6, 55.5 ppm; IR (neat): $\tilde{\nu}$ = 2918, 2850, 1636, 1503, 1452, 1378, 1245, 1145, 1083, 996, 958, 790, 633 cm$^{-1}$; MS (TOF ES+): *m*/*z* (%): 288.1 (100) [*M*+H]$^+$; HRMS (TOF ES+): *m*/*z* calcd for [C$_{16}$H$_{18}$NO$_4$]$^+$: 288.1236; found: 288.1252.

**Compound 24**: This compound was prepared by method A. It was isolated as a brownish solid (93%). $^1$H NMR (300 MHz, [D]CHCl$_3$, 25°C): $\delta$ = 8.20 (s, 1H), 8.14 (d, $^3J$(H,H) = 8.7 Hz, 1H), 7.86 (d, $^3J$(H,H) = 7.5 Hz, 1H), 7.76 (ddd, $^4J$(H,H) = 1.1 Hz, $^3J$(H,H) = 6.8 Hz, $^3J$(H,H) = 8.3 Hz, 1H), 7.56 (t, $^3J$(H,H) = 7.9 Hz, 1H), 6.52 (s, 1H), 5.96 (d, $^3J$(H,H) = 7.9 Hz, 1H), 5.67 (d, $^3J$(H,H) = 7.9 Hz, 1H), 3.79–3.75 (m, 2H), 3.68–3.63 (m, 2H), 3.55 (s, 3H), 1.25 ppm (t, $^3J$(H,H) = 7.2 Hz, 6H); $^{13}$C NMR (75 MHz, [D]CHCl$_3$, 25°C): $\delta$ = 152.7, 150.0, 131.4, 130.6, 129.8, 128.4, 127.8, 104.7, 98.4, 97.0, 60.9, 60.9, 55.0, 15.3 ppm; MS CI+: *m*/*z* (%): 316 (100) [*M*+H]$^+$; HRMS (CI +): *m*/*z* calcd for [C$_{18}$H$_{22}$NO$_4$]$^+$: 316.1549; found: 316.1555.

**Compound 25**: This compound was prepared by method A. It was isolated as a brownish solid (95%). $^1$H NMR (300 MHz, [D]CHCl$_3$, 25°C): $\delta$ = 7.96 (d, $^3J$(H,H) = 8.7 Hz, 1H), 7.93 (s, 1H), 7.72 (d, $^3J$(H,H) = 8.3 Hz, 1H), 7.62 (ddd, $^4J$(H,H) = 1.1 Hz, $^3J$(H,H) = 6.8 Hz, $^3J$(H,H) = 8.7 Hz, 1H), 7.38 (ddd, $^4J$(H,H) = 1.1 Hz, $^3J$(H,H) = 6.8 Hz, $^3J$(H,H) = 7.9 Hz, 1H), 6.6 (s, 1H), 6.13 (s, 1H), 5.01 (s, 1H), 3.66 (m, 2H), 3.58 (m, 2H), 3.57 (s, 3H), 1.21 ppm (td, $^4J$(H,H) = 1.1 Hz, $^3J$(H,H) = 7.2 Hz, 6H); $^{13}$C NMR (75 MHz, [D]CHCl$_3$, 25°C): $\delta$ = 155.4, 148.7, 133.6, 130.3, 128.8, 127.9, 127.2, 125.8, 122.7, 104.7, 100.0, 98.7, 62.0, 61.6, 55.8, 15.1 ppm; IR (neat): $\tilde{\nu}$ = 2973, 2920, 2849, 1651, 1621, 1497, 1433, 1354, 1155, 1114, 997, 965, 754, 637 cm$^{-1}$; MS CI+: *m*/*z* (%): 316 (100) [*M*+H]$^+$; HRMS (CI+): *m*/*z* calcd for [C$_{18}$H$_{22}$NO$_4$]$^+$: 316.1549; found: 316.1549.

**Compound 27**: This compound was prepared by method A. It was isolated as a yellow solid (quantitative). $^1$H NMR (300 MHz, [D]CHCl$_3$, 25°C): $\delta$ = 8.16 (s, 1H), 8.10 (d, $^3J$(H,H) = 8.7 Hz, 1H), 7.83 (d, $^3J$(H,H) = 7.9 Hz, 1H), 7.74 (ddd, $^4J$(H,H) = 1.5 Hz, $^3J$(H,H) = 7.2 Hz, $^3J$(H,H) = 8.7 Hz, 1H), 7.53 (ddd, $^4J$(H,H) = 0.8 Hz, $^3J$(H,H) = 6.8 Hz, $^3J$(H,H) = 7.9 Hz, 1H), 6.5 (s, 1H), 5.85 (s, 1H), 3.52 (s, 3H), 1.33 ppm (s, 9H); $^{13}$C NMR (75 MHz, [D]CHCl$_3$, 25°C): $\delta$ = 155.0, 149.8, 148.7, 131.3, 130.4, 129.3, 128.4, 128.2, 127.5, 126.4, 112.1, 103.8, 54.4, 31.8, 30.3 ppm; MS ES+: *m*/*z* (%): 270 (100) [*M*+H]$^+$; HRMS (TOF ES+): *m*/*z* calcd for [C$_{17}$H$_{20}$NO$_2$]$^+$: 270.1494; found: 270.1498.

**Compound 28**: This compound was prepared by method A. It was isolated as a yellow solid (quantitative). $^1$H NMR (300 MHz, [D]CHCl$_3$, 25°C): $\delta$ = 8.14 (s, 1H), 8.08 (d, $^3J$(H,H) = 8.3 Hz, 1H), 7.77 (d, $^3J$(H,H) = 8.3 Hz, 1H), 7.59 (t, $^3J$(H,H) = 8.3 Hz, 1H), 7.40 (d, $^3J$(H,H) = 7.4 Hz, 1H), 6.30 (s, 1H), 6.16 (s, 1H), 3.56 (s, 3H), 1.07 ppm (s, 9H); $^{13}$C NMR (75 MHz, [D]CHCl$_3$, 25°C): $\delta$ = 172.9, 151.1, 146.7, 136.7, 132.2, 129.0, 127.8, 127.6, 126.8, 123.1, 100.0, 98.9, 56.8, 37.0, 28.1 ppm; IR (neat): $\tilde{\nu}$ = 2965, 2931, 2359, 1617, 1503, 1436, 1262, 1237, 1157, 1071, 1028, 993, 754, 687 cm$^{-1}$; TOF MS ES+: *m*/*z* (%): 270 (100) [*M*+H]$^+$; HRMS (TOF ES+): *m*/*z* calcd for [C$_{17}$H$_{20}$NO$_2$]$^+$: 270.1494; found: 270.1508.

**Compound 30**: This compound was prepared by method A. It was isolated as a pale yellow powder ( quantitative); $^1$H NMR (300 MHz, [D]CHCl$_3$, 25°C): $\delta$ = 7.99 (d, $^3J$(H,H) = 8.3 Hz, 1H), 7.92 (s, 1H), 7.72 (d, $^3J$(H,H) = 7.9 Hz, 1H), 7.65 (td, $^3J$(H,H) = 6.8 Hz, $^4J$(H,H) = 1.5 Hz, 1H), 7.39 (td, $^3J$(H,H) = 6.8 Hz, $^4J$(H,H) = 1.1 Hz, 1H), 6.26 (s, 1H), 6.08 (s, 1H), 3.57 (s, 3H), 1.75 (m, 1H), 1.06 (m, 1H), 0.90 ppm (m, 4H); $^{13}$C NMR (75 MHz, [D]CHCl$_3$, 25°C): $\delta$ = 162.4, 149.8, 148.3, 133.4, 130.2, 128.1, 127.8, 126.6, 125.1, 122.0, 100.8, 99.9, 55.7, 14.8, 7.5, 6.0 ppm; IR (neat): $\tilde{\nu}$ = 3008, 2919, 2848, 1635, 1617, 1497, 1428, 1078, 1046, 1004, 962, 961, 752, 624 cm$^{-1}$; TOF MS ES+: *m*/*z* (%): 254 (100) [*M*+H]$^+$; HRMS (TOF ES+): *m*/*z* calcd for [C$_{16}$H$_{16}$NO$_2$]$^+$: 254.1181; found: 254.1177.

**Compound 32**: This compound was prepared by method A. It was isolated as a pale oil (85%). $^1$H NMR (300 MHz, [D]CHCl$_3$, 25°C): $\delta$=8.02 (d, $^3J$(H,H)=8.7 Hz, 1H), 7.99 (s, 1H), 7.77 (d, $^3J$(H,H)=8.3 Hz, 1H), 7.68 (ddd, $^4J$(H,H)=1.1 Hz, $^3J$(H,H)=6.8 Hz, $^3J$(H,H)=8.3 Hz, 1H), 7.45 (ddd, $^4J$(H,H)=0.8 Hz, $^3J$(H,H)=6.8 Hz, $^3J$(H,H)=7.5 Hz, 1H), 6.45 (s, 1H), 6.19 (s, 1H), 4.81 (q, $^4J$(H,H)=3.8 Hz, 1H), 4.43 (dt, $^4J$(H,H)= 1.1 Hz, $^2J$(H,H)=13.9 Hz, 1H), 4.24 (dd, $^4J$(H,H)=0.8 Hz, $^2J$(H,H)= 13.9 Hz, 1H), 3.97–3.87 (m, 1H), 3.61 (s, 3H), 1.80–1.55 (m, 5H), 1.07–0.90 ppm (m, 3H); $^{13}$C NMR (75 MHz, [D]CHCl$_3$, 25°C): $\delta$=mixture of 2 diastereoisomers 157.6, 157.3, 149.6, 149.5, 149.2, 133.9, 133.8, 130.6, 129.2, 128.3, 127.5, 126.1, 122.9, 104.6, 104.2, 100.4 (×2), 98.5, 97.9, 66.2, 65.9, 62.3 (×2), 56.1, 43.9, 30.6, 30.1, 27.3, 25.8, 19.4, 19.3 ppm; TOF MS ES+: $m/z$ (%): 328 (100) $[M+H]^+$; HRMS (TOF ES+): $m/z$ calcd for $[C_{19}H_{22}NO_4]^+$: 328.1549; found: 328.1548.

**Compound 34**: This compound was prepared by method A. It was isolated as a pale oil (95%). $^1$H NMR (300 MHz, [D]CHCl$_3$, 25°C): $\delta$=8.06 (s, 1H), 8.02 (d, $^3J$(H,H)=8.7 Hz, 1H), 7.80 (dd, $^4J$(H,H)=1.5 Hz, $^3J$(H,H)=7.5 Hz, 1H), 7.79 (dd, $^4J$(H,H)=1.1 Hz, $^3J$(H,H)=7.9 Hz, 1H), 7.69 (ddd, $^4J$(H,H)=1.1 Hz, $^3J$(H,H)=6.8 Hz, $^3J$(H,H)=8.3 Hz, 1H), 7.65 (dd, $^4J$(H,H)=1.5 Hz, $^3J$(H,H)=7.9 Hz, 1H), 7.56 (td, $^4J$(H,H)=1.5 Hz, $^3J$(H,H)=7.5 Hz, 1H), 7.49 (ddd, $^4J$(H,H)=1.9 Hz, $^3J$(H,H)=7.9 Hz, $^3J$(H,H)=9.4 Hz, 1H), 7.45 (dd, $^4J$(H,H)=1.1 Hz, $^3J$(H,H)=6.8 Hz, 1H), 6.56 (s, 1H), 6.35 (s, 1H), 3.88 (s, 3H), 3.68 ppm (s, 3H); $^{13}$C NMR (75 MHz, [D]CHCl$_3$, 25°C): $\delta$=168.5, 157.9, 150.4, 148.7, 134.9, 132.6, 131.4, 131.2, 130.1, 129.7, 129.6, 128.7, 128.0, 127.3, 125.7, 122.7, 105.2, 101.7, 56.5, 52.3 ppm; MS ES+: $m/z$ (%): 348 (100) $[M+H]^+$; HRMS (TOF ES+): $m/z$ calcd for $[C_{21}H_{18}NO_4]^+$: 348.1236; found: 348.1230.

**Compound 35**: This compound was prepared by method A. It was isolated as a pale oil (96%); $^1$H NMR (300 MHz, [D]CHCl$_3$, 25°C): $\delta$=8.40 (dd, $^4J$(H,H)=0.8 Hz, $^3J$(H,H)=7.9 Hz, 1H), 8.24–8.22 (m, 2H), 7.94 (dd, $^4J$(H,H)=1.5 Hz, $^3J$(H,H)=7.9 Hz, 1H), 7.87 (d, $^3J$(H,H)=8.3 Hz, 1H), 7.78 (ddd, $^4J$(H,H)=1.1 Hz, $^3J$(H,H)=7.2 Hz, $^3J$(H,H)=8.7 Hz, 1H), 7.65 (s, 1H), 7.56 (td, $^4J$(H,H)=0.8 Hz, $^3J$(H,H)=7.2 Hz, 2H), 7.33–7.28 (m, 1H), 6.66 (s, 1H), 3.99 (s, 3H), 3.61 ppm (s, 3H); $^{13}$C NMR (75 MHz, [D]CHCl$_3$, 25°C): $\delta$=168.3, 154.3, 151.8, 150.1, 135.6, 131.6, 131.4, 130.5, 130.5, 130.4, 129.8, 129.1, 128.4, 128.2, 127.7, 126.8, 126.2, 105.4, 97.9, 55.0, 52.2 ppm; MS ES+: $m/z$ (%): 348 (100) $[M+H]^+$; HRMS (TOF ES+): : $m/z$ calcd for $[C_{21}H_{18}NO_4]^+$: 348.1236; found: 348.1254.

**Compound 37**: This compound was prepared by method A. It was isolated as a pale oil (89%); $^1$H NMR (300 MHz, [D]CHCl$_3$, 25°C): $\delta$=8.49 (d, $^3J$(H,H)=7.9 Hz, 1H), 8.25–8.20 (m, 2H), 7.88 (dd, $^4J$(H,H)=1.1 Hz, $^3J$(H,H)=7.2 Hz, 1H), 7.79 (ddd, $^4J$(H,H)=1.5 Hz, $^3J$(H,H)=7.2 Hz, $^3J$(H,H)=8.7 Hz, 1H), 7.71 (d, $^3J$(H,H)=7.5 Hz, 1H), 7.60–7.56 (m, 2H), 7.32 (t, $^3J$(H,H)=7.5 Hz, 1H), 7.10 (q, $^4J$(H,H)=1.9 Hz, 1H), 6.68 (s, 1H), 3.60 ppm (s, 3H); MS ES+; $m/z$ (%): 358 (100) $[M+H]^+$; HRMS (TOF ES+): $m/z$ calcd for $[C_{20}H_{15}NO_2F_3]^+$: 358.1055; found: 358.1069.

**Compound 39**: This compound was prepared by method A. It was isolated as a yellow solid (94%). $^1$H NMR (300 MHz, [D]CHCl$_3$, 25°C): $\delta$= 8.07 (d, $^3J$(H,H)=8.7 Hz, 1H), 8.03 (s, 1H), 7.93 (dd, $^4J$(H,H)=1.9 Hz, $^3J$(H,H)=7.9 Hz, 1H), 7.79 (dd, $^4J$(H,H)=1.1 Hz, $^3J$(H,H)=8.3 Hz, 1H), 7.69 (ddd, $^4J$(H,H)=1.5 Hz, $^3J$(H,H)=6.8 Hz, $^3J$(H,H)=8.3 Hz, 1H), 7.45 (ddd, $^4J$(H,H)=1.1 Hz, $^3J$(H,H)=6.8 Hz, $^3J$(H,H)=7.9 Hz, 1H), 7.41 (s, 1H), 7.38 (ddd, $^4J$(H,H)=1.5 Hz, $^3J$(H,H)=7.2 Hz, $^3J$(H,H)=8.3 Hz, 1H), 7.06 (dd, $^4J$(H,H)=1.5 Hz, $^3J$(H,H)=7.5 Hz, 1H), 7.01 (app. d, $^3J$(H,H)=7.9 Hz, 1H), 6.31 (s, 1H), 3.97 (s, 3H), 3.68 ppm (s, 3H); $^{13}$C NMR (75 MHz, [D]CHCl$_3$, 25°C): $\delta$=158.1, 150.3, 133.1, 130.7, 130.2, 128.5, 128.3, 127.9, 127.1, 125.5, 122.8, 120.4, 111.3, 107.3, 99.9, 55.9, 55.5 ppm; IR (neat): $\tilde{\nu}$=2919, 2850, 2325, 1713, 1614, 1490, 1428, 1243, 1170, 1122, 1009, 954, 900, 810, 610 cm$^{-1}$; MS (TOF ES+): $m/z$ (%): 320 (100) $[M+H]^+$; HRMS (TOF ES+): $m/z$ calcd for $[C_{20}H_{18}NO_3]^+$: 320.1287; found: 320.1291.

**Compound 41**: This compound was prepared by method A. It was isolated as a yellow solid (94%). $^1$H NMR (300 MHz, [D]CHCl$_3$, 25°C): $\delta$= 8.76 (t, $^4J$(H,H)=1.9 Hz, 1H), 8.27 (ddd, $^4J$(H,H)=0.8 Hz, $^4J$(H,H)= 2.3 Hz, $^3J$(H,H)=9.0 Hz, 1H), 8.19 (dt, $^4J$(H,H)=1.5 Hz, $^3J$(H,H)= 7.9 Hz, 1H), 8.10 (s, 1H), 8.08 (d, $^3J$(H,H)=8.7 Hz, 1H), 7.85 (dd, $^4J$(H,H)=1.1 Hz, $^3J$(H,H)=8.3 Hz, 1H), 7.75 (ddd, $^4J$(H,H)=1.5 Hz, $^3J$(H,H)=5.3 Hz, $^3J$(H,H)=6.8 Hz, 1H), 7.65 (t, $^3J$(H,H)=7.9 Hz, 1H), 7.53 (ddd, $^4J$(H,H)=0.8 Hz, $^3J$(H,H)=6.8 Hz, $^3J$(H,H)=7.9 Hz, 1H), 7.10 (s, 1H), 6.42 (s, 1H), 3.73 ppm (s, 3H); $^{13}$C NMR (75 MHz, [D]CHCl$_3$, 25°C): $\delta$=153.4, 149.4, 149.3, 149.1, 136.1, 133.9, 131.2, 131.0, 130.1, 129.3, 128.4, 127.7, 126.6, 124.6, 122.9, 120.6, 104.6, 100.9, 56.6 ppm; MS (TOF ES+): $m/z$ (%): 335 (100) $[M+H]^+$; HRMS (TOF ES+): $m/z$ calcd for $[C_{19}H_{15}N_2O_4]^+$: 335.1032; found: 335.1024.

**Compound 42**: This compound was prepared by method A. It was isolated as a yellow solid (94%); $^1$H NMR (300 MHz, [D]CHCl$_3$, 25°C): $\delta$= 8.86 (s, 1H), 8.27 (s, 1H), 8.17 (d, $^3J$(H,H)=8.7 Hz, 1H), 8.09–8.02 (m, 2H), 7.90 (d, $^3J$(H,H)=7.9 Hz, 1H), 7.83 (ddd, $^4J$(H,H)=0.8 Hz, $^3J$(H,H)=6.8 Hz, $^3J$(H,H)=7.9 Hz, 1H), 7.60 (t, $^3J$(H,H)=7.2 Hz, 1H), 7.52 (t, $^3J$(H,H)=7.9 Hz, 1H), 6.78 (s, 1H), 6.71 (s, 1H), 3.71 ppm (s, 3H); $^{13}$C NMR (75 MHz, [D]CHCl$_3$, 25°C): $\delta$=153.8, 152.8, 150.0, 148.6, 137.0, 134.6, 131.7, 130.9, 129.6, 129.2, 128.6, 128.5, 127.9, 127.2, 123.4, 121.0, 106.0, 98.5, 55.8 ppm; MS (TOF ES+): $m/z$ (%): 335 (100) $[M+H]^+$; HRMS (TOF ES+): $m/z$ calcd for $[C_{19}H_{15}N_2O_4]^+$: 335.1032; found: 335.1049.

**Compound 44**: This compound was prepared by method A. It was isolated as a brown solid (92%). $^1$H NMR (300 MHz, [D]CHCl$_3$, 25°C): $\delta$= 7.97 (s, 1H), 7.91 (m, 2H), 7.68 (d, $^3J$(H,H)=8.3 Hz, 1H), 7.45 (m, 4H), 7.14 (dd, $^3J$(H,H)=9.0 Hz, $^4J$(H,H)=2.6 Hz, 1H), 6.97 (s, 1H), 6.35 (s, 1H), 3.97 (s, 1H), 3.70 ppm (s, 1H); $^{13}$C NMR (75 MHz, [D]CHCl$_3$, 25°C): $\delta$=161.4, 155.7, 150.6, 149.9, 133.8, 133.0, 129.8, 128.9, 125.4, 122.2, 120.3, 118.8, 106.6, 101.9, 100.2, 77.1, 55.7, 55.5 ppm; IR (neat): $\tilde{\nu}$= 2918, 2849, 1608, 1503, 1451, 1379, 1241, 1157, 1077, 1046, 954, 907, 765, 689, 630 cm$^{-1}$; MS ESI+: $m/z$ (%): 320 (100) $[M+H]^+$; HRMS (ESI+): $m/z$ calcd for $[C_{20}H_{18}NO_3]^+$: 320.1287; found: 320.1276.

**Compound 46**: This compound was prepared by method A. It was isolated as a dark oil (89%). $^1$H NMR (300 MHz, [D]CHCl$_3$, 25°C): $\delta$=8.05 (s, 1H), 8.03 (d, $^3J$(H,H)=8.9 Hz, 1H), 7.92–7.87 (m, 2H), 7.79 (dd, $^4J$(H,H)=1.3 Hz, $^3J$(H,H)=8.1 Hz, 1H), 7.70 (ddd, $^4J$(H,H)=1.5 Hz, $^3J$(H,H)=7.0 Hz, $^3J$(H,H)=8.5 Hz, 1H), 7.49–7.43 (m, 4H), 6.84 (s, 1H), 3.36 (s, 3H), 1.97 ppm (s, 3H); $^{13}$C NMR (75 MHz, [D]CHCl$_3$, 25°C): $\delta$= 155.8, 151.4, 150.6, 136.2, 132.5, 131.4, 130.8, 130.7, 130.4, 129.0, 128.4, 127.1, 126.0, 125.9, 110.8, 100.7, 51.3, 27.1 ppm; IR (neat): $\tilde{\nu}$=2928, 2848, 1749, 1633, 1443, 1255, 1094, 749 cm$^{-1}$; MS ESI+: $m/z$ (%): 304 (100) $[M+H]^+$; HRMS (ESI+): $m/z$ calcd for $[C_{20}H_{18}NO_2]^+$: 304.1338; found: 304.1341.

**Compound 48**: This compound was prepared by method A. It was isolated as a yellow oil (quantitative). $^1$H NMR (300 MHz, [D]CHCl$_3$, 25°C): $\delta$=7.50–7.47 (m, 1H), 7.42–7.37 (m, 2H), 6.39 (s, 1H), 5.20 (t, $^2J$(H,H)= 7.2 Hz, 1H), 4.34–4.20 (m, 2H), 3.43 (s, 3H), 3.39 ppm (s, 3H); $^{13}$C NMR (75 MHz, [D]CHCl$_3$, 25°C): $\delta$=155.5, 138.1, 134.5, 130.2, 129.7, 123.4, 120.5, 106.9, 94.1, 66.7, 58.1, 54.7 ppm; MS (TOF ES+): $m/z$ (%): 207 (100) $[M+H]^+$; HRMS (TOF ES+): $m/z$ calcd for $[C_{12}H_{15}O_3]^+$: 207.1021; found: 207.1034.

**Compound 49**: This compound was prepared by method A. It was isolated as a yellow oil (quantitative). $^1$H NMR (300 MHz, [D]CHCl$_3$, 25°C): $\delta$=7.32 (qd, $^4J$(H,H)=1.9 Hz, $^3J$(H,H)=8.7 Hz, 1H), 7.24–7.27 (m, 2H), 7.12 (d, $^3J$(H,H)=7.2 Hz, 1H), 6.07 (s, 1H), 6.00 (s, 1H), 4.08 (dd, $^2J$(H,H)=12.4 Hz, $^2J$(H,H)=38.8 Hz, 2H), 3.56 (s, 3H), 3.41 ppm (s, 3H); further characterization was consistent with published data.[6a]

**Compound 51**: This compound was prepared by method A. It was isolated as a brown oil (96%). $^1$H NMR (300 MHz, [D]CHCl$_3$, 25°C): $\delta$=7.85 (d, $^3J$(H,H)=6.9 Hz, 1H), 7.44–7.36 (m, 5H), 7.25–7.30 (m, 3H), 6.64 (s, 1H), 6.18 (s, 1H), 3.64 ppm (s, 3H); MS (TOF ES+): $m/z$ (%): 239 (100) $[M+H]^+$; HRMS (ESI+): $m/z$ calcd for $[C_{16}H_{15}O_2]^+$: 239.1072; found: 239.1059. further characterization was consistent with published data.[5a]

**Compound 52**: This compound was prepared by method A. It was isolated as a brown oil (96%); $^1$H NMR (300 MHz, [D]CHCl$_3$, 25°C): $\delta$=7.77 (d, $^3J$(H,H)=7.5 Hz, 2H), 7.58 (dd, $^4J$(H,H)=1.5 Hz, $^3J$(H,H)=6.8 Hz, 1H), 7.48–7.33 (m, 5H), 7.22–7.16 (m, 1H), 6.57 (s, 1H), 6.00 (s, 1H), 3.51 ppm (s, 3H); $^{13}$C NMR (75 MHz, [D]CHCl$_3$, 25°C): $\delta$=171.1, 135.8, 135.5, 129.9, 128.9, 128.4, 128.3, 125.9, 123.1, 119.8, 107.4, 98.2, 60.3 ppm; MS (TOF ES+): $m/z$ (%): 239 (100) $[M+H]^+$; HRMS (ESI+): $m/z$ calcd for $[C_{16}H_{15}O_2]^+$: 239.1072; found: 239.1086.

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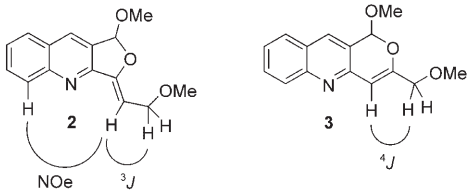


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