EurJOC
European Journal of Organic Chemistry

Research Article
doi.org/10.1002/ejoc.202400013

Chemistry Europe
European Chemical Societies Publishing

www.eurjoc.org

Synthesis and Photochemical Characterization of Indolizine Fluorophores Obtained by a Multicomponent Palladium Iodide–Catalyzed Oxidative Aminocarbonylation Approach

Ida Ziccarelli,[a] Roberta Amuso,[a] Raffaella Mancuso,[a] Antonio Maggiore,[b] Giuseppe Lamberti,[b] Paola Vitale,[c] Vincenzo Maiorano,[b] Lucia Veltri,*[a] and Bartolo Gabriele*[a]

A catalytic carbonylative method for the direct, multicomponent synthesis of indolizine fluorophores has been developed. The process is based on the PdI_2/KI-catalyzed oxidative aminocarbonylation of 2-(pyridin-2-yl)pent-4-yn-1-carbonyl compounds leading to the corresponding 2-ynamide intermediates, followed in situ by 5-*exo*-*dig* cyclization (by amine-promoted conjugate addition of the pyridine ring nitrogen) and aromatization, to give the finally isolated *N*,*N*-disubstituted 2-(indolizin-3-yl)acetamides. Reactions are carried out under relatively mild conditions (100 °C under 20 atm of a 4:1 mixture CO–air for 6–15 h) in MeCN as the solvent and with a low catalyst loading (0.33 mol% PdI_2), in the presence of 0.5 equiv. of KI and 3 equiv. of a secondary amine. The optical properties of representative 2-(indolizin-3-yl)acetamide products have also been investigated.

Introduction

Indolizines are an important class of heterocyclic derivatives, which display a wide range of biological activities (including anticancer, antitubercular, antioxidant, antimicrobial and anti-inflammatory activities), with a number of indolizine-based drugs being currently tested in different phases of clinical trials.[1] Moreover, some interesting organic fluorophores possess the indolizine core as the key structural unit,[2] and indolizine derivatives are useful substrates for the preparation of more complex molecular architectures.[3] Accordingly, several synthetic efforts have been devoted to the synthesis of indolizines,[4] and the development of new efficient synthetic approaches for their production is still of considerable interest in current research.

Among functionalized indolizines, 2-(indolizin-3-yl)acetamides are of particular interest, as they are known to act as orexin receptor antagonists, and are therefore useful for the treatment of several diseases and disorders, such as eating disorders, sleep disorders, cognitive dysfunctions in psychiatric and neurological disorders, drug dependence, obesity, and type II diabetes.[5,6] These indolizine derivatives are currently prepared by functionalization of the indolizine nucleus[7] or by an annulation approach based on a multistep procedure, in particular starting from 2-(chloromethyl)pyridine.[6] Another method, leading to dihydroindolizine-fused pyrrolidinones, is based on Cu-catalyzed bis-annulation of malonate-tethered *O*-acyl oximes (obtained from a three-step procedure).[8] To the best of our knowledge, however, no direct carbonylation[9] method has been reported so far for the preparation of this important subclass of indolizine derivatives, in spite of their interest as bioactive molecules as well as compounds with potential luminescent properties.

Based on our PdI_2/KI-catalyzed carbonylation reaction,[10–12] in this work we have envisaged the possibility to achieve a carbonylative multicomponent[13] synthesis of *N*,*N*-disubstituted 2-(indolizin-3-yl)acetamides **3** starting from simple building blocks, namely, 2-(pyridin-2-yl)pent-4-yn-1-carbonyl compounds **1**, CO, amines **2**, and O_2 (from air, used as external oxidant). As shown in Scheme 1, an approach like this would take place through the sequential PdI_2/KI-catalyzed oxidative monoaminocarbonylation[12c,d, m, 14] of the terminal triple bond of **1** to give 2-ynamide intermediates **I** followed by in situ amine-promoted cyclization of **I** to give **3**. 2-Ynamide intermediates **I** would be formed through amine-promoted palladation of the triple bond of **1**, followed by CO insertion, nucleophilic displacement by the amine, and Pd(0) reoxidation. In situ C-2

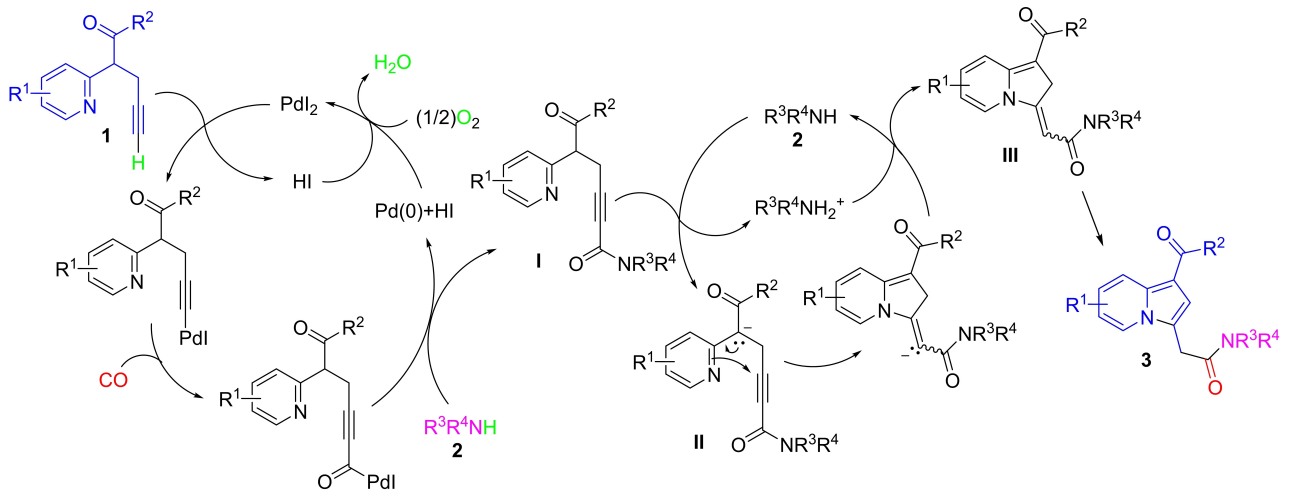
[a] Dr. I. Ziccarelli, Dr. R. Amuso, Prof. Dr. R. Mancuso, Prof. Dr. L. Veltri, Prof. Dr. B. Gabriele
Laboratory of Industrial and Synthetic Organic Chemistry (LISOC), Department of Chemistry and Chemical Technologies
University of Calabria
Via Pietro Bucci 12/C, 87036 Arcavacata di Rende (CS), Italy
E-mail: lucia.veltri@unical.it
bartolo.gabriele@unical.it

[b] Dr. A. Maggiore,+ Dr. G. Lamberti, Dr. V. Maiorano
CNR-NANOTEC – Institute of Nanotechnology, c/o Campus Ecotekne, Via Monteroni, Lecce, 73100, Italy

[c] P. Vitale
Department of Pharmacy – Pharmaceutical Sciences, University of Bari "Aldo Moro", Via E. Orabona 4, 70125 Bari, Italy

Supporting information for this article is available on the WWW under https://doi.org/10.1002/ejoc.202400013

Research Article
doi.org/10.1002/ejoc.202400013



Scheme 1. *Work hypothesis:* Sequential PdI_2/KI-catalyzed monoaminocarbonylation of 2-(pyridin-2-yl)pent-4-yn-1-carbonyl compounds **1** with CO, amines **2** and O_2 to give 2-ynamide intermediates **I** followed by amine-promoted intramolecular conjugate addition and aromatization to give *N,N*-disubstituted 2-(indolizin-3-yl)acetamides **3**.

deprotonation of **I** by the amine **2** would then lead to the relatively stabilized carbanion **II**, which would undergo dearomative intramolecular conjugated addition (by 5-*exo-dig* attack of the pyridine ring nitrogen) to give **III** followed by rearomatization to afford the target compounds **3** (Scheme 1; anionic iodide ligands are omitted for clarity).

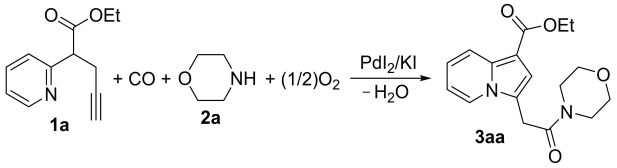
Results and Discussion

PdI_2/KI-Catalyzed Carbonylative Synthesis of *N,N*-Disubstituted 2-(Indolizin-3-yl)acetamides 3

To test our work hypothesis for the carbonylative synthesis of 2-(indolizin-3-yl)acetamides, shown in Scheme 1, we initially allowed to react ethyl 2-(pyridin-2-yl)pent-4-ynoate **1a** with morpholine **2a** (3 equiv) under 20 atm of a 4:1 mixture CO-air in MeCN (0.2 mmol of **1a** per mL of MeOH) at 100 °C and in the presence of 1 mol% of PdI_2 and 1 equiv. of KI. Gratifingly, after 6 h, the desired ethyl 3-(2-morpholino-2-oxoethyl)indolizine-1-carboxylate **3aa** was obtained in 78% isolated yield at total **1a** conversion (Table 1, entry 1). This very promising initial result could be further improved after a brief optimization study (Table 1, entries 2–8). In particular, we were pleased to find that a **3aa** yield as high as 85% could be achieved using 0.5 equiv. of KI under more concentrated conditions (0.4 mmol of **1a** per mL of MeCN; Table 1, entry 7) and that practically the same yield (86%) was obtained by decreasing the catalyst loading to 0.33 mol% of palladium (Table 1, entry 8).

We then assessed the generality of the process by applying the optimized conditions to different amines **2a-h** and differently substituted 2-(pyridin-2-yl)pent-4-yn-1-carbonyl compounds **1a-j**, and the results are shown in Table 2. As can be seen from Table 2, excellent results (71–93% isolated product yield, 213–279 TONs) could be attained when the parent substrate **1a** was aminocarbonylated with different secondary amines, including cyclic amines (such as morpholine **2a**, piperidine **2b**, and pyrrolidine **2c**, Table 2, entries 1–3), unhindered dialkylamines (like dimethylamine **2d** and dibutylamine **2e**, Table 2, entries 4 and 5, respectively) or more hindered amines such as benzylmethylamine **2f** or diisopentylamine **2g** (Table 2, entries 6 and 7, respectively). The presence of a strong electron-withdrawing group like the nitro group at the C-5 position of the pyridine ring resulted in a slower process (15 h reaction time instead of 6 h were necessary to achieve complete substrate conversion), with a lower but still satisfac-

Table 1. PdI_2/KI-catalyzed oxidative aminocarbonylation of ethyl 2-(pyridin-2-yl)pent-4-ynoate **1a** with morpholine **2a** to ethyl 3-(2-morpholino-2-oxoethyl)indolizine-1-carboxylate **3aa** under different conditions.[a]



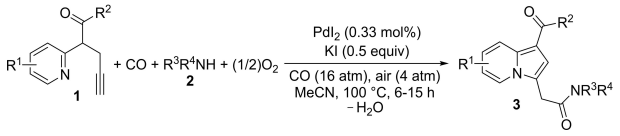
Entry	PdI_2 [mol%]	KI [equiv]	**2a** [equiv]	**1a** concn.[b]	T [°C]	Yield of **3a** [%][c]
1	1	1	3	0.2	100	78
2	1	1	2	0.2	100	74
3	1	1	4	0.1	100	77
4[d]	1	1	3	0.2	80	56
5	1	0.5	3	0.2	100	81
6	1	1	3	0.4	100	80
7	1	0.5	3	0.4	100	85
8	0.33	0.16	3	0.4	100	86

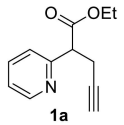
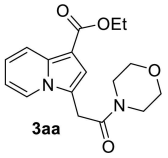
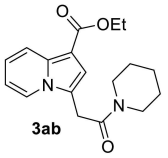
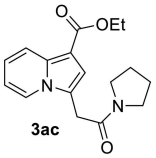
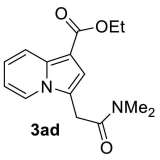
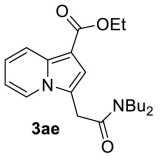
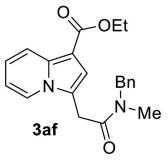
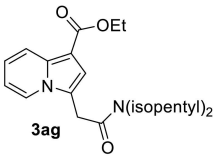
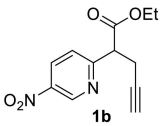
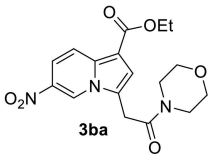
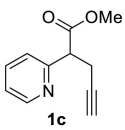
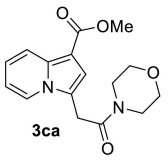
[a] Unless otherwise noted, all reactions were carried out in MeCN for 6 h and substrate conversion was quantitative. Formation of unidentified heavy products (chromatographically immobile materials) accounted for the difference between substrate conversion and product yield. [b] Mmol of **1a** per mL of solvent. [c] Isolated yield based on starting **1a**. [d] Substrate conversion was 83%.

Research Article
doi.org/10.1002/ejoc.202400013

Chemistry Europe
European Chemical Societies Publishing

Table 2. Synthesis of indolizines **3** by PdI_2/KI-catalyzed oxidative aminocarbonylation of **1** with CO and amines **2**.[a]

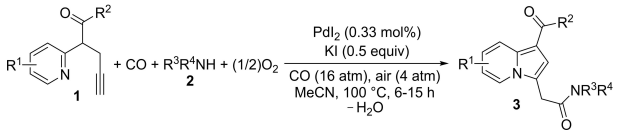


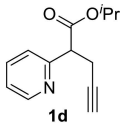
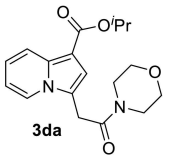
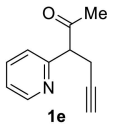
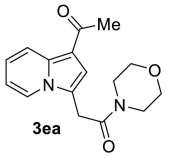
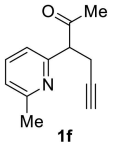
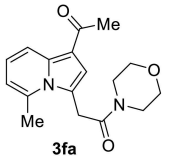
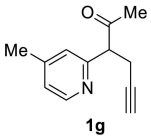
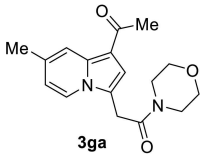
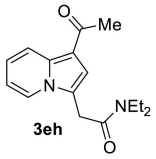
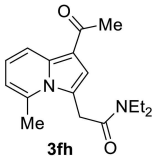
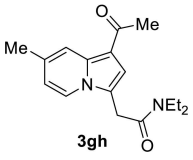
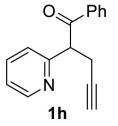
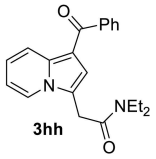
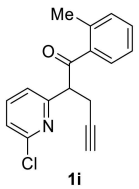
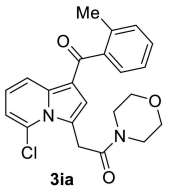
Entry	1	2	3	Yield of 3 [%][b]
1	 **1a**	 **2a**	 **3aa**	86
2	**1a**	 **2b**	 **3ab**	82
3	**1a**	 **2c**	 **3ac**	71
4	**1a**	Me_2NH **2d**	 **3ad**	83
5	**1a**	Bu_2NH **2e**	 **3ae**	93
6	**1a**	BnNHMe **2f**	 **3af**	85
7	**1a**	$(isopentyl)_2NH$ **2g**	 **3ag**	74
8[c]	 **1b**	**2a**	 **3ba**	60
9	 **1c**	**2a**	 **3ca**	95

Research Article
doi.org/10.1002/ejoc.202400013

Chemistry Europe
European Chemical Societies Publishing

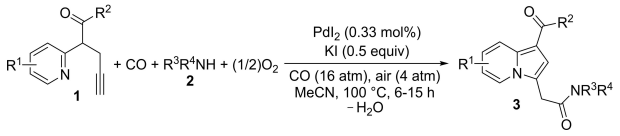
Table 2. continued

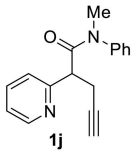
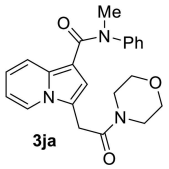
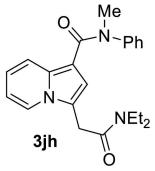


Entry	1	2	3	Yield of **3** [%][b]
10	 **1d**	**2a**	 **3da**	85
11	 **1e**	**2a**	 **3ea**	51[d]
12	 **1f**	**2a**	 **3fa**	56[e]
13	 **1g**	**2a**	 **3ga**	55[f]
14	**1e**	Et_2NH **2h**	 **3eh**	79
15	**1f**	**2h**	 **3fh**	81
16	**1g**	**2h**	 **3gh**	80
17	 **1h**	**2h**	 **3hh**	91
18	 **1i**	**2a**	 **3ia**	74

Research Article
doi.org/10.1002/ejoc.202400013

Table 2. continued



Entry	1	2	3	Yield of 3 [%][b]
19	 1j	2a	 3ja	69
20	1j	2h	 3jh	66

[a] Unless otherwised noted, all reactions were carried out at 100 °C for 6 h in MeCN (0.4 mmol of **1** per mL of MeCN) under 20 atm (at 25 °C) of a 4:1 mixture of CO−air, in the presence of 0.33 mol% of PdI_2 and 0.16 equiv. of KI and 3 equiv. of **2**. [b] Isolated yield based on starting **1**. [c] The reaction was carried out for 15 h. [d] The GLC yield was 75%. See text for details. [e] The GLC yield was 78%. See text for details. [f] The GLC yield was 76%. See text for details.

tory yield of the corresponding ethyl 3-(2-morpholino-2-oxoethyl)-6-nitroindolizine-1-carboxylate **3ba** (60%, Table 2, entry 8). On the other hand, extension of the method to methyl 2-(pyridin-2-yl)pent-4-ynoate **1c** as well as to more hindered isopropyl 2-pyridin-2-yl)pent-4-ynoate **1d** led to high yields of the corresponding indolizine derivatives **3ca** (95%; Table 2, entry 9) and **3da** (85%; Table 2, entry 10). Switching from the ester to the keto group also led to good yields of the corresponding 2-(1-acylindolizin-3-yl)-*N*,*N*-dialkylacetamide derivatives (Table 2, entries 11–18), although in same cases the final isolated yield was affected by the difficulty to separate the desired product from the oxamide coproduct (1,2-dimorpholinoethane-1,2-dione, formed by concomitant PdI_2/KI-catalyzed oxidative double carbonylation of the excess amine).[15] In particular, from the reactions of 3-(pyridin-2-yl)hex-5-yn-2-one **1e**, 3-(6-methylpyridin-2-yl)hex-5-yn-2-one **1f**, and 3-(4-methylpyridin-2-yl)hex-5-yn-2-one **1g** with morpholine **2a**, the corresponding acetylindolizines **3ea**, **3fa**, and **3ga** were isolated in 51%, 56%, and 55% yields, respectively, while their GLC yield were 75%, 78% and 76%, respectively (Table 2, entries 11–13). With diethylamine **2h**, however, the corresponding 2-(1-acetylindolizin-3-yl)-*N*,*N*-diethylacetamides **3eh**, **3fh**, and **3gh** could be isolated in high yields (79%, 81% and 80%; Table 2, entries 14, 15, and 16, respectively). An even higher isolated yield was observed in the case of aminocarbonylation of 1-phenyl-2-(pyridin-2-yl)pent-4-yn-1-one **1h** with diethylamine **2h** (yield of 2-(1-benzoylindolizin-3-yl)-*N*,*N*-diethylacetamide **3hh**, 91%; Table 2, entry 17). Also, the imidazoline product **3ia**, deriving from aminocarbonylation with morpholine **2a** of a substrate bearing a chloro substituent on the C-6 position of the pyridine ring and an *o*-tolyl group bonded to the carbonyl (2-(6-chloropyridin-2-yl)-1-(*o*-tolyl)pent-4-yn-1-one **1i**), could be efficiently isolated, with a yield of 74% (Table 2, entry 18). Finally, we also tested the reactivity of an amide substrate such as *N*-methyl-*N*-phenyl-2-(pyridin-2-yl)pent-4-ynamide **1j** under aminocarbonylation conditions with both morpholine **2a** and diethylamine **2h** as the nucleophilic partner, and were pleased to find that the process worked nicely even in this substrate, with formation of the corresponding 3-(2-(dialkylamino)-2-oxoethyl)-indolizine-1-carboxamides **3ja** and **3jh** in 69% and 66% yields, respectively (Table 2, entries 19 and 20).

Photochemical Characterization of *N*,*N*-Disubstituted 2-(Indolizin-3-yl)acetamides 3 as New Indolizine Fluorophores

In this section, we present the optical properties of 1,3-disubstituted indolizines bearing the ethyl ester functional group at position C-1 and substituted with various groups at the C-3 position (**3aa**-**3ae**). Additionally, to investigate the impact of an additional substituent, we conducted a photophysical study on 1,3,5- and 1,3,6-trisubstituted indolizines (**3ba**, **3fa**). Specifically, **3ba** shares the same structure as **3aa** but with the inclusion of a nitro substituent at C-6. Comparing **3aa** with **3fa**, it is evident that the carboxyethyl group at C-1 is replaced by an acetyl group, and an additional methyl substituent is present at C-5. We examined these compounds through UV/Vis absorption, as well as steady-state and time-resolved fluorescence spectroscopy.

The photophysical properties in solution were initially studied in diluted solutions (5^{-10} M) in three different air-equilibrated solvents with increasing polarity: cyclohexane (CH), toluene (TOL), and dichloromethane (DCM). Subsequently, we investigated the solid-state photophysical properties of isolated

Research Article
doi.org/10.1002/ejoc.202400013

molecules in a rigid polymer matrix of poly(methyl methacrylate) (PMMA). The photophysical data for all compounds are summarized in Tables S1 and S2 (Supporting Information).

Figure 1a shows a comparison of the UV-Vis absorption spectra of **3aa**-**3ae** in dichloromethane (DCM), while Figure 1b illustrates the comparison of the UV-Vis absorption spectra of **3aa**, **3ba**, and **3fa** in DCM. It is evident that **3aa**-**3ae** molecules exhibit similar absorption spectra in the UV-Vis region, specifically between 375 and 400 nm. Consequently, these transitions can be attributed to the indolizine central core[16] substituted with the ethyl ester. Conversely, transitions at higher energies (between 220 and 375 nm) may be assigned to both the different substituent groups on the indolizine core and other transitions typical of indolizine.[17] In Figure 1a we observe that the molar extinction coefficients of the transitions between 375 and 400 nm are nearly identical for all **3aa**-**3ae** molecules. This observation confirms that the absorption in this region remains unaffected by the presence of diverse substituents at position C-3. Supplementary Figure S1 and Figure S2 display the UV-Vis absorption spectra of **3aa**-**3ae** in three different solvents and in PMMA, respectively. It is noteworthy that the lower-energy band centered around 370 nm exhibits vibronic resolution in cyclohexane (CH) and becomes Gaussian in DCM. Additionally, this band experiences a slight shift with solvent polarity, consistent with solvatochromism.

Figure 1b and Figure S3 and S4 (Supporting Information) present the UV-Vis absorption spectra of the trisubstituted indolizines **3ba** and **3fa**). Specifically, in Figure 2b we compare the absorption features of **3ba** and **3fa** with those of **3aa**, as they share the same indolizine core substituted with the same group at C-3. We observe the following trends: i) In **3fa**, compared to **3aa**, the ester group at C-1 is replaced by a acetyl group, and an additional methyl group is present at C-5. This results in a shift of absorption to lower energy and the disappearance of transition peaks between 225 and 325 nm; ii) Remarkably, in **3ba**, where an additional nitro group is present

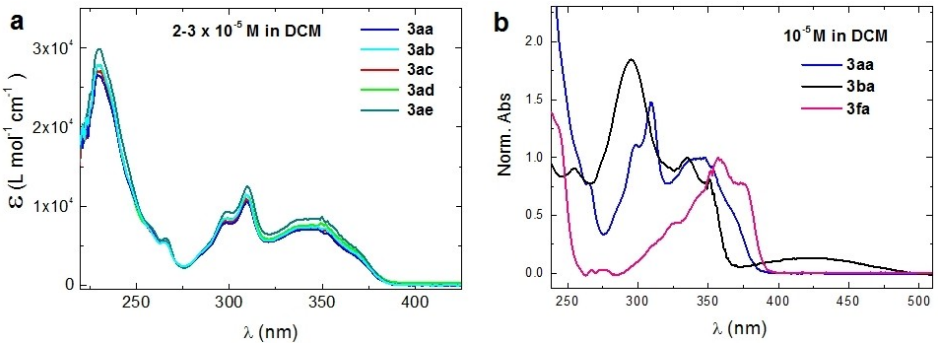


Figure 1. a) UV-Vis absorption spectra in DCM of **3aa**-**3ae**; b) UV-Vis absorption spectra in DCM of **3aa**, **3ba**, and **3fa**.

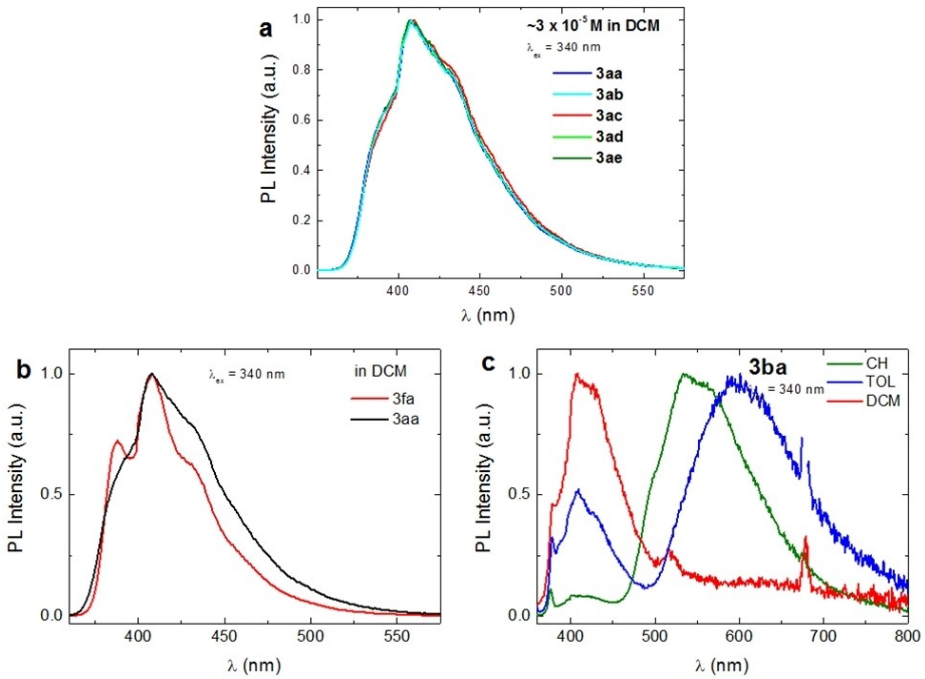


Figure 2. a) Photoluminescence (PL) emission spectra in cyclohexane, toluene and DCM of **3aa**-**3ae**. b) PL emission spectra in DCM of **3fa** and **3aa**. c) PL emission spectra in cyclohexane, toluene and DCM of **3ba**.

at C-6 compared to **3 aa**, in addition to a blue shift in the absorption bands of indolizine, a new weak Gaussian band emerges between 360 and 500 nm. As shown in Supplementary Figure S3, this band exhibits a clear bathochromic shift with increasing solvent polarity. We attribute this band to the intramolecular charge transfer state (ICT) formed between the indolizine and the nitro group, consistent with the strong acceptor strength of the nitro group.

The fluorescence spectral characteristics of the compounds were investigated in a solution (10^{-5} M) in cyclohexane (CH), toluene (TOL), and dichloromethane (DCM), as well as in poly(methyl methacrylate) (PMMA) thin films (concentration = 0.1 weight %) (Figure 2 and Figures S5–S8, Supporting Information). Similar to the UV-Vis results, the PL emission of **3 aa**-**3 ae** compounds remained almost constant, exhibiting an emission band centered at λ_{max} = 408–409 nm in DCM (Figure 2, and Table S1, Supporting Information). In PMMA (Figure S6, Supporting Information), a slight blue shift is observed (λ_{max} = 401–402), attributed to the rigidochromic effect in the solid environment. From Figure S5 and Table S1 (Supporting Information), it is apparent that, similar to the UV-Vis spectra, the PL emission of all **3 aa**-**3 ae** compounds undergoes a slight red shift with an increase in solvent polarity, consistent with the presence of a permanent dipole on the molecule. The bathochromic effect on the PL of **3 aa**-**3 ae** compounds is minimal for the PL maxima but becomes more pronounced for peaks at lower energy (Table S1, Supporting Information). For all **3 aa**-**3 ae** samples, the photoluminescence quantum yield (φ_{PL}) is high in all solvents and also in the solid matrix (Table S2, Supporting Information). Notably, φ_{PL} decreases from CH to TOL (especially for **3 ab**, **3 ac**, and **3 ae**) but subsequently increases in DCM. This trend is attributed to the higher polarity of DCM, allowing the stabilization of the charge transfer (CT) state component, leading to a higher φ_{PL}. In PMMA, φ_{PL} remains similar or even lower compared to that in solution (Table S2, Supporting Information), indicating that the molecules do not present non-radiative decay channels due to roto-vibrational motions.

Regarding the PL properties of the tri-substituted indolizines (**3 ba** and **3 fa**), we can first notice that, compared to **3 aa**, **3 fa** presents similar PL spectra (Figure 2b), but with narrowed emission and vibronic transitions at almost the same energy, albeit with a relatively different intensity. This behavior indicates that the additional methyl group in C-5 and the substitution of acetyl for ethoxycarbonyl in C-1 only slightly affect the PL spectra of the indolizine core. Nevertheless, the φ_{PL} of **3 fa** is much higher compared to the other compounds (87 % in TOL, Table S2, Supporting Information). More interestingly, the presence of a nitro group in C-6 has a profound impact on the photophysical behavior of **3 ba**. In fact, the PL spectra of **3 ba** show double emission in solvents and PMMA (Figure 2c, and Figure S8a, Supporting Information). Particularly, we can note that the band at higher energy, similar to the other compounds, is centered around 400 nm, and therefore is assigned to the indolizine moiety. On the other hand, the band at lower energy presents a clear intramolecular charge transfer (ICT) behavior, with vibronic resolution in CH and bathochromic shift with Gaussian emission in TOL and PMMA (Figure 2c, and Figure S8a, Supporting Information). Simultaneously, in DCM, the CT band appears strongly quenched, indicating an over-stabilization effect due to higher polarity. Nevertheless, as seen in Table S2 (Supporting Information), the φ_{PL} strongly decreases compared to all the other systems, indicating that the formation of the CT state results in a strong quenching of the PL properties of these systems. This effect aligns with the well-known fluorescence quenching properties of nitro groups.[18]

Photophysical properties of the samples were further studied using time-resolved emission spectroscopy (Figures S9-S12, Supporting Information). In particular, the luminescence decays of **3 aa**-**3 ae** in the three solvents (Figure S9, Supporting Information) were fitted with two characteristic lifetimes (Table S2, Supporting Information): one shorter, which slightly increases with solvent polarity, and the other much longer, especially in DCM. We attribute these two components to locally excited (LE) states, suggesting the possible presence of two different indolizine conformations arising from distinct interactions with the solvent. Consequently, the ratio between these lifetimes can vary with different solvent polarities. Nevertheless, we cannot exclude the possibility that the bi-exponential decay could also be influenced by a strong propensity for π-π stacking, even in diluted solution.

Conclusions

In conclusion, we have reported a catalytic multicomponent approach to an important class of fused heterocycles, namely, *N*,*N*-disubstituted 2-(indolizin-3-yl)acetamides. These compounds have been efficiently synthesized by allowing to react readily available 2-(pyridin-2-yl)pent-4-yn-1-carbonyl compounds with carbon monoxide, a secondary amine and oxygen (from air, used as benign external oxidant) under relatively mild conditions (100 °C under 20 atm of a 4 : 1 mixture CO−air for 6–15 h, in MeCN as the solvent and in the presence of 0.33 mol% of PdI_2, 0.5 equiv. of KI, and 3 equiv. of the secondary amine). The process occurs through an ordered sequence of mechanistic steps, involving PdI_2/KI-catalyzed oxidative aminocarbonylation of the substrate to give the corresponding 2-ynamide intermediates followed by amine-promoted dearomative 5-*exo*-*dig* cyclization (by intramolecular conjugate addition of the pyridine ring nitrogen) and rearomatization (by double bond shift from exocyclic to endocyclic position).

While 2-(indolizin-3-yl)acetamides have been reported in the literature to possess interesting pharmacological properties,[5,6] in this work we have demonstrated that our newly synthesized *N*,*N*-disubstituted 2-(indolizin-3-yl)acetamides are also interesting fluorophores. In particular, the representative compounds tested (**3 aa-3 ae**, **3 ba**, and **3 fa**) absorb (λ_{abs}) in the UV region (374.5–386.0 nm), and emit (λ_{em}) in the visible or blue region (442–448.6 nm).

Research Article
doi.org/10.1002/ejoc.202400013

Experimental Section

General Experimental Methods

Melting points are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded at 25 °C in $CDCl_3$ at 500 MHz and 125 MHz, respectively, with Me_4Si as internal standard. Chemical shifts (δ) and coupling constants (*J*) are given in ppm and in Hz, respectively. IR spectra were taken with an FT-IR spectrometer. All reactions were analyzed by TLC on silica gel 60 F254 and by GC-MS analysis using a GC–MS apparatus at 70 eV ionization voltage equipped with a 95% methyl polysiloxane – 5% phenyl polysiloxane capillary columns (30 m ×0.25 mm, 0.25 μm). Column chromatography was performed on silica gel 60 (70–230 mesh). Evaporation refers to the removal of solvent under reduced pressure. The HRMS spectra were taken on Q-TOF-MS mass spectrometer, equipped with an electrospray ion source (ESI) operated in dual ion mode. 10 μL of the sample solutions (CH_3OH) were introduced by continuous infusion at a flow rate of 200 L min-1 with the aid of a syringe pump. Experimental conditions were performed as follows: capillary voltage, 4000 V; nebulizer pressure, 20 psi; flow rate of drying gas, 10 L/min; temperature of sheath gas, 325 °C; flow rate of sheath gas, 10 L/min; skimmer voltage, 60 V; OCT1 RF Vpp, 750 V; fragmentor voltage, 170 V. The spectra data were recorded in the m/z range of 100–1000 Da in a centroid pattern of full-scan MS analysis mode. The MS/MS data of the selected compounds were obtained by regulating diverse collision energy (18–45 eV).

Substrates **1** were prepared and characterized as described in the Supplementary data. All other materials were commercially available and were used without further purification.

Fluorescence spectroscopic studies were performed at 25 °C with an Edinburgh FLS980 spectrometer equipped with a peltier-cooled Hamamatsu R928 photomultiplier tube (185–850 nm). The studies in solution were performed in diluted solution with an absorbance lower than 0.1 by using as holder a rectangular 10 mm path length quartz cuvettes from Hellma. For studies in solid state, the materials where dispersed in rigid polymers matrix (PMMA and Zeonex) at different concentrations and deposited on quartz substrates. Corrected spectra were obtained via a calibration curve supplied with the instrument. For the excitation and emission spectra, the slits widths were adjusted between 1–5 nm, integration time = 0.1 s, 1 nm step. The relative photoluminescence quantum yields (PLQY Φ_{PL}) in solution were determined at 25 °C, from corrected emission spectra using quinine sulphate in 0.1 M $HClO_4$ as standard. For each QY measurements, slit width, excitation wavelength, scan rate, integration time and emission range were kept identical for the reference and the sample. The fluorescence QY was determined according to the following formula:

$$\Phi_{PL} = \Phi_R \bullet \left(\frac{Abs_R}{Abs_S}\right) \bullet \left(\frac{\eta_S^2}{\eta_R^2}\right) \bullet \left(\frac{I_S}{I_R}\right)$$

Where: Φ_{PL} = Fluorescence quantum yield, *Abs* = absorbance of the solution, η = refractive index of the solvent, *I* = Integrated fluorescence intensity of the emitted light, and subscripts '*R*' and '*S*' refer to the reference and sample respectively. For all solid films, PLQYs have been calculated by corrected emission spectra obtained from an apparatus consisting of a barium sulphate coated integrating sphere (4 or 6 inches), a 450 W Xe lamp (λ_{exc} = tunable by a monochromator supplied with the instrument) as light sources, and a R928 photomultiplier tube as signal detectors, following the procedure described by De Mello and coworkers.[19] Lifetime experiments were done using 10 mm path length quartz cuvettes or directly on the solid-state samples deposited on the quartz substrate. Emission lifetimes were determined by the time-correlated single-photon counting (TCSPC) technique by means of the same Edinburgh FLS980 spectrometer using two different laser diodes as excitation source (EPL 1 MHz, λ_{exc} = 407 nm.) and an peltier-cooled Hamamatsu tube R928 photomultiplier tube as detector. Analysis of the luminescence decay profiles *vs.* time was accomplished with the DAS6 Decay Analysis Software provided by the manufacturer. The quality of the fit was estimated by visual inspection of the weighted residuals and calculation of χ^2. Experimental uncertainties were estimated to be ±8% for lifetime determinations, ±20% for emission quantum yields, ±2 nm and ±5 nm for absorption and emission peaks, respectively.

General Procedure for the Synthesis of *N*,*N*-disubstituted 2-(Indolizin-3-yl)acetamides 3

A 35 mL stainless steel autoclave was charged in the presence of air with PdI_2 (1.9. mg, 5.3 × 10^{-3} mmol), KI (43.2 mg, 0.26 mmol) anhydrous CH_3CN (4 mL), α-propargylpyridinyl carbonylic compounds **1** (1.6 mmol) [**1a**, 326 mg; **1b**, 397 mg; **1c**, 303 mg; **1d**, 348 mg; **1e**, 277 mg; **1f**, 300 mg; **1g**, 300 mg; **1h**, 376 mg; **1i**, 454 mg; **1j**, 423 mg] and the amine (4.8 mmol) [**2a**, 418 mg; **2b**, 409 mg; **2c**, 341 mg, **2d**, 180 mg (2.4 mL of dimethylamine solution 2 M in THF); **2e**, 620 mg; **2f**, 582 mg, **2g**, 755 mg, **2h**: 351 mg]. The autoclave was sealed and, while the mixture was stirred, the autoclave was pressurized with CO (16 atm) and air (up to 20 atm). After being stirred at 100 °C for 6 h (for **1a**, **1c-j**) or 15 h (**1b**), the autoclave was cooled, degassed and opened. After evaporation of the solvent, products **3** were purified by column chromatography on silica gel (eluent: hexane - acetone from 9:1 to 7:3).

*Ethyl 3-(2-morpholino-2-oxoethyl)indolizine-1-carboxylate(**3aa**).* Yield: 434 mg, starting from 326 mg of **1a** (86%). Colorless solid, mp 128–130 °C. IR (film): ν = 1686 (s), 1651 (s), 1512 (m), 1447 (m), 1408 (w), 1234 (m), 1115 (w), 1076 (w), 1038 (m), 768 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.22 (dist dt, *J* = 6.9, 1.1, 1 H), 8.19 (dt, *J* = 9.1, 1.1, 1 H), 7.10 (s, 1 H), 7.08 (ddd, *J* = 9.1, 6.9, 1.1, 1 H), 6.77 (td, *J* = 6.9, 1.1, 1 H), 4.36 (q, *J* = 7.1, 2 H), 3.95 (s, 2 H), 3.65-3.55 (m, 8 H), 1.40 (t, *J* = 7.1, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.9, 164.9, 136.2, 124.2, 122.2, 119.9, 117.9, 116.1, 112.7, 103.3, 66.8, 66.5, 59.5, 46.7, 42.3, 32.6, 14.7; GC-MS (EI): *m/z* = 316 (M^+, 27), 202 (100), 174 (45), 128 (16); HRMS (ESI - TOF) *m/z*: $[M + Na]^+$ Calcd. for $C_{17}H_{20}N_2NaO_4^+$ 339.1315; Found 339.1323.

*Ethyl 3-(2-oxo-2-(piperidin-1-yl)ethyl)indolizine-1-carboxylate (**3ab**).* Yield: 412 mg, starting from 326 mg of **1a** (82%). Yellow solid, mp 82–84 °C. IR (film): ν = 1674 (s), 1636 (s), 1512 (m), 1443 (m), 1381 (w), 1304 (w), 1234 (s), 1072 (m), 1042 (w), 1007 (w), 775 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.24 (dist dt, *J* = 6.9, 1.0, 1 H), 8.18 (dist dt, *J* = 9.0, 1.1, 1 H), 7.09 (s, 1 H), 7.04 (ddd, *J* = 9.0, 6.9, 1.0, 1 H), 6.73 (td, *J* = 6.9, 1.0, 1 H), 4.35 (q, *J* = 7.1, 2 H), 3.93 (s, 2 H), 3.56–3.46 (m, 4 H), 1.62–1.56 (m, 2H), 1.52–1.41 (m, 4 H), 1.39 (t, *J* = 7.1, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.6, 164.9, 136.3, 124.4, 121.9, 119.8, 118.7, 116.1, 112.5, 103.5, 59.4, 47.5, 43.2, 32.9, 26.4, 25.6, 24.4, 14.7; GC-MS (EI): *m/z* = 314 (M^+, 23), 269 (5), 202 (100), 174 (39), 128 (15); HRMS (ESI - TOF) *m/z*: $[M + Na]^+$ Calcd. for $C_{18}H_{22}N_2NaO_3^+$ 337.1523; Found 337.1520.

*Ethyl 3-(2-oxo-2-(pyrrolidin-1-yl)ethyl)indolizine-1-carboxylate (**3ac**).* Yield: 342 mg, starting from 326 mg of **1a** (71%). Yellow solid, mp 113–115 °C. IR (film): ν = 1682 (s), 1647 (s), 1516 (m), 1443 (s), 1339 (w), 1231 (m), 1196 (m), 1076 (m), 1053 (w), 775 (m), 741 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.35 (dist dt, *J* = 6.9, 1.1, 1 H), 8.18 (dist dt, *J* = 9.0, 1.1, 1 H), 7.11 (s, 1 H), 7.07 (ddd, *J* = 9.0, 6.9, 1.1, 1 H), 6.76 (td, *J* = 6.9, 1.1, 1 H), 4.36 (q, *J* = 7.1, 2 H), 3.88 (s, 2 H), 3.53 (t, *J* = 6.9, 2 H), 3.44 (t, *J* = 6.9, 2 H), 1.94 (quintuplet, *J* = 6.9, 2H), 1.82 (quintuplet, *J* = 6.9, 2 H), 1.40 (t, *J* = 7.1, 3 H); ^{13}C NMR

(125 MHz, $CDCl_3$): δ = 166.6, 165.0, 136.2, 124.6, 122.1, 119.6, 118.1, 116.3, 112.4, 103.0, 59.4, 47.0, 46.1, 34.2, 26.2, 24.2, 14.7; GC-MS (EI): *m/z* = 300 (M^+, 27), 255 (6), 202 (100), 174 (44), 128 (16); HRMS (ESI - TOF) *m/z*: $[M + Na]^+$ Calcd. for $C_{17}H_{20}N_2NaO_3^+$ 323.1366; Found 323.1368.

*Ethyl 3-(2-(dimethylamino)-2-oxoethyl)indolizine-1-carboxylate (**3 ad**).* Yield: 365 mg, starting from 326 mg of **1 a** (83 %). Yellow solid, mp 131–132 °C. IR (film): ν = 1686 (s), 1639 (s), 1501 (m), 1439 (m), 1400 (w), 1335 (w), 1304 (w), 1180 (m), 1146 (m), 1072 (m), 1034 (w), 779 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 8.23 (dist dt, *J* = 6.9, 1.1, 1 H), 8.18 (dist dt, *J* = 9.1, 1.1, 1 H), 7.10 (s, 1 H), 7.03 (ddd, *J* = 9.1, 6.9, 1.1, 1 H), 6.73 (td, *J* = 6.9, 1.1, 1 H), 4.35 (q, *J* = 7.1, 2 H), 3.92 (s, 2 H), 3.09 (s, 3 H), 2.93 (s, 3 H), 1.39 (t, *J* = 7.1, 3 H, OCH_2CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.3, 164.9, 136.4, 124.4, 122.0, 119.8, 118.4, 116.2, 112.5, 103.4, 59.4, 37.9, 35.8, 32.8, 14.7; GC-MS (EI): *m/z* = 274 (M^+, 28), 229 (8), 202 (100), 174 (64), 128 (22); HRMS (ESI - TOF) *m/z*: $[M + Na]^+$ Calcd. for $C_{15}H_{18}N_2NaO_3^+$ 297.1210; Found 297.1213.

*Ethyl 3-(2-(dibutylamino)-2-oxoethyl)indolizine-1-carboxylate (**3 ae**).* Yield: 535 mg, starting from 326 mg of **1 a** (93 %). Yellow oil, IR (film): ν = 1682 (s), 1651 (s), 1514 (m), 1454 (w), 1381 (w), 1315 (w), 1223 (m), 1130 (w), 1070 (m), 820 (m), 775 (m), cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 8.24 (dist dt, *J* = 7.0, 1.1, 1 H), 8.19 (dt, *J* = 9.1, 1.1, 1 H), 7.09 (s, 1 H), 7.06 (ddd, *J* = 9.1, 7.0, 1.1, 1 H), 6.76 (td, *J* = 7.0, 1.1, 1 H), 4.36 (q, *J* = 7.1, 2 H), 3.93 (s, 2 H), 3.37–3.25 (m, 4 H), 1.52–1.44 (m, 4 H), 1.39 (t, *J* = 7.1, 3 H), 1.37–1.30 (m, 2 H), 1.30–1.21 (m, 2 H), 0.95 (t, *J* = 7.3, 3 H), 0.88 (t, *J* = 7.3, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.8, 165.0, 136.3, 124.4, 122.0, 119.7, 118.8, 116.0, 112.4, 103.1, 59.4, 48.3, 46.1, 32.9, 31.2, 29.8, 20.2, 20.1, 14.67, 14.65, 13.8; GC-MS (EI): *m/z* = 358 (M^+, 15), 313 (4), 281 (4), 202 (100), 174 (25), 128 (8); HRMS (ESI - TOF) *m/z*: $[M + Na]^+$ Calcd. for $C_{21}H_{30}N_2NaO_3^+$ 381.2149; Found 381.2162.

*Ethyl 3-(2-(benzyl(methyl)amino)-2-oxoethyl)indolizine-1-carboxylate (**3 af**).* (Mixture of rotamers A + B, deriving from hindered rotation around the (CO)-N amide bond: A/B ca 1.4 by ^1H NMR). Yield: 478 mg, starting from 326 mg of **1 a** (85 %). Yellow solid, mp 91–93 °C. IR (film): ν = 1694 (s), 1643 (s), 1508 (m), 1447 (m), 1416 (w), 1389 (w), 1342 (w), 1315 (m), 1192 (m), 1076 (m), 772 (m), 694 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 8.26–8.14 [m, 2 H (A) + 2 H (B)], 7.37 −7.18 [m, 4 H (A) + 4 H(B)], 7.16 - 7.08 [m, 2 H (A) + 2 H (B)], 7.07–7.00 [m, 1 H (A) + 1 H (B)], 6.77–6.69 [m, 1 H (A) + 1 H (B)], 4.63 [s, 2 H (B)], 4.55 [s, 2 H (A)], 4.38–4.30 [m, 4 H, 2 H (A) + 2 H (B)], 3.97 [s, 2 H (A)], 3.95 [s, 2 H (B)], 2.99 [s, 3 H (A)], 2.94 [s, 3 H (B)],1.41–1.34 [m, 3 H (A) + 3 H (B)]; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.9 (B), 168.4 (A), 164.8 (A + B), 137.0 (B), 136.4 (A), 129.1 (B), 128.7 (A), 128.0 (A), 127.8 (B), 127.5 (A + B), 126.3 (A + B), 124.3 (A + B), 121.9 (A + B), 119.8 (A + B), 118.2 (A + B), 116.34 (B), 116.29 (A), 112.5 (A + B), 103.5 (A + B), 59.4 (A + B), 53.9 (B), 51.4 (A), 35.4 (A), 34.4 (B), 33.0 (A), 32.7 (B), 14.7 (A + B); GC-MS (EI): *m/z* = 350 (M^+, 22), 305 (5), 202 (100), 174 (39), 128 (14), 91 (9); HRMS (ESI - TOF) *m/z*: $[M + Na]^+$ Calcd. for $C_{21}H_{22}N_2NaO_3^+$ 373.1523; Found 373.1518.

*Ethyl 3-(2-(diisopentylamino)-2-oxoethyl)indolizine-1-carboxylate (**3 ag**).* Yield: 457 mg, starting from 326 mg of **1 a** (74 %). Yellow oil, IR (film): ν = 1682 (s), 1651 (s), 1506 (s), 1456 (m), 1385 (m), 1339 (w), 1315 (w), 1223 (m), 1128 (w), 1070 (m), 775 (m), 743 (m), cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 8.24 (dist dt, *J* = 6.9, 1.0, 1 H), 8.19 (dist dt, *J* = 9.0, 1.0, 1 H), 7.09 (s, 1 H), 7.06 (ddd, *J* = 9.0, 6.9, 1.0, 1 H), 6.76 (td, *J* = 6.9, 1.0, 1 H), 4.36 (q, *J* = 7.1, 2 H), 3.92 (s, 2 H), 3.38–3.28 (m, 4 H), 1.60 (heptuplet, *J* = 6.7, 1 H), 1.52 (heptuplet, *J* = 6.7, 1 H), 1.43–1.36 (m, 4 H), 1.40 (t, *J* = 7.1, 3 H), 0.95 (d, *J* = 6.7, 3 H), 0.89 (d, *J* = 6.7, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.7, 165.0, 136.3, 124.4, 122.0, 119.7, 118.9, 116.1, 112.5, 103.2, 59.4, 47.0, 44.8, 37.9, 36.5, 32.8, 26.3, 22.6, 22.5, 14.73, 14.69; GC-MS (EI): *m/z* = 386 (M^+, 12), 341 (3), 202 (100), 174 (22), 128 (8); HRMS (ESI - TOF) *m/z*: $[M + Na]^+$ Calcd. for $C_{23}H_{34}N_2NaO_3^+$ 409.2462; Found 409.2472.

*Ethyl 3-(2-morpholino-2-oxoethyl)-6-nitroindolizine-1-carboxylate (**3 ba**).* Yield: 348 mg, starting from 397 mg of **1 b** (60 %). Yellow solid, mp 154–156 °C. IR (KBr): ν = 1690 (s), 1651 (s), 1543 (m), 1512 (w), 1450 (s), 1389 (w), 1319 (s), 1234 (vs), 1119 (s), 1034 (m), 795 (w), 772 (m), cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 9.28 (d, *J* = 1.6, 1 H), 8.23 (d, *J* = 9.9, 1 H), 7. 75 (dd, *J* = 9.9, 1.6, 1 H), 7.25 (s, 1 H), 4.37 (q, *J* = 7.1, 2 H), 4.04 (s, 2 H), 3.76–3.59 (m, 8 H), 1.40 (t, *J* = 7.1); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.2, 163.9, 137.3, 135.7, 125.1, 121.7, 119.54, 119.46, 115.2, 106.8, 66.8, 66.4, 60.2, 46.6, 42.4, 31.3, 14.6; GC/MS (EI): *m/z* = 361 (M^+, 17), 316 (3), 247 (100), 231 (7), 219 (25), 201 (15), 173 (16), 128 (15), 114 (7); HRMS (ESI - TOF) *m/z*: $[M + Na]^+$ Calcd. for $C_{17}H_{19}N_3NaO_6^+$ 384.1166; Found 384.1179.

*Methyl 3-(2-morpholino-2-oxoethyl)indolizine-1-carboxylate (**3 ca**).* Yield: 460 mg, starting from 303 mg of **1 c** (95 %). Colorless solid, mp 204–207 °C. IR (film): ν = 1690 (s), 1639 (s), 1508 (m), 1439 (m), 1385 (w), 1234 (m), 1115 (m), 1072 (m), 775 (m), cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 8.21 (dt, *J* = 6.8, 1.2, 1 H), 8.19 (dist dt, *J* = 9.0, 1.2, 1 H), 7.08 (s, 1 H), 7.08 (ddd, *J* = 9.0, 6.8, 1.2, 1 H), 6.78 (td, *J* = 6.8, 1.2, 1 H), 3.95 (s, 2 H), 3.88 (s, 3 H), 3.65–3.56 (m, 8 H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.8, 165.2, 136.3, 124.2, 122.3, 119.7, 118.0, 116.0, 112.7, 102.9, 66.7, 66.4, 50.9, 46.6, 42.3, 32.5; GC-MS (EI): *m/z* = 302 (M^+, 15), 271 (4), 188 (100), 158 (2), 128 (16); HRMS (ESI - TOF) *m/z*: $[M + Na]^+$ Calcd. for $C_{16}H_{18}N_2NaO_4^+$ 325.1159; Found 325.1167.

*Isopropyl 3-(2-morpholino-2-oxoethyl)indolizine-1-carboxylate (**3 da**).* Yield: 450 mg, starting from 348 mg of **1 d** (85 %). Colorless solid, mp 149–150 °C. IR (film): ν = 1690 (vs), 1508 (m), 1443 (m), 1408 (w), 1227 (s), 1119 (m), 1076 (s), 1037 (m), 1018 (m), 775 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 8.21–8.16 (m, 2 H), 7.09 (s, 1 H), 7.09–7.04 (m, 1 H), 6.75 (dist t, *J* = 6.7, 1 H, H-7), 5.26 (heptuplet, *J* = 6.0, 1 H), 3.94 (s, 2 H), 3.65–3.54 (m, 8 H), 1.38 (d, *J* = 6.0, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.9, 164.4, 136.1, 124.1, 122.0, 119.8, 117.8, 116.1, 112.5, 103.6, 66.7, 66.6, 66.4, 46.6, 42.3, 32.4, 22.3; GC-MS (EI): *m/z* = 330 (M^+, 27), 271 (8), 216 (97), 174 (100), 128 (14); HRMS (ESI - TOF) *m/z*: $[M + Na]^+$ Calcd. for $C_{18}H_{22}N_2NaO_4^+$ 353.1472; Found 353.1464.

*2-(1-Acetylindolizin-3-yl)-1-morpholinoethan-1-one (**3 ea**).* Yield: 233 mg, starting from 277 mg of **1 e** (51 %). Yellow solid, mp 179–181 °C; IR (KBr): ν = 1643 (s), 1620 (s), 1504 (s), 1443 (m), 1366 (m), 1304 (w), 1234 (m), 1111 (m), 1034 (w), 925 (w), 748 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 8.46–8.41 (m, 1 H), 8.15–8.11 (m, 1 H), 7.19–7.13 (m, 1 H), 7.01 (s, 1 H), 6.84 (td, *J* = 6.8, 1.2, 1 H), 3.96 (s, 2 H), 3.68–3.56 (m, 8 H), 2.49 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 192.5, 166.9, 135.9, 123.8, 123.7, 120.6, 118.1, 116.3, 113.6, 112.7, 66.8, 66.4, 46.6, 42.3, 32.1, 27.9; GC/MS (EI): *m/z* = 286 (M^+, 22), 172 (100), 129 (13); HRMS (ESI - TOF) *m/z*: $[M + Na]^+$ Calcd. for $C_{16}H_{18}N_2NaO_3^+$ 309.1210; Found 309.1215.

*2-(1-Acetyl-5-methylindolizin-3-yl)-1-morpholinoethan-1-one (**3 fa**).* Yield: 270 mg, starting from 300 mg of **1 f** (56 %). Yellow solid, mp 173–175 °C; IR (KBr): ν = 1643 (vs), 1504 (s), 1443 (s), 1358 (w), 1265 (m), 1150 (w), 1111 (m), 1034 (m), 949 (m), 795 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 8.42 (d, *J* = 8.9, 1 H), 6.98 (dd, *J* = 8.9, 6.7, 1 H), 6.92 (s, 1 H), 6.48 (d, *J* = 6.7, 1 H), 4.19 (s, 2 H), 3.73–3.64 (m, 6 H), 3.55–3.51 (m, 2 H), 2.73 (s, 3 H), 2.46 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 192.3, 168.9, 138.5, 135.4, 124.0, 120.0, 119.4, 119.0, 115.6, 112.1, 66.9, 66.6, 46.2, 42.3, 35.2, 28.0, 21.0; GC/MS (EI): *m/z* = 300 (M^+, 13), 186 (100), 168 (3), 143 (12); HRMS (ESI - TOF) *m/z*: $[M + Na]^+$ Calcd. for $C_{17}H_{20}N_2NaO_3^+$ 323.1366; Found 323.1373.

*2-(1-Acetyl-7-methylindolizin-3-yl)-1-morpholinoethan-1-one (**3 ga**).* Yield: 263 mg, starting from 300 mg of **1 g** (55 %). Yellow solid, mp 201–203 °C; IR (KBr): ν = 1643 (vs), 1504 (m), 1435 (m), 1358 (m), 1277 (w), 1231 (m), 1119 (m), 1072 (w), 1038 (w), 941 (m), 856 (w), 802 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 8.25 (s, br, 1 H), 8.04 (d,

J = 7.1, 1 H), 6.94 (s, 1 H), 6.68 (dd, *J* = 7.1, 1.7, 1 H), 3.93 (s, 2 H), 3.67–3.55 (m, 8 H), 2.47 (s,3 H), 2.39 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 192.3, 167.0, 136.5, 135.1, 123.4, 119.1, 117.4, 116.21, 116.19, 111.5, 66.8, 66.5, 46.6, 42.3, 32.2, 27.9, 21.3; GC-MS (EI): *m/z* = 300 (M^+, 14), 186 (100), 143 (16); HRMS (ESI - TOF) *m/z*: [M + Na]$^+$ Calcd. for $C_{17}H_{20}N_2NaO_3^+$ 323.1366; Found 323.1373.

*2-(1-Acetylindolizin-3-yl)-N,N-diethylacetamide (**3eh**).* Yield: 344 mg, starting from 277 mg of **1e** (79%).Yellow solid, mp: 110–113 °C; IR (KBr): ν = 1643 (s), 1628 (s), 1497 (s), 1435 (m), 1373 (m), 1265 (m), 1142 (m), 1011 (w), 926 (m), 756 (s) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.44 (d, *J* = 9.0, 1 H), 8.15 (d, *J* = 7.0, 1 H), 7.17–7.11 (m, 1 H), 7.01 (s, 1 H), 6.82 (t, *J* = 7.0, 1 H), 3.93 (s, 2 H), 3.45 (q, *J* = 7.1, 2 H), 3.40 (q, *J* = 7.1, 2 H), 2.50 (s, 3 H), 1.18 (t, *J* = 7.1, 3 H), 1.13 (t, *J* = 7.1, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 192.5, 167.4, 135.9, 124.0, 123.6, 120.5, 118.9, 116.4, 113.4, 112.6, 42.6, 40.6, 32.3, 27.9, 14.4, 13.0; GC/MS (EI): *m/z* = 272 (M^+, 20), 172 (100), 154 (1), 143 (2), 129 (13), 100 (2); HRMS (ESI - TOF) *m/z*: [M + Na]$^+$ Calcd. for $C_{16}H_{20}N_2NaO_2^+$ 295.1417; Found 295.1424.

*2-(1-Acetyl-5-methylindolizin-3-yl)-N,N-diethylacetamide (**3fh**).* Yield: 370 mg, starting from 300 mg of **1f** (81%). Yellow solid, mp 111–114 °C; IR (KBr): ν = 1636 (s), 1612 (s), 1512 (s), 1443 (s), 1358 (m), 1265 (m), 1157 (m), 1080 (w), 949 (m), 779 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.45-8.41 (m, 1 H), 6.97 (dd, *J* = 8.9, 6.7, 1 H), 6.92 (s, 1 H), 6.47 (d, *J* = 6.7, 1 H), 4.17 (s, 2 H), 3.43 (q, *J* = 7.1, 2 H), 3.39 (q, *J* = 7.1, 2 H), 2.72 (s, 3 H), 2.47 (s, 3 H), 1.26 (t, *J* = 7.1, 3 H), 1.17 (t, *J* = 7.1, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 192.4, 169.3, 138.5, 135.5, 123.8, 120.9, 119.4, 119.0, 115.5, 112.1, 42.2, 40.6, 35.4, 27.9, 20.9, 14.3, 12.9; GC/MS (EI): *m/z* = 286 (M^+, 13), 186 (100), 168 (2), 143 (10); HRMS (ESI - TOF) *m/z*: [M + Na]$^+$ Calcd. for $C_{17}H_{22}N_2NaO_2^+$ 309.1573; Found 309.1576.

*2-(1-Acetyl-7-methylindolizin-3-yl)-N,N-diethylacetamide (**3gh**).* Yield: 366 mg, starting from 300 mg of **1g** (80%). Yellow solid, mp 149–150 °C; IR (KBr): ν = 1628 (vs), 1504 (m), 1358 (m), 1250 (m), 1138 (w), 1077 (w), 941 (m), 802 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.27–8.21 (m, 1 H), 8.07 (d, *J* = 7.0, 1 H), 6.93 (s, 1 H), 6.66 (dd, *J* = 7.0, 1.8, 1 H), 3.90 (s, 2 H), 3.44 (q, *J* = 7.1, 2 H), 3.38 (q, *J* = 7.1, 2 H), 2.48 (s, 3 H), 2.38 (s, 3 H), 1.16 (t, *J* = 7.1, 3 H), 1.12 (t, *J* = 7.1, 3 H) ^{13}C NMR (125 MHz, $CDCl_3$): δ = 192.4, 167.5, 136.5, 135.0, 123.6, 119.1, 118.3, 116.3, 116.1, 111.5, 42.6, 40.6, 32.5, 27.9, 21.3, 14.4, 13.0; GC/MS (EI): *m/z* = 286 (M^+, 18), 186 (100), 143 (13); HRMS (ESI - TOF) *m/z*: [M + Na]$^+$ Calcd. for $C_{17}H_{22}N_2NaO_2^+$ 309.1573; Found 309.1582.

*2-(1-Benzoylindolizin-3-yl)-N,N-diethylacetamide (**3hh**).* Yield: 487 mg, starting from 376 mg of **1h** (91%). Yellow solid, mp 85–87 °C; IR (KBr): ν = 1628 (s), 1597 (s), 1493 (s), 1420 (s), 1358 (m), 1250 (m), 1130 (s), 1018 (m), 872 (s), 760 (s) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.49–8.44 (m, 1 H), 8.24 (d, *J* = 6.9, 1 H), 7.82–7.77 (m, 2 H), 7.52–7.42 (m, 3 H), 7.21–7.16 (m, 1 H), 6.91 (s, 1 H), 6.86 (td, *J* = 6.9, 1.1, 1 H), 3.92 (s, 2 H), 3.43–3.33 (m, 4 H), 1.14 (t, *J* = 7.1, 3 H), 1.09 (t, *J* = 7.1, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 190.1, 167.3, 141.3, 137.5, 130.6, 128.8, 128.1, 124.3, 123.9, 120.6, 119.2, 118.2, 113.8, 111.5, 42.5, 40.5, 32.5, 14.3, 12.9; GC/MS (EI): *m/z* = 334 (M^+, 15), 234 (100), 204 (5), 129 (4); HRMS (ESI - TOF) *m/z*: [M + Na]$^+$ Calcd. for $C_{21}H_{22}N_2NaO_2^+$ 357.1573; Found 357.1577.

*2-(5-Chloro-1-(2-methylbenzoyl)indolizin-3-yl)-1-morpholinoethan-1-one (**3ia**).* Yield: 469 mg, starting from 454 mg of **1i** (74%). Yellow oil; IR (KBr): ν = 1643 (s), 1586 (m), 1555 (m), 1454 (m), 1273 (w), 1246 (m), 1115 (s), 1038 (m), 988 (w), 775 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.37–7.32 (m, 3 H), 7.31–7.28 (m, 1 H), 7.25–7.21 (m, 1 H), 7.07 (dd, *J* = 7.8, 0.7, 1 H), 6.92 (t, *J* = 0.7, 1 H), 6.87 (dd, *J* = 7.8, 0.7, 1 H), 3.82 (d, *J* = 0.6, 2 H), 3.70–3.61 (m, 6 H), 3.60–3.55 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.9, 152.9, 151.16, 150.92, 148.2, 138.6, 137.9, 130.6, 129.6, 126.0, 123.1, 121.6, 119.5, 109.2, 66.8, 66.6, 46.6, 42.3, 33.9, 19.9; GC/MS (EI): *m/z* = 398 [(M+2)$^+$, 11], 396 (M^+, 29), 360 (46), 284 (35), 282 (100), 246 (36), 219 (15), 129 (27), 114 (48); HRMS (ESI - TOF) *m/z*: [M + Na]$^+$ Calcd. for $C_{22}H_{21}ClN_2NaO_3^+$ 419.1133; Found 419.1142.

*N-Methyl-3-(2-morpholino-2-oxoethyl)-N-phenylindolizine-1-carboxamide (**3ja**).* Yield: 417 mg, starting from 423 mg of **1j** (69%). Colorless solid, mp 137–138 °C; IR (KBr): ν = 1651 (s), 1589 (s), 1504 (m), 1431 (m), 1223 (m), 1088 (m), 961 (m), 764 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.36 (dt, *J* = 9.1, 1.2, 1 H), 8.09 (dt, *J* = 6.9, 1.2, 1 H,), 7.36–7.31 (m, 2 H), 7.30–7.20 (m, 3 H), 7.00 (ddd, *J* = 9.1, 6.9, 1.2, 1 H), 6.70 (td, *J* = 6.9, 1.2, 1 H), 5.62 (s, 1 H), 3.67 (s, 2 H), 3.59–3.54 (m, 2 H), 3.52–3.45 (m, 2 H,), 3.46 (s, 3 H), 3.43–3.39 (m, 2 H), 3.15–3.09 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.8, 166.1, 146.4, 137.0, 129.4, 127.6, 126.4, 123.4, 121.1, 120.6, 116.0, 115.5, 112.5, 106.0, 66.7, 66.3, 46.5, 42.1, 38.4, 32.7; GC/MS (EI): *m/z* = 377 (M^+, 24), 271 (100), 263 (38), 184 (22), 158 (7), 129 (56); HRMS (ESI - TOF) *m/z*: [M + Na]$^+$ Calcd. for $C_{22}H_{23}N_3NaO_3^+$ 400.1632; Found 400.1645.

*3-(2-(Diethylamino)-2-oxoethyl)-N-methyl-N-phenylindolizine-1-carboxamide (**3jh**).* Yield: 384 mg, starting from 423 mg of **1j** (66%). Colorless solid, mp 182–183 °C; IR (KBr): ν = 1647 (s), 1605 (s), 1497 (m), 1381 (m), 1261 (m), 1157 (m), 1084 (m), 744 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.35 (dt, *J* = 9.1, 1.2, 1 H), 8.11 (dt, *J* = 6.9, 0.9, 1 H,), 7.34–7.27 (m, 2 H), 7.26–7.19 (m, 3 H), 6.98 (ddd, *J* = 9.1, 6.9, 0.9, 1 H), 6.68 (td, *J* = 6.9, 1.2, 1 H), 5.60 (s, 1 H), 3.62 (s, 2 H), 3.47 (s, 3 H), 3.27 (q, *J* = 7.1, 2 H), 3.05 (q, *J* = 7.1, 2 H), 1.03 (t, *J* = 7.1, 3 H), 0.97 (t, *J* = 7.1, 3 H);^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.4, 166.2, 146.3, 137.0, 129.3, 127.6, 126.4, 123.5, 121.0, 120.5, 117.0, 115.4, 112.3, 105.8, 42.4, 40.5, 38.4, 33.1, 14.2, 13.0; GC/MS (EI): *m/z* = 363 (M^+, 23), 263 (64), 257 (100), 184 (19), 158 (8), 129 (61); HRMS (ESI - TOF) *m/z*: [M + Na]$^+$ Calcd. for $C_{22}H_{25}N_3NaO_2^+$ 386.1839; Found 386.1852.

Supporting Information

The authors have cited additional references within the Supporting Information.[20–25]

Acknowledgements

Financial support by MUR PRIN 20223B4JWC project (Valorization of carbon oxides by sequential catalysis: Combining the reverse water gas shift reaction with catalytic carbonylation for the synthesis of high value added compounds – COXSECAT) to B.G. is acknowledged.

Conflict of Interests

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Keywords: carbonylation · cyclization · fluorophores · indolizines · palladium catalysis

[1] For reviews on bioactivity of indolizines, see: a) K. M. Dawood, A. A. Abbas, *Expert Opin. Ther. Pat.* **2020**, *30*, 695–714; b) V. Sharma, V. Kumar, *Med. Chem. Res.* **2014**, *23*, 3593–3606; c) G. S. Singh, E. E. Mmatli, *Eur. J. Med. Chem.* **2011**, *46*, 5237–5257; d) V. R. Vemula, S. Vurukonda, C. K. Bairi, *Int. J. Pharm. Sci. Res.* **2011**, *11*, 159–163.

[2] For a review, see: E. Kim, Y. Lee, S. Lee, S. B. Park, *Acc. Chem. Res.* **2015**, *48*, 538–547.

[3] For reviews, see: a) Priyanka, P. Rani, Kiran, J. Sindhu, *ChemistrySelect* **2023**, *8*, e202203531; b) E. V. Babaev, I. A. Shadrin, *Molecules* **2021**, *26*, 2050; c) K. M. Elattar, I. Youssef, A. A. Fadda, *Synth. Commun.* **2016**, *46*, 719–744.

[4] For reviews, see: a) J. Hui, Y. Ma, J. Zhao, H. Cao, *Org. Biomol. Chem.* **2021**, *19*, 10245–10258; b) S. Dong, X. Fu, X. Xu, *Asian J. Org. Chem.* **2020**, *9*, 1133–1143; c) L.-X. Wang, Y.-L. Tang, *Eur. J. Org. Chem.* **2017**, 2207–2213; d) B. Sadowski, J. Klajn, D. T. Gryko, *Org. Biomol. Chem.* **2016**, *14*, 7804–7828.

[5] a) T. P. Lebold, P. Bonaventure, B. T. Shireman, *Bioorg. Med. Chem. Lett.* **2013**, *23*, 4761–4769; b) K. S. Takaki, J. R. Epperson, *Ann. Rep. Med. Chem.* **1999**, *34*, 41–50.

[6] J. M. Bentley, T. Davenport, D. J. Hallett, *PCT Pat. Appl.* WO 2011/138266, **2011**.

[7] a) K. D. Mane, S. S. Bagwe, S. G. More, G. Suryavanshi, *Tetrahedron Lett.* **2023**, *118*, 154386; b) E. Sathish, A. K. Gupta, Deeksha, S. K. Mishra, D. M. Sawant, R. Singh, *J. Org. Chem.* **2022**, *87*, 14168–14176; c) M. Van Eis, P. Von Matt, J. Wagner, *PCT Pat. Appl.* WO 2008/074752, **2008**.

[8] C.-B. Miao, H.-R. Guan, Y. Tang, K. Wang, W.-L. ren, X. Lyu, C. Yao, H.-T. Yang, *Org. Lett.* **2021**, *23*, 8699–8704.

[9] For recent books and reviews on carbonylation chemistry, see: a) B. Gabriele, Ed. *Carbon Monoxide in Organic Synthesis–Carbonylation Chemistry*, Wiley-VCH, Weinheim, 2021; b) B. Gabriele, R. Mancuso, N. Della Ca', L. Veltri, I. Ziccarelli, *Catalysts* **2023**, *13*, 1025; c) A. Yamini, A. Kumar, P. Das, *ChemistrySelect* **2023**, *8*, e202204453; d) C. M. A. Afsina, R. M. Philip, P. V. Sanarya, G. Anikumar, *Curr. Org. Synth.* **2023**, *20*, 308–331; e) Q. Tian, X. Yin, R. Sun, X.-F. Wu, Y. Li, *Coord. Chem. Rev.* **2023**, *475*, 214900; f) X. Yan, L. Fan, X. Zhang, G. Liu, *Org. Chem. Front.* **2022**, *9*, 6749–6765; g) J.-X. Xu, L.-C. Wang, X.-F. Wu, *Chem. Asian J.* **2022**, *17*, e202200928; h) N. T. Sevostyanova, S. A. Batashev, *Russ. J. Appl. Chem.* **2022**, *95*, 1085–1106; i) D. Y. de Albuquerque, W. K. O. Teixeira, S. Narayanaperumal, R. S. Schwab, *J. Braz. Chem. Soc.* **2022**, *33*, 637–663; j) T. Kawamoto, T. Fukuyama, B. Picard, I. Ryu, *Chem. Commun.* **2022**, *58*, 7608–7617; k) J.-X. Xu, C.-S. Kuai, B. Chen, X.-F. Wu, *Chem. Catal.* **2022**, *2*, 477–498; l) J.-B. Peng, X.-L. Liu, L. Li, X.-F. Wu, *Sci. China Chem.* **2022**, *65*, 441–461; m) T. R. Kegl, L. T. Mika, T. Kegl, *Molecules* **2022**, *27*, 460; n) Shaifali, Sheetal, P. Das, *Chem. Rec.* **2022**, *22*, e202100157; o) Y. Shi, C. Xia, Y. Huang, L. He, *Chem. Asian J.* **2021**, *16*, 2830–2841; p) V. Botla, A. Voronov, E. Motti, C. Carfagna, R. Mancuso, B. Gabriele, N. Della Ca', *Catalysts* **2021**, *11*, 918; q) L.-J. Cheng, N. P. Mankad, *Acc. Chem. Res.* **2021**, *54*, 2261–2274; r) Y. Tan, J. Lang, M. Tang, J. Li, P. Mi, X. Zheng, *ChemistrySelect* **2021**, *6*, 2343–2349; s) S. Cai, H. Zhang, H. Huang, *Trends Chem.* **2021**, *3*, 218–230; t) R. Sang, Y. Hu, R. Razzaq, R. Jackstell, R. Franke, M. Beller, *Org. Chem. Front.* **2021**, *8*, 799–811; u) S. Zhang, H. Neumann, M. Beller, *Chem. Soc. Rev.* **2020**, *49*, 3187–3210; v) J. B. Peng, H, -Q. Geng, X.-F. Wu, *Chem* **2019**, *5*, 526–552.

[10] a) B. Gabriele, M. Costa, G. Salerno, G. P. Chiusoli, *J. Chem. Soc. Chem. Commun.* **1992**, 1007–1008; b) B. Gabriele, M. Costa, G. Salerno, G. P. Chiusoli, *J. Chem. Soc. Perkin Trans. 1* **1994**, 83–87.

[11] For reviews and accounts, see: a) R. Mancuso, N. Della Ca', L. Veltri, I. Ziccarelli, B. Gabriele, *Catalysts* **2019**, *9*; 610; b) B. Gabriele, *Targets Heterocycl. Syst.* **2018**, *22*, 41–55; c) B. Gabriele, Synthesis of Heterocycles by Palladium-Catalyzed Carbonylation Reactions. In: *Advances in Transition-Metal Mediated Heterocyclic Synthesis*, Chapter 3; D. Solé, I. Fernández (Eds.), Academic Press-Elsevier, London, 2018; d) B. Gabriele, R. Mancuso, G. Salerno, *Eur. J. Org. Chem.* **2012**, *2012*, 6825–6839; e) B. Gabriele, G. Salerno, M. Costa, *Top. Organomet. Chem.* **2006**, *18*, 239–272; f) B. Gabriele, G. Salerno, M. Costa, G. P. Chiusoli, *Curr. Org. Chem.* **2004**, *8*, 919–946; g) B. Gabriele, PdI_2, in: D. Crich (Ed.), *e*-EROS (electronic Encyclopedia of Reagents for Organic Synthesis), Wiley-Interscience, **2006**; h) B. Gabriele, G. Salerno, M. Costa, *Synlett* **2004**, 2468–2483; i) B. Gabriele, G. Salerno, M. Costa, G. P. Chiusoli, *J. Organomet. Chem.* **2003**, *687*, 219–228.

[12] For very recent examples, see: a) R. Mancuso, A. De Salvo, P. Russo, A. Falcicchio, N. Della Ca', L. Pantoja Munoz, B. Gabriele, *Chin. J. Chem.* **2023**, *41*, DOI: 10.1002/cjoc.202300277; b) R. Mancuso, S. Cuglietta, R. Strangis, B. Gabriele, *J. Org. Chem.* **2023**, *88*, 5180–5186; c) L. Veltri, R. Amuso, T. Prestia, P. Vitale, B. Gabriele, *Eur. J. Org. Chem.* **2022**, e202200916; d) I. Ziccarelli, R. Mancuso, F. Giacalone, C. Calabrese, V. La Parola, A. De Salvo, N. Della Ca', M. Gruttadauria, B. Gabriele, *J. Catal.* **2022**, *413*, 1098–1110; e) R. Mancuso, I. Ziccarelli, M. Novello, C. Cuocci, R. Centore, N. Della Ca', D. Olivieri, C. Carfagna, B. Gabriele, *J. Catal.* **2022**, *405*, 164–182; f) R. Mancuso, P. Russo, R. Miliè, M. Dell'Aera, F. Grande, N. Della Ca', B. Gabriele, *Catal. Today* **2022**, *397–399*, 631–638; g) R. Mancuso, P. Russo, M. Lettieri, D. Santandrea, C. Cuocci, B. Gabriele, *Adv. Synth. Catal.* **2022**, *364*, 3917–3926; h) R. Mancuso, M. Lettieri, I. Ziccarelli, P. Russo, A. Palumbo Piccionello, B. Gabriele, *Adv. Synth. Catal.* **2021**, *363*, 4612–4620; i) R. Mancuso, I. Ziccarelli, M. Brindisi, C. D. Altomare, L. Frattaruolo, A. Falcicchio, N. Della Ca', A. Cappello, B. Gabriele, *Catalysts* **2021**, *11*, 227; j) L. Veltri, T. Prestia, P. Russo, C. Carfagna, C. Clementi, P. Vitale, F. Ortica, B. Gabriele, *ChemCatChem* **2021**, *13*, 990–998; k) R. Mancuso, R. Strangis, I. Ziccarelli, N. Della Ca', B. Gabriele, *J. Catal.* **2021**, *393*, 335–343; l) F. Pancrazzi, N. sarti, P. P. Mazzeo, A. Bacchi, C. Carfagna, R. Mancuso, B. Gabriele, M. Costa, A. Stirling, N. Della Ca', *Org. Lett.* **2020**, *22*, 1569–1574; m) L. Veltri, P. Russo, T. Prestia, P. Vitale, R. Romeo, B. Gabriele, *J. Catal.* **2020**, *386*, 53–59.

[13] For a recent interesting work on a Pd-catalyzed multicomponent reaction, see: H. Hikawa, T. Nakayama, M. Takahashi, S. Kikkawa, I. Azumaya, *Adv. Synth. Catal.* **2021**, *363*, 4075–4084.

[14] B. Gabriele, G. Salerno, L. Veltri, M. Costa, *J. Organomet. Chem.* **2001**, *622*, 84–88.

[15] R. Mancuso, D. S. Raut, N. Della Ca', F. Fini, C. Carfagna, B. Gabriele, *ChemSusChem* **2015**, *8*, 2204–2211.

[16] a) R. Sarkar, T. Chaudhuri, A. Karmakar, C. Mukhopadhyay, *Org. Biomol. Chem.* **2015**, *13*, 11674–11686; b) Y.-C. Yuan, T.-Z. Liu, B.-X. Zhao, *J. Org. Chem.* **2021**, *86*, 12737–12744.

[17] a) D. A. Lerner, P. M. Horowitz, E. M. Evleth, *J. Phys. Chem.* **1977**, *81*, 12–17; b) D. A. Lerner, E. M. Evleth, *Chem. Phys. Lett.* **1972**, *15*, 260–262.

[18] C.-X. Zhao, T. Liu, M. Xu, H. Lin, C.-J. Zhang, *Chin. Chem. Lett.* **2021**, *32*, 1925–1928.

[19] J. C. De Mello, H. F. Wittmann, R. H. Friend, *Adv. Mater.* **1997**, *9*, 230–232.

[20] J. L. Chen, S. Namirembe, L. T. Lauchert, J. H. Tsougranis, A. K. Isaacs, *Tetrahedron Lett.* **2015**, *56*, 4105–4108.

[21] R. C. Illig, S. K. Ballentine, J. Chen, R. L. Desjariais, S. K. Meegalla, M. Wall, K. Wilson (Janssen pharmaceutica), *Pat. Appl.* WO 2011/138266, **2011**.

[22] H. B. Jalani, D. Lee, J.-Y. Lee, J.-H. Jeong, *J. Heterocycl. Chem.* **2023**, *60*, 825–833.

[23] T. Broese, P. Ehlers, P. Langer, J. Von Langermann, *ChemBioChem* **2021**, *22*, 3314–3318.

[24] M. Graser, H. Kopacka, K. Wurst, T. Müller, B. Bildstein, *Inorg. Chim. Acta* **2013**, *401*, 38–49.

[25] C. Dey, E. Larionov, E. P. Kuendig, *Org. Biomol. Chem.* **2013**, *11*, 6734–6743.

Manuscript received: January 4, 2024
Revised manuscript received: January 18, 2024
Accepted manuscript online: January 19, 2024
Version of record online: February 2, 2024