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[2+2+2] Cycloadditions

Air-Stable CpCo^{I}–Phosphite–Fumarate Precatalyst in Cyclization Reactions: Comparing Different Methods of Energy Supply

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Abstract: The robust Co^{I} precatalyst [CpCo(P{OEt}$_3$)(*trans*-MeO$_2$CHC=CHCO$_2$Me)] was investigated in cyclotrimerizations, furnishing benzenes and pyridines from triynes, diynes and nitriles, comparing the influence of different ways of energy supply; namely, irradiation and conventional (thermal) or microwave heating. The precatalyst was found to work under all conditions, including the possibility to catalyze cyclotrimerizations at room temperature under photochemical conditions at longer reaction times. Performance of the reactions in a microwave reactor proved to be the most time-efficient way to rapidly assemble the expected reaction products; however, careful selection of reaction conditions can be required. The synthesis of pyridines and isoquinolines successfully involved the utilization of versatile functionalized nitriles, affording structurally interesting reaction products. Comparison with the known and often applied precatalyst CpCo(CO)$_2$ demonstrated the significantly higher reactivity of the CpCo^{I}–phosphite–olefin precatalyst.

Introduction

The development of isolable transition-metal catalysts for organic transformations is today often outrun by the invention of in situ generated transition-metal catalyst system. The most significant advantage of the latter approach is the flexibility in terms of the broad choice of metal sources and ligands that can be screened together, including different metal-to-ligand ratios and the additional use of different beneficial additives. An area that is currently intensively investigated and includes both approaches, isolated precatalysts as well as in situ catalyst generation, lies the field of C–H activation by base metal complexes such as cobalt.[1] Inherent to the application of molecularly defined transition-metal precatalysts is that they usually yield only a single defined reactive species upon activation. This way, cleaner catalytic reactions are usually observed and mechanistic studies of a certain reaction becomes possible without the interference of additional substances from an alternative in situ generation procedure.

The recent developments in the area of cyclotrimerization reactions of alkynes, diynes, oligoynes and heterocumulenes were nursed by both approaches of catalyst employment.[2,3] Numerous studies by the groups of Okamoto, Hilt and others promoted the application of catalysts generated from simple cobalt(II) salts, appropriate ligands and reductants for the application in cyclotrimerizations.[2c,4] However, the prime catalyst source for cobalt-mediated and -catalyzed [2+2+2] cycloadditions is cyclopentadienyl cobalt(I) dicarbonyl [CpCo(CO)$_2$, **1**], introduced by Vollhardt et al. in their classical synthetic studies applying the cobalt-catalyzed cyclizations for the synthesis of annelated benzenes and finally in estrone total synthesis.[5,6] Even today, this commercially available complex remains the catalyst of choice for many cobalt-catalyzed cyclotrimerizations, although it usually requires significant amounts of energy for activation. Applications include the synthesis of natural products, especially those containing heterocyclic cores; examples for both include angucyclinones,[7] (dehydro)tylophorine,[8] (+)-complanadine A,[9] xylarinol A,[10] and, recently, cyclopropylallocolchicinoid[11] and (±)-allocolchicine.[12] Earlier reports on the photochemistry of CpCo(CO)$_2$ (**1**) discussing the possibility of the formation of clusters being regularly responsible for catalyzing the cyclotrimerizations have not been corroborated yet.[13] Recent studies only discuss mononuclear CpCo^{I} species as being responsible catalytic species.

When comparing the reaction conditions in the different synthetic routes, in most cases, rather high temperatures up to 150 °C (conventional heating) or 200 °C (microwave) are required, in some cases together with additional irradiation.[14] Such reaction conditions are necessitated by the tight bonding of the CO groups to the Co^{I} center in **1** (Scheme 1). Highly reactive CpCo(olefin)$_2$ complexes such as **2** were introduced by Jonas et al. in the beginning of the 1980s and were utilized in a number of cases for cyclotrimerizations under very mild conditions.[15] Butenschön et al. found that phosphoryl-tethered Cp′Co(C_2H_4) complexes are still active catalysts at 25 °C.[16] Aubert and Gandon et al. presented the first "upgraded" and air-stable CpCo^{I} carbonyl complex **3**, containing an electron-

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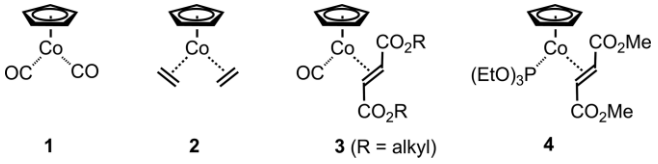
deficient dialkyl fumarate ligand instead of the second CO ligand, obtained by heating in toluene under reflux and irradiation.[17] Whereas precatalysts such as **3** are easy to handle, high temperatures are still required for application in cyclotrimerizations [typically refluxing toluene (110 °C) or microwave conditions (DMF, 200 °C)] due to strong bonding to the carbonyl ligand. Recently, the direct thermolysis of several examples of substituted enediynes and enynenitriles applying microwave heating (200 °C) without a catalyst was reported to yield highly substituted benzenes and pyridines.[18]



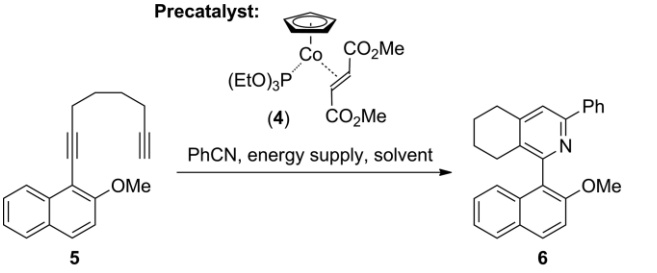
Scheme 1. CpCo^{I} catalysts: often utilized and novel precatalysts.

During our studies on novel derivatives of the Jonas complex **2**, we found that trimethylvinylsilane was a particular alkene ligand, and the Jonas complex congener with this alkene was extremely reactive in co-cyclotrimerizations with diynes and nitriles.[19] Taming the reactivity by selectively exchanging one alkene with a phosphite ligand led to CpCo^{I} complexes with mixed ligand sets, which could be used for cyclizations already at 50 °C.[20] With the clearly attractive olefin/phosphite combination we set out for further exploration and found that a phosphite ligand together with dimethylfumarate furnished air-stable and recyclable CpCo^{I} complexes such as **4**, which can easily be applied to cyclotrimerization reactions[21] and has since become commercially available.[22] This particular ligand combination also allows the efficient stabilization of functionalized Cp'Co-fragments.[23]

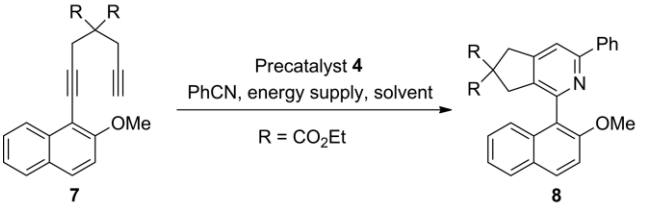
Showcase applications of **4** in several synthetic projects already proved to be beneficial,[24] leaving us with the idea to explore different reaction conditions in terms of the energy supply to determine more precisely the requirements and circumstances under which complex **4** can be successfully applied. Especially the application of irradiation vs. conventional heating/microwave to activate the catalyst appears to be attractive, as there are not many reports on precatalysts that can be efficiently activated under both activation methods. Microwave irradiation of Co-mediated cyclotrimerizations in glass reaction vessels is reported to be additionally favored by reduced induction periods and increased triplet life time of organometallic reaction intermediates.[25] Accordingly, we report here the study of the cyclization of different triyne and diyne/nitrile substrates utilizing precatalyst **4** under thermal as well as photochemical conditions.

Results and Discussion

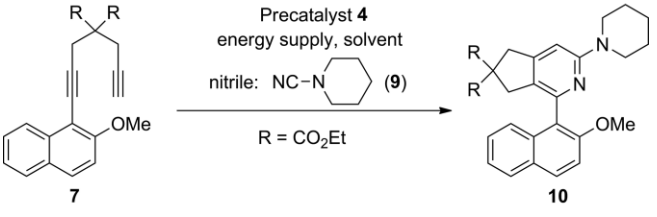
Since we have found that catalysts of the type CpCoL^{1}L^{2} (L^{1}, L^{2} = olefin, olefin/phosphite or phosphite) can be applied using conventional heating as well as microwave heating or irradiation for successful cyclization reactions, the generality of a single catalyst for such reactions for all ways of energy supply and under generally mild conditions and even "wet" solvents would be highly practical. We therefore started our investigation with selected substrates and evaluated precatalyst **1** under all conditions mentioned above. In Scheme 2 the results obtained with diynes **5** and **7** for the reaction with benzonitrile and *N*-cyanopiperidine (**9**) are displayed. Biaryl **6** has been prepared stereoselectively before by the photochemical approach.[27b] The results (Scheme 2, top) show here that the photochemical approach is superior to pure heating to 100 °C in toluene, furnishing product **6** in better yield even after only 4 h irradiation time vs. the 17 h for heating and also better than the microwave-assisted reaction after 4 h. Dipropargylmalonates such as **7** have rarely been used for co-cyclotrimerizations under such conditions for the synthesis of pyridines. Reaction with benzonitrile (2 equiv.) furnished biaryl **8** with 36 % on conventional heating to 100 °C oil-bath temperature for 17 h. Performance under microwave conditions yielded 53 % product after only 0.5 h reaction time. Irradiation for 5.5 h, however, yielded **8** with quantitative yield. In the final example, using



Nitrile	Solvent	Energy supply	T [°C]	t [h]	Yield [%]
2 equiv.	toluene	Δ	100	17 h	55 %
2 equiv.	toluene	mw	120	0.5 h	63 %
2 equiv.	THF	hν	25	4 h	68 %



Nitrile	Solvent	Energy supply	T [°C]	t [h]	Yield [%]
2 equiv.	toluene	Δ	100	17 h	36 %
2 equiv.	toluene	mw	120	0.5 h	53 %
2 equiv.	THF	hν	25	5.5 h	quant.



Nitrile	Solvent	Energy supply	T [°C]	t [h]	Yield [%]
2 equiv.	toluene	Δ	100	22 h	82 %
2 equiv.	toluene	mw	160	0.5 h	96 %
2 equiv.	THF	hν	25	22 h	82 %

Scheme 2. Comparison of thermal and photochemical energy supply for co-cyclotrimerization reactions of selected diynes and nitriles.

only 2 equiv. heterocyclic nitrile **9** in the reaction with diyne **7** gave excellent yields of **10** with each method of energy supply, again with the shortest reaction time for the microwave-assisted reaction. Conducting the microwave-assisted reaction completely under air led to a lower yield of product **10**, resulting in a mixture of substrate and product that is difficult to separate.

The results clearly show that photochemically assisted reactions often give excellent results at convenient temperatures; however, long reaction times are frequently required. The latter is also true for thermal reactions, taking up to 22 h for maximum conversion at 100 °C.

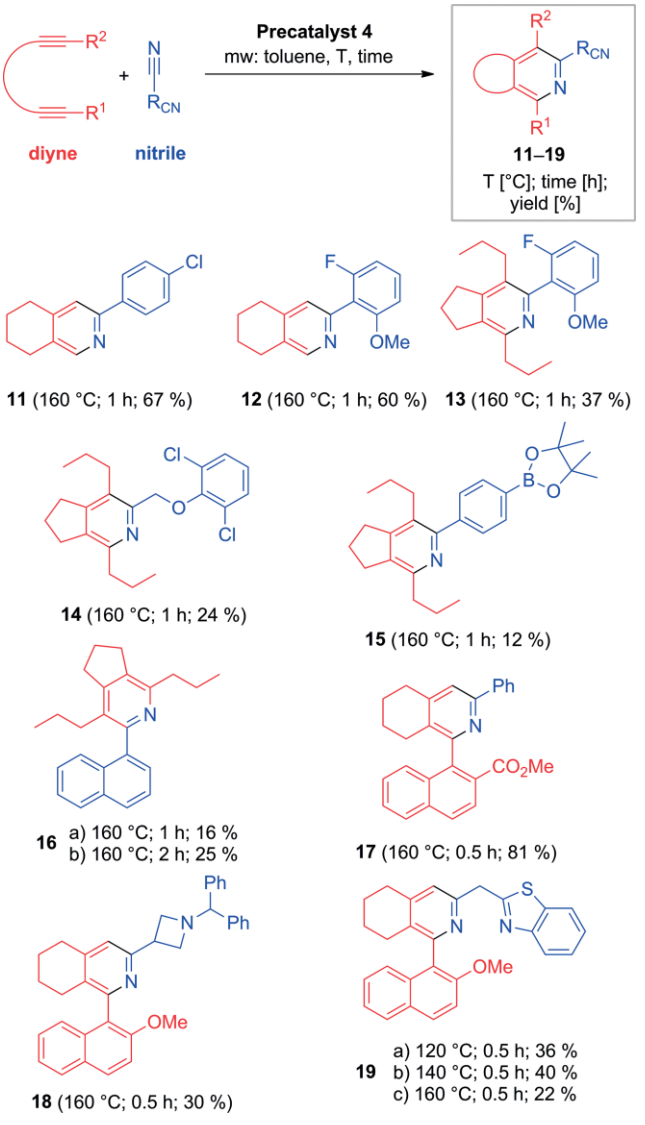
Microwave heating often gives superior results at higher reaction temperatures within short reaction times and therefore we applied catalyst **4** in exemplary syntheses to rapidly assemble different functionalized pyridines.[26] We were focusing on the broadness of application and screening of different nitrile substrates rather than general optimization of the reaction conditions towards yield to display instructive examples. In Scheme 3 cyclization results for internal, terminal, as well as monosubstituted diynes with different nitriles are presented.

The results establish that the co-cyclotrimerization using complex **4** allows a very broad array of differently functionalized nitriles to be used. Examples **11** and **12** nicely illustrate the higher reactivity of terminal alkynes compared with internal diynes such as trideca-4,9-diyne in compound **13**. In particular, the direct comparison between the diynes in the cyclization of 2-fluoro-6-methoxybenzonitrile corroborates the difference with the significantly higher yield obtained for **12**. The reaction with a dichlorinated phenyl-derivative to compound **14** is possible with significantly lower yield when using trideca-4,9-diyne as coupling partner. Reactions of benzonitril-4-pinacolylboronat and 1-cyano-naphthalene with trideca-4,9-diyne yielded products **15** and **16** in yields not exceeding 25 %, which again could be attributed to the lower reactivity of this internal diyne. Extended reaction time did not improve the yield significantly. The reaction of carboxynaphthyl-substituted 1,7-octadiynes delivered compound **17** with very good yield. Synthesis of biaryl products **18** and **19** corroborated the ability of complex **4** to mediate reactions with unusual nitriles even containing heteroatoms, leading to products that could act as ligands inhibiting the catalyst by coordination and preventing further catalysis.[27] Interestingly, for the conversion of 2-(benzo[*d*]thiazol-2-yl)-acetonitrile into biaryl **19**, a maximum in the yield was reached at 140 °C reaction temperatures, whereas a higher temperature gave a significantly lower yield of isolated product.

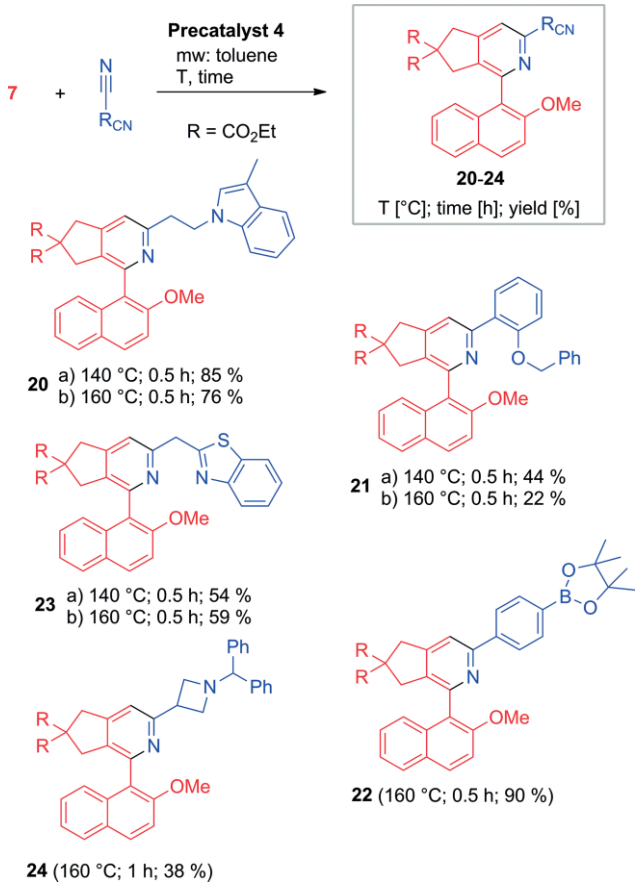
We extended the scope of the investigation and included the malonyl-substituted diyne **7** as substrate in our investigations (Scheme 4).

The yields obtained with diyne **7** and the different nitriles are in general acceptable to very good, even under unoptimized conditions. They were also higher than in comparable cases with compound **5** as the diyne component (compare to structurally related products **19** and **23**), which possibly could be traced back to the easier formation of the five-membered annulated pyridine ring.[28] For compounds **20** and **21**, higher yields at 140 °C compared with 160 °C reaction temperature were observed. Curiously, attempts to prepare an analogue of compound **21** using diyne **5** instead **7** did not work at all. The cyclization of **7** with a borylated benzonitrile led to triaryl **22** in excellent 90 % yield. Finally, an azetidine-based nitrile could be cyclized within an hour at 160 °C furnishing pyridine **24**, albeit in mediocre yield. In summary, an interesting array of structurally more sophisticated nitriles was successfully reacted, allowing access to novel bi- and triaryl motifs.

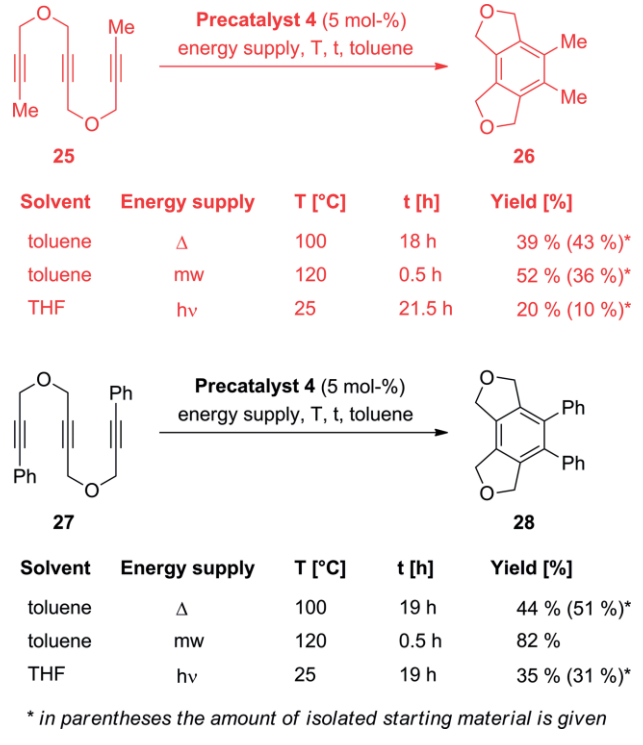
After investigating the synthesis of pyridine derivatives under the different conditions, we also evaluated such conditions in the cyclization of triynes. For the study we focused on methyl- or phenyl-terminated triynes **25** and **27**; the results are shown in Scheme 5. Cyclization of **25** under conventional thermal conditions with precatalyst **4** yielded product **26** and unreacted **25** in nearly equal amounts (Scheme 5, top). Use of microwave conditions improved the yield of **26** to 52 %,[29] whereas irradiation gave only 20 % yield and most of the substrate must have reacted to different other products, which were not identified.



Scheme 3. Synthesis of pyridines from different diynes and nitriles (2 equiv.) using precatalyst **4** under microwave conditions.



Scheme 4. Preparation of different substituted pyridines from diyne **7** and nitriles (2 equiv.) under microwave conditions.



Solvent	Energy supply	T [°C]	t [h]	Yield [%]
toluene	Δ	100	18 h	39 % (43 %)*
toluene	mw	120	0.5 h	52 % (36 %)*
THF	hν	25	21.5 h	20 % (10 %)*

Solvent	Energy supply	T [°C]	t [h]	Yield [%]
toluene	Δ	100	19 h	44 % (51 %)*
toluene	mw	120	0.5 h	82 %
THF	hν	25	19 h	35 % (31 %)*

** in parentheses the amount of isolated starting material is given*

Scheme 5. Comparison of thermal and photochemical energy supply for [2+2+2] cycloaddition reactions of triynes **25** and **27**.

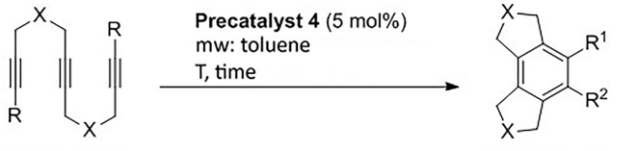
The results for triyne **27** were partially different compared to those achieved for **25**. Conventional heating led to rather sluggish conversion of **27**, delivering product **28** with only 44 % yield after 19 h and leaving half of the starting material unchanged. Irradiation for the same time worked even less well and gave just 35 % product. However, in both cases at least unreacted substrate **27** could be retained and clearly no side reaction has occurred. Applying microwave conditions, the cyclization ran smoothly and gave a very good yield of **28** after just 30 minutes reaction time. This yield is superior to the experiment conducted under microwave conditions in DMF for 10 min reaction time, giving only 52 % yield of **28** with catalyst **4**.[21]

The results presented above clearly provided evidence for the differences in the reaction outcome under the chosen conditions.

However, which would be the conditions to choose for initial screening of reaction parameters? Whereas photochemical conditions have the advantage to proceed under very mild conditions, the reaction times are usually relatively long and yields compared to pyridine synthesis rather low, as the examples showed. Conventional heating in toluene solution requires at least 100 °C to proceed over mostly long reaction times to drive the reaction towards completion. Therefore, microwave heating appears to be most compelling, especially due to the short reaction times, although reaction temperatures of at least 120 °C for triynes are frequently required.

We investigated the cyclization of other triyne derivatives with **4** under microwave conditions; the results are given in Table 1. Entries 1 und 2 are interesting as they show that even 20 °C difference in reaction temperature for the transformation of **29** into **30** can make the difference between complete conversion and no reaction at all. The reaction time is very short

Table 1. [2+2+2] Cycloadditions of triynes under microwave conditions.

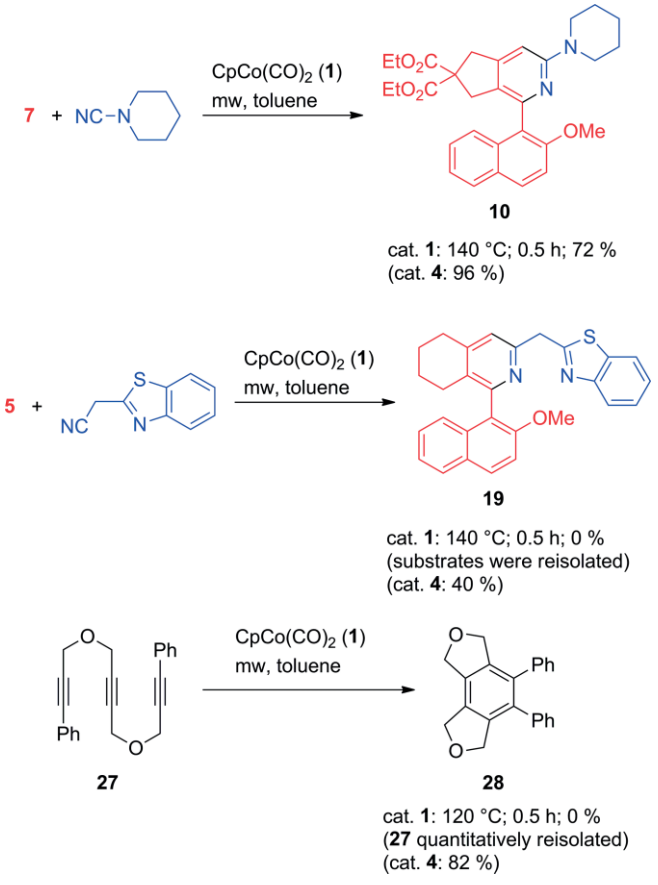


Entry	Triyne/ product	X	R^1, R^2	T [°C]	t [min]	Yield[a]
1	**29/30**	O	1-naphthyl	100	10	0 %
2	**29/30**	O	1-naphthyl	120	10	98 %
3	**29/30**	O	1-naphthyl	120	10	78 %[b]
4	**31/32**	O	2-MeO-1-naphthyl	120	10	34 %
5	**33/34**	O	R^1 = 2-MeO-1-naphthyl R^2 = Ph	120	20	62 %
6	**35/36**	O	R^1 = 1-naphthyl R^2 = Ph	120	20	83 %
7	**37/38**	$(EtO_2C)_2C$	1-naphthyl	120	30	15 %
8	**39/40**	$(EtO_2C)_2C$	R^1 = 1-naphthyl R^2 = Ph	120	30	40 %
9	**41/42**	$(EtO_2C)_2C$	R^1 = 2-MeO-1-naphthyl R^2 = Me	120	30	15 %

[a] Isolated yield. [b] 2.5 mol-% precatalyst **4**.

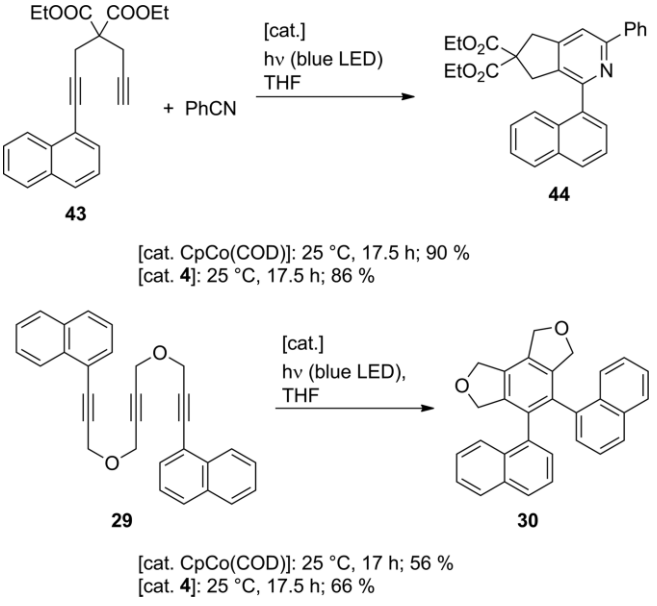
(10 min) and the comparable cyclization using $CoCl(PPh_3)_3$ as catalyst gave identical yield (92 %), but required 36 h at 25 °C.[30] The reaction temperature is in general lower than the pyridine synthesis discussed before. Also here, the structure of the triyne appears to play a role for the reaction outcome, demonstrated by the lower yields for the malonyl-substituted triynes **37**, **39** and **41**, even at prolonged reaction times.

As discussed in the introduction, complex **1** has a longstanding history as catalyst for [2+2+2] cycloaddition reactions. We were keen to benchmark this precatalyst vs. complex **4** in selected reactions to see their performance compared (Scheme 6). In the first investigated reaction yielding pyridine **10** (Scheme 6, top) the yields were high in both cases under identical reaction conditions; however, complex **4** gave an even higher conversion. The outcome with the preparation of **19** as the second example (Scheme 6, middle) was even more impressive, as complex **1** failed to catalyze this transformation at all. The cyclization of triyne **27** emphasizes the versatility of complex **4** even further (Scheme 6, below), as the product **28** was obtained with 82 % whereas complex **1** again failed to give any product again.



Scheme 6. Comparison of precatalysts $CpCo(CO)_2$ (**1**) and **4** in [2+2+2] cycloaddition reactions.

We showed in Scheme 2 that photochemically assisted reactions using precatalyst **4** proceeded very smoothly when a high-power medium-pressure mercury lamp in thermostatted reaction vessels was used.[24] Although the outcome of photochemical reactions is often quite depending on the experimental setup, we decided to showcase reactions using a convenient setup involving LED lamps for irradiation without the requirement of extensive cooling for temperature control required for powerful mercury pressure or metal halide lamps (Scheme 7, see the Supporting Information for details).[31]



Scheme 7. Comparison of precatalysts CpCo(COD) and **4** in [2+2+2] cycloaddition reactions using LED irradiation.

Initial experiments using diyne **5** and PhCN as substrates gave biaryl **6** with good yield (68 %) after 4 h reaction time using precatalyst **4**. The reaction of diyne **40** with PhCN in the presence of **4** proceeded with excellent 86 % yield after 17.5 h (Scheme 7, top), which matches the results obtained by applying CpCo(COD) (COD = 1,5-cyclooctadiene) as often used precatalyst for photoassisted [2+2+2] cycloadditions (90 %). Comparable results were obtained for the cyclotrimerization of triyne **29** with a yield of 56 % for triaryl **30** applying CpCo(COD) as catalyst and slightly higher 66 % for precatalyst **4** (Scheme 7, below). These investigations further corroborate the usefulness of complex **4** under a variety of reaction conditions and also different setups for cyclizations performed under photochemical conditions.

Conclusions

The presented investigation concentrated on the influence that different kinds of energy supply can exert on the application of $CpCo^{I}$ precatalysts in [2+2+2] cycloaddition reactions. Investigation of the air-stable and commercially available complex $CpCo[P(OEt)_3]$(dimethyl fumarate) (**4**) under conventional thermal, microwave and photochemical conditions confirmed that cyclization reactions can be performed succesfully under all three types of reaction conditions. Applying microwave heating takes advantage of providing consistent high temperatures in a confined reaction chamber and allows short reaction times. Other methods can be equally successful, however, they require significantly longer reaction times. We applied complex **4** under

microwave conditions for the synthesis of pyridines from terminal and internal alkynes and substituted alkyl and aryl nitriles, which allowed rapid access to more complex structures. This is also possible for the cyclization of triynes, even at temperatures as low as 120 °C, which can otherwise require explicitly higher temperatures. Benchmarking the reactivity of **4** against the routinely applied complex $CpCo(CO)_2$ (**1**) in pyridine and triaryl synthesis impressively demonstrated that application of **4** as catalyst can lead to excellent yields even when complex **1** shows no reactivity at all. Successful use of **4** in photocatalyzed cyclizations with a convenient photoreactor under irradiation by a LED device further substantiated the broad scope of application of this particular precatalyst.

Experimental Section

[2+2+2] Cycloaddition Reactions under Photochemically Assisted Conditions; General Procedure 1 (GP1): A thermostatted photochemical reactor[24a] was loaded with precatalyst **4** (5 mol-%) under inert conditions and a solution of diyne (0.125 mmol) and the appropriate nitrile (2–5 equiv.) THF or toluene was added. The reaction mixture was irradiated for the indicated time at 25 °C using medium-pressure metal halide lamps (2 × 450 W). To stop the reaction the lamps were turned off and the reaction vessel was opened to air. The reaction solution was evaporated to dryness and loaded on a small amount of silica gel, yielding a fine powder. The crude product was purified by flash chromatography, furnishing the pure product.

Synthesis of 10; Typical Procedure: For the preparation of biaryl **10**, diyne **7** (49 mg, 0.125 mmol), piperidine-1-carbonitrile (28 mg, 0.25 mmol, 2 equiv.), and catalyst **4** (2.7 mg, 5 mol-%) dissolved in anhydrous THF (2 mL) was irradiated according to General Procedure GP1 for the indicated time at 25 °C. Upon completion of the reaction, the solvent was removed in vacuo and the crude product charged to a small amount of silica gel in Et_2O and dried, to give a dark free-flowing powder. Column chromatography on silica gel using cyclohexane (c-hex)/ethyl acetate (3:1, v/v) as eluent furnished one main fraction of product **10** (51 mg, 82 %) of a yellowish syrup. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.12 (t, J = 7.1 Hz, 3 H), 1.23 (t, J = 7.0 Hz, 3 H), 1.58–1.65 (m, 4 H), 2.98 (d, J = 16.3 Hz, 1 H), 3.36 (d, J = 16.3 Hz, 1 H), 3.47–3.54 (m, 4 H), 3.58–3.61 (m, 2 H), 3.88 (s, 3 H), 4.08 (q, J = 7.0 Hz, 1 H), 4.10 (q, J = 7.0 Hz, 1 H), 4.19 (q, J = 7.1 Hz, 2 H), 6.61 (s, 1 H), 7.29–7.35 (m, 2 H), 7.35 (d, J = 9.2 Hz, 1 H), 7.47–7.53 (m, 1 H), 7.77–7.83 (m, 1 H), 7.87 (d, J = 9.2 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.0, 14.1, 24.9, 25.7, 27.0, 38.0, 40.8, 47.1 (2 ×), 56.9, 60.2, 61.7 (2 ×), 101.8, 114.0, 123.6, 125.4, 126.1, 126.3, 127.8, 129.3, 129.8, 133.2, 149.3, 151.6, 154.1, 159.7, 171.6, 171.7 ppm. HRMS (EI): m/z calcd. for $C_{30}H_{34}O_5N_2$: 502.2462; found: 502.2459.

[2+2+2] Cycloaddition Reactions under Standard Thermal Conditions; General Procedure 2 (GP2): In a Schlenk flask, precatalyst **4** was weighted under inert conditions, followed by addition of a solution of diyne (0.125 mmol) and the appropriate nitrile (2–5 equiv.) in THF or toluene. The reaction mixture was heated to 100 °C for the indicated time. After cooling the reaction solution, the solvent was removed in vacuo. The crude product was purified by flash chromatography.

Compound 10; Typical Procedure: Diyne **7** (49 mg, 0.125 mmol), piperidine-1-carbonitrile (28 mg, 0.25 mmol, 2 equiv.) and catalyst **4** (2.7 mg, 5 mol-%) dissolved in anhydrous toluene (2 mL) were reacted according to GP2 (22 h, 100 °C oil-bath temperature). Isolation of **10** according to the aforementioned procedure gave the pure product (51 mg, 82 %). The analytical data were consistent with the data determined before.

[2+2+2] Cycloaddition Reactions under Microwave Conditions; General Procedure 3 (GP3): In a Schlenk flask, precatalyst **4** was weighted under inert conditions, followed by addition either of a solution of diyne (0.125 mmol) and the appropriate nitrile (2–5 equiv.) in toluene or the substrate triyne (0.125 mmol) in toluene (2 mL). The solution was filled under inert conditions into the microwave reaction vial equipped with a stir bar mixture. The reaction in the microwave was executed according to the specified temperature and time. After cooling the reaction solution, the solvent was removed in vacuo. The crude product was purified by automated flash chromatography.

Compound 10; Typical Procedure: Diyne **7** (49 mg, 0.125 mmol), piperidine-1-carbonitrile (28 mg, 0.25 mmol, 2 equiv.) and catalyst **4** (2.7 mg, 5 mol-%) dissolved in anhydrous toluene (2 mL) were reacted according to above General Procedure (0.5 h, 160 °C). Isolation of **10** according to the aforementioned procedure gave the product with 96 % yield (60 mg). The analytical data were consistent with the above data.

Heterocyclic Cyclization Products

3-(4-Chlorophenyl)-5,6,7,8-tetrahydroisoquinoline (11): Compound **11** was synthesized from 1,7-octadiyne (26.5 mg, 0.25 mmol) and 4-chloro benzonitrile (69 mg, 0.5 mmol, 2 equiv.) and catalyst **4** (5.4 mg, 5 mol-%) in anhydrous toluene (4 mL) according to **GP3** (1 h, 160 °C). Column chromatography on silica gel using c-hex/ethyl acetate (1:1, v/v) as eluent gave pure product **11** (41 mg, 67 % yield) as a solid. M.p. 96–99 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.81–1.88 (m, 4 H), 2.75–2.84 (m, 4 H), 7.38 (s, 1 H), 7.41 (d, J = 8.7 Hz, 2 H), 7.89 (ddd, J = 8.7 Hz, 2 H), 8.36 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 22.6, 22.8, 26.2, 29.1, 120.6, 128.1, 128.9, 132.2, 134.5, 138.3, 147.2, 150.5, 153.3 ppm. HRMS (EI): m/z calcd. for $C_{15}H_{14}ClN$: 243.0809; found: 243.0810.

3-(2-Fluoro-6-methoxyphenyl)-5,6,7,8-tetrahydroisoquinoline (12): Compound **12** was synthesized from 1,7-octadiyne (106 mg, 0.13 mL, 1.0 mmol) and 2-fluoro-6-methoxy benzonitrile (302.3 mmg, 2.0 mmol, 2 equiv.) and catalyst **4** (21.7 mg, 5 mol-%) in anhydrous toluene (6 mL) according to **GP3** (1 h, 160 °C). Reaction monitoring via TLC with c-hex/ethyl acetate (1:1, v/v) showed complete conversion of the diyne starting material. The solvent was removed, and the crude product charged to a small amount of silica gel to give a dark free-flowing solid. Column chromatography on silica gel using c-hex/ethyl acetate (2:1, v/v) as eluent gave two main fractions, which were identified as pure recovered benzonitrile starting material (196 mg, according to 70 % conversion) and product **12** (162 mg, 60 % yield) of transparent syrupy consistency. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.80–1.87 (m, 4 H), 2.76–2.82 (m, 4 H), 3.78 (s, 3 H), 6.74–6.81 (m, 2 H), 7.09 (s, 1 H), 7.28 (ddd, J = 8.7, 8.3, 6.6 Hz, 1 H), 8.42 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 22.5, 22.7, 26.2, 28.9, 56.3, 106.8 [d, $J_{C,F}$ = 3.0 Hz]; 108.4 (d, $J_{C,F}$ = 23.1 Hz), 126.2, 129.7 (d, $J_{C,F}$ = 11.1 Hz), 132.0, 146.3, 148.2, 150.2, 158.5 (d, $J_{C,F}$ = 7.1 Hz), 159.4, 162.4 ppm. ^{19}F NMR ($CDCl_3$, 282 MHz): δ = 115.8 ppm. HRMS (EI): m/z calcd. for $C_{16}H_{15}ONF$: 256.1132; found: 256.1132.

3-(2-Fluoro-6-methoxyphenyl)-1,4-di-*n*-propyl-6,7-dihydro-5*H*-cyclopenta[*c*]pyridine (13): Pyridine **13** was synthesized from 4,9-tridecadiyne (176.3 mg, 1.0 mmol) and 2-fluoro-6-methoxy benzonitrile (302.3 mmg, 2.0 mmol, 2 equiv.) and catalyst **4** (21.7 mg, 5 mol-%) in anhydrous toluene (6 mL) according to **GP3** (1 h,

160 °C). After completion of the reaction cycle the solvent was removed in vacuo and the crude product charged to a small amount of silica gel in Et_2O and dried, to give a dark free-flowing powder. Column chromatography on silica gel using c-hex/ethyl acetate (2:1, v/v) as eluent furnished two main fractions, which were identified as pure recovered benzonitrile starting material (216 mg, according to 57 % conversion) and product **13** (122 mg, 37 % yield) of a transparent syrup. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.76 (t, 3 H), 0.97 (t, 3 H), 1.28–1.42 (m, 2 H), 1.63–1.76 (m, 2 H), 2.07–2.19 (m, 2 H), 2.28–2.36 (m, 2 H), 2.68–2.77 (m, 2 H), 2.91–2.99 (m, 4 H), 3.73 (s, 3 H), 6.72–6.79 (m, 2 H), 7.27 (ddd, J = 8.7, 8.3, 6.6 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.2, 14.4, 22.5, 22.8, 24.5, 30.9, 31.9, 32.5, 38.3, 56.1, 106.9 (d, $J_{C,F}$ = 2.7 Hz); 108.4 (d, $J_{C,F}$ = 22.8 Hz), 129.4 (d, $J_{C,F}$ = 9.8 Hz), 131.4, 137.1, 148.0, 152.8, 155.0, 158.6 (d, $J_{C,F}$ = 7.4 Hz), 159.4, 162.7 ppm. ^{19}F NMR ($CDCl_3$, 282 MHz): δ = 114.3 ppm. HRMS (EI): *m/z* calcd. for $C_{21}H_{26}ONF$: 327.1986; found: 327.1993.

3-[(2,6-Dichlorophenoxy)methyl]-1,4-dipropyl-6,7-dihydro-5*H*-cyclopenta[*c*]pyridine (14): For the preparation of compound **14** the 4,9-tridecadiyne (88 mg, 0.5 mmol) and 2-(2,6-dichlorophenoxy)acetonitrile (202 mg, 1 mmol, 2 equiv.) and catalyst **4** (10.8 mg, 5 mol-%) in anhydrous toluene (4 mL) according to **GP3** (1 h, 160 °C). After performing the microwave-assisted reaction, the solvent was removed in vacuo and the crude product charged to a small amount of silica gel in ethyl acetate and dried. Column chromatography on silica gel using c-hex/ethyl acetate (3:1, v/v) as eluent furnished two main fractions, which were identified as pure recovered nitrile starting material (70 mg, according to 62 % conversion) and product **14** (45 mg, 24 % yield) as orange syrup. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.94 (t, J = 7.4 Hz, 3 H), 1.03 (t, J = 7.4 Hz, 3 H), 1.58–1.71 (m, 4 H), 2.06–2.15 (m, 2 H), 2.62–2.67 (m, 2 H), 2.82–2.87 (m, 2 H), 2.91 (ddd, J = 8.0, 7.6, 2.7 Hz, 4 H), 5.21 (s, 2 H), 6.90 (dd, J = 8.3, 7.8 Hz, 1 H), 7.28 (d, J = 8.1 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 14.3, 14.7, 22.3, 23.9, 24.7, 30.9, 31.6, 31.7, 37.8, 75.6, 125.0, 129.0 (2 C), 130.1 (2 C), 131.9, 138.1, 150.5, 151.8, 153.3, 154.5 ppm. HRMS (EI): *m/z* calcd. for $C_{21}H_{25}Cl_2NO$: 377.1308; found: 377.1301.

1,4-Dipropyl-3-[4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]-6,7-dihydro-5*H*-cyclopenta[*c*]pyridine (15): For the preparation of triaryl **15** the 4,9-tridecadiyne (44 mg, 0.25 mmol) and pinacol 4-(cyanophenyl)boronate (114.5 mg, 0.5 mmol, 2 equiv.) and catalyst **4** (5.4 mg, 5 mol-%) in anhydrous toluene (4 mL) according to **GP3** (1 h, 160 °C). After performing the microwave-assisted reaction, the solvent was removed in vacuo and the crude product charged to a small amount of silica gel in ethyl acetate and dried. Column chromatography on silica gel using c-hex/ethyl acetate (3:1, v/v) as eluent furnished and product **15** (23 mg, 24 % yield) of yellowish syrup. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.80 (t, J = 7.3 Hz, 3 H), 0.98 (t, J = 7.3 Hz, 3 H), 1.36 (s, 12 H), 1.38–1.46 (m, 2 H), 1.67–1.78 (m, 2 H), 2.08–2.18 (m, 2 H), 2.45–2.52 (m, 2 H), 2.68–2.75 (m, 2 H), 2.90–2.98 (m, 4 H), 7.42 (d, J = 8.2 Hz, 2 H), 7.84 (d, J = 8.2 Hz, 2 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.36, 14.44, 22.6, 23.4, 24.8, 25.0 (4 ×), 30.9, 32.0, 32.2, 38.2, 83.9 (2 C), 128.5 (2 C), 129.4, 134.6 (2 C), 144.7, 153.2, 154.6, 156.3 (1 C could not be detected due to C-B coupling) ppm. ^{11}B NMR ($CDCl_3$, 96 MHz): δ = 30.9 ppm. HRMS (EI): *m/z* calcd. for $C_{26}H_{36}BO_2N$: 405.2834; found: 405.2830.

3-(Naphthalen-1-yl)-1,4-dipropyl-6,7-dihydro-5*H*-cyclopenta[*c*]-pyridine (16): Pyridine **16** was synthesized from 4,9-tridecadiyne (176.3 mg, 1.0 mmol) and 1-naphthonitrile (308 mg, 2.0 mmol, 2 equiv.) and catalyst **4** (21.7 mg, 5 mol-%) in 6 mL toluene according to **GP3** (2 h, 160 °C). After completion of the reaction cycle the solvent was removed in vacuo and the crude product charged to a small amount of silica gel in ethyl acetate and dried. Column chromatography on silica gel using c-hex/ethyl acetate (3:1, v/v) as eluent furnished two main fractions, which were identified as pure recovered 1-naphthonitrile starting material (238 mg, according to 78 % recovery) and product **16** (80 mg, 25 % yield) as orange syrup. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.64 (t, J = 7.4 Hz, 3 H), 0.98 (t, J = 7.4 Hz, 3 H), 1.27 (q, J = 7.4 Hz, 2 H), 1.72 (q, J = 7.4 Hz, 2 H), 2.11–2.25 (m, 3 H), 2.32–2.45 (m, 1 H), 2.71–2.79 (m, 2 H), 2.95–3.05 (m, 4 H), 7.30–7.47 (m, 4 H), 7.51 (dd, J = 8.2, 7.0 Hz, 1 H), 7.86 (dd, J = 8.2, 3.4 Hz, 2 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.3, 14.4, 22.9, 23.3, 24.8, 31.0, 32.0, 32.4, 38.2, 125.3, 125.7, 125.9, 126.2, 126.8, 127.7, 128.2, 130.9, 132.6, 133.9, 136.7, 139.1, 153.1, 154.7, 155.4 ppm. HRMS (EI), $C_{24}H_{27}N$: calcd. 329.2138, found 329.2126.

Methyl 1-(3-Phenyl-5,6,7,8-tetrahydroisoquinolin-1-yl)-2-naphthoate (17): Pyridine **17** was synthesized from methyl 1-(octa-1,7-diyn-1-yl)-2-naphthoate (37 mg, 0.125 mol) and benzonitrile (26 mg, 0.25 mmol, 2 equiv.) and catalyst **4** (2.7 mg, 5 mol-%) in anhydrous toluene (2 mL) according to **GP3** (0.5 h, 160 °C). After completion of the reaction cycle the solvent was removed in vacuo and the crude product charged to a small amount of silica gel in ethyl acetate and dried. Column chromatography on silica gel using c-hex/ethyl acetate (3:1, v/v) as eluent furnished one main fraction, which were product **17** (40 mg, 81 %) of a yellowish solid. The identification was accomplished by comparison with published NMR spectroscopic data.[27b]

3-(1-Benzhydrylazetidin-3-yl)-1-(2-methoxynaphthalen-1-yl)-5,6,7,8-tetrahydroisoquinoline (18): Compound **18** was synthesized from diyne **5** (33 mg, 0.125 mmol) and 1-benzhydrylazetidine-3-carbonitrile (62 mg, 0.25 mmol, 2 equiv.) and catalyst **4** (2.7 mg, 5 mol-%) in toluene (2 mL) according to **GP3** (0.5 h, 160 °C). After completion of the reaction cycle the solvent was removed in vacuo and the crude product charged to a small amount of silica gel in ethyl acetate and dried. Column chromatography on silica gel using c-hex/ethyl acetate (3:1, v/v) as eluent furnished two main fractions, which were identified as pure recovered 1-benzhydrylazetidine-3-carbonitrile starting material (40 mg, according to 65 % recovery) and product **18** (19 mg, 30 % yield) as syrup. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.56–1.82 (m, 4 H), 2.05–2.17 (m, 1 H), 2.33–2.46 (m, 1 H), 2.89 (dd, J = 7.1, 6.2 Hz, 2 H), 3.34 (ddd, J = 7.2, 7.1, 2.4 Hz, 2 H), 3.60–3.69 (m, 2 H), 3.81–3.91 (m, 1 H), 3.83 (s, 3 H), 4.46 (s, 1 H), 7.09–7.21 (m, 4 H), 7.23–7.33 (m, 6 H), 7.35 (d, J = 9.1 Hz, 1 H), 7.41–7.46 (m, 1 H), 7.79–7.84 (m, 1 H), 7.89 (d, J = 9.1 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 22.5, 23.1, 25.5, 29.8, 36.7, 56.9, 59.6, 59.7, 78.1, 114.0, 120.5, 123.6, 123.8, 124.7, 126.6, 127.1 (2 C), 127.71 (4 ×), 127.74 (4 ×), 128.0, 128.5 (2 C), 129.4, 129.7, 131.0, 133.3, 142.5, 146.8, 154.0, 158.6 ppm. HRMS (EI): *m/z* calcd. for $C_{36}H_{34}ON_2$: 510.2666; found: 510.2669.

2-{[1-(2-Methoxynaphthalen-1-yl)-5,6,7,8-tetrahydroisoquinolin-3-yl]methyl}benzo[*d*]thiazole (19): Biaryl **19** was synthesized from diyne **5** (33 mg, 0.125 mmol) and 2-(benzo[*d*]thiazol-2-yl) acetonitrile (44 mg, 0.25 mmol, 2 equiv.) and catalyst **4** (2.7 mg, 5 mol-%) in toluene (2 mL) according to **GP3** (0.5 h, 140 °C). After completion of the reaction cycle the solvent was removed in vacuo and the crude product charged to a small amount of silica gel in ethyl acetate and dried. Column chromatography on silica gel using c-hex/ethyl acetate (1:1, v/v) as eluent furnished two main fractions, which were identified as pure recovered 2-(benzo[*d*]thiazol-2-yl)-acetonitrile starting material (27 mg, according to 61 % recovery) and product **19** (22 mg, 40 % yield) as yellow-orange solid. M.p. 129–131 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.55–1.81 (m, 4 H), 2.09–2.21 (m, 1 H), 2.36–2.48 (m, 1 H), 2.81 (t, J = 6.2 Hz, 2 H), 3.88 (s, 3 H), 4.67 (s, 2 H), 7.13 (s, 1 H), 7.17–7.21 (m, 1 H), 7.30–7.37 (m, 3 H),

7.38 (d, J = 9.0 Hz, 1 H), 7.46 (ddd, J = 8.3, 7.0, 1.3 Hz, 1 H), 7.79–7.86 (m, 2 H), 7.92 (d, J = 9.0 Hz, 1 H), 8.04–8.0 (m, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 22.3, 22.9, 25.5, 27.0, 29.6, 43.2, 56.8, 113.8, 121.6, 122.8, 123.1, 123.7, 124.7, 124.8, 125.9, 126.7, 128.1, 129.4, 130.0, 136.2, 153.2 (2 C), 154.2, 170.3 ppm (two carbon resonances are missing presumably due to signal overlay). HRMS (EI): m/z calcd. for $C_{28}H_{23}ON_2S$: 435.1526; found: 435.1525.

Diethyl 1-(2-Methoxynaphthalen-1-yl)-3-[2-(3-methyl-1*H*-indol-1-yl)ethyl]-5,7-dihydro-6*H*-cyclopenta[*c*]pyridine-6,6-dicarboxylate (20): Compound **20** was synthesized from diyne **7** (49 mg, 0.125 mmol) and 3-(3-methyl-1*H*-indol-1-yl)propanenitrile (46 mg, 0.25 mmol, 2 equiv.) and catalyst **4** (2.7 mg, 5 mol-%) in anhydrous toluene (2 mL) according to **GP3** (0.5 h, 140 °C). After completion of the reaction cycle the solvent was removed in vacuo and the crude product charged to a small amount of silica gel in ethyl acetate and dried. Column chromatography on silica gel using c-hex/ethyl acetate (3:1, v/v) as eluent furnished one main fraction, which were identified as product **20** (61 mg, 85 % yield) of off-white syrupy consistency. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.13 (t, J = 7.2 Hz, 3 H), 1.22 (t, J = 7.2 Hz, 3 H), 2.29 (d, J = 0.8 Hz, 3 H), 3.08 (d, J = 16.8 Hz, 1 H), 3.30 (t, J = 6.8 Hz, 2 H), 3.34 (d, J = 16.8 Hz, 1 H), 3.48–3.60 (m, 2 H), 3.91 (s, 3 H), 4.04–4.15 (m, 2 H), 4.18 (q, J = 7.2 Hz, 2 H), 4.50 (t, J = 6.8 Hz, 2 H), 6.80 (d, J = 9.1 Hz, 2 H), 7.06–7.11 (m, 1 H), 7.14–7.19 (m, 1 H), 7.23–7.29 (m, 2 H), 7.34–7.37 (m, 2 H), 7.40 (d, J = 9.1 Hz, 1 H), 7.55 (d, J = 7.7 Hz, 1 H), 7.82–7.87 (m, 1 H), 7.95 (d, J = 9.1 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 9.7, 14.0, 14.1, 38.5, 39.2, 40.6, 46.4, 56.7, 59.8, 61.9 (2 C), 109.4, 110.2, 113.6, 118.5, 118.8, 119.0, 121.3, 123.8, 124.6, 125.8, 126.9, 128.1, 128.8, 129.3, 130.4, 133.0, 135.4, 136.4, 150.7, 151.9, 154.3, 157.3, 171.2, 171.3 ppm. HRMS (EI): m/z calcd. for $C_{36}H_{36}O_5N_2$: 576.2619; found: 576.2619.

Diethyl 3-[2-(Benzyloxy)phenyl]-1-(2-methoxynaphthalen-1-yl)-5,7-dihydro-6*H*-cyclopenta[*c*]pyridine-6,6-dicarboxylate (21): Triaryl **21** was synthesized from diyne **7** (49 mg, 0.125 mmol) and 2-(benzyloxy)benzonitrile (52 mg, 0.25 mmol, 2 equiv.) and catalyst **4** (2.7 mg, 5 mol-%) in anhydrous toluene (2 mL) according to **GP3** (0.5 h, 140 °C). After completion of the reaction cycle the solvent was removed in vacuo and the crude product charged to a small amount of silica gel in ethyl acetate and dried. Column chromatography on silica gel using c-hex/ethyl acetate (3:1, v/v) as eluent furnished one main fraction, which were identified as product **21** (33 mg, 44 % yield) of a transparent syrup. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.14 (t, J = 7.1 Hz, 3 H), 1.25 (t, J = 7.1 Hz, 3 H), 3.18 (d, J = 17 Hz, 1 H), 3.54 (t, J = 17 Hz, 1 H), 3.71 (br. s, 2 H), 3.88 (s, 3 H), 4.06–4.18 (m, 2 H), 4.22 (q, J = 7.1 Hz, 2 H), 5.18 (t, J = 1.6 Hz, 2 H), 6.97–7.05 (m, 2 H), 7.27–7.49 (m, 10 H), 7.79–7.85 (m, 3 H), 7.92 (d, J = 9.1 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.0, 14.1, 38.8, 40.8, 56.7, 59.9, 61.9, 70.8, 113.4, 113.6, 120.1, 121.2, 121.6, 123.7, 125.0, 126.7, 127.1, 127.2 (2 C), 127.8, 128.0, 128.3, 128.6 (2 C), 128.8, 129.3, 129.6, 130.3, 131.9, 133.2, 135.7, 137.4, 151.6, 154.4, 154.7, 156.3, 171.4, 171.5 ppm. HRMS (EI): m/z calcd. for $C_{38}H_{35}NO_6$: 601.2459; found: 601.2448.

Diethyl 1-(2-Methoxynaphthalen-1-yl)-3-[4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]-5,7-dihydro-6*H*-cyclopenta[*c*]pyridine-6,6-dicarboxylate (22): For the preparation of triaryl **22**, diyne **7** (49 mg, 0.125 mmol), 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzonitrile (57 mmg, 0.25 mmol, 2 equiv.) and catalyst **4** (2.7 mg, 5 mol-%) were dissolved in anhydrous toluene (2 mL), and reacted according to **GP3** (0.5 h, 160 °C). After performing the microwave-assisted reaction, the solvent was removed in vacuo and the crude product charged to a small amount of silica gel in ethyl acetate and dried. Column chromatography on silica gel using c-hex/ethyl acetate (5:1, v/v) as eluent furnished one main fraction, which were identified as pure product **22** (70 mg, 90 % yield) of yellowish syrupy consistency. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.14 (t, J = 7.1 Hz, 3 H), 1.25 (t, J = 7.1 Hz, 3 H), 1.35 (s, 12 H), 3.15 (d, J = 17.1 Hz, 1 H), 3.54 (d, J = 17.1 Hz, 1 H), 3.76 (br. s, 2 H), 3.89 (s, 3 H), 4.07–4.16 (m, 2 H), 4.22 (qd, J = 7.1, 0.8 Hz, 2 H), 7.32–7.37 (m, 2 H), 7.38 (d, J = 9.2 Hz, 1 H), 7.42–7.46 (m, 1 H), 7.70 (s, 1 H), 7.82–7.87 (m, 3 H), 7.94 (d, J = 9.0 Hz, 1 H), 8.00–8.04 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.0, 14.2, 25.0 (2 C), 38.8, 40.8, 56.7, 59.9, 62.0, 83.9, 113.7, 115.8, 122.5, 123.8, 125.0, 126.5, 126.8, 128.0, 129.4, 130.4, 133.2, 135.2, 136.4, 142.4, 150.9, 152.1, 154.3, 156.3, 171.3, 171.4 ppm. HRMS (EI): m/z calcd. for $C_{37}H_{40}BNO_7$: 621.2892; found: 621.2892.

Diethyl 3-(Benzo[*d*]thiazol-2-ylmethyl)-1-(2-methoxynaphthalen-1-yl)-5,7-dihydro-6*H*-cyclopenta[*c*]pyridine-6,6-dicarboxylate (23): Pyridine **23** was synthesized from diyne **7** (49 mg, 0.125 mmol) and 2-(benzo[*d*]thiazol-2-yl)acetonitrile (44 mg, 0.25 mmol, 2 equiv.) and catalyst **4** (2.7 mg, 5 mol-%) dissolved in anhydrous toluene (2 mL) according to **GP3** (0.5 h, 160 °C). After completion of the reaction cycle the solvent was removed in vacuo and the crude product charged to a small amount of silica gel in ethyl acetate and dried. Column chromatography on silica gel using c-hex/ethyl acetate (1:1, v/v) as eluent furnished product **23** (42 mg, 59 % yield, orange-brown solid). M.p. 155–158 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.20 (t, J = 7.1 Hz, 3 H), 1.22 (t, J = 7.1 Hz, 3 H), 3.12 (d, J = 17 Hz, 1 H), 3.46 (d, J = 17 Hz, 1 H), 3.67 (br. s, 2 H), 3.88 (s, 3 H), 4.03–4.14 (m, 2 H), 4.18 (qd, J = 7.2, 0.7 Hz, 2 H), 4.72 (d, J = 1.5 Hz, 2 H), 7.29 (br. s, 1 H), 7.30–7.34 (m, 3 H), 7.34–7.39 (m, 2 H), 7.46 (ddd, J = 8.5, 7.2, 1.3 Hz, 1 H), 7.80–7.85 (m, 2 H), 7.93 (d, J = 9.1 Hz, 1 H), 8.01–8.05 (m, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.0, 14.1, 38.6, 40.7, 43.3, 56.6, 59.8, 61.9, 113.5, 118.5, 121.6, 122.9, 123.8, 124.9 (2 ×), 126.0, 126.8, 128.0, 129.3, 130.5, 132.9, 136.1, 136.2, 151.4, 152.1, 153.2, 154.3, 155.5, 171.2 (2 ×), ppm (two carbon resonances are missing presumably due to signal overlay). HRMS (EI): m/z calcd. for $C_{33}H_{30}N_2O_5S$: 566.1870; found: 566.1861.

Diethyl 3-(1-Benzhydrylazetidin-3-yl)-1-(2-methoxynaphthalen-1-yl)-5,7-dihydro-6*H*-cyclopenta[*c*]pyridine-6,6-dicarboxylate (24): The cyclization of diyne **7** (98 mg, 0.25 mmol) and 1-benzhydrylazetidine-3-carbonitrile (124 mg, 0.5 mmol, 2 equiv.) and catalyst **4** (5.4 mg, 5 mol-%) dissolved in anhydrous toluene (4 mL) was conducted according to **GP3** (1 h, 160 °C). For workup the solvent was removed and the crude product charged to a small amount of silica gel in ethyl acetate and dried. Purification by column chromatography on silica gel eluting with c-hex/ethyl acetate (3:1, v/v) furnished product **24** (61 mg, 38 % yield, yellowish syrup). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.15 (t, J = 7.1 Hz, 3 H), 1.25 (t, J = 7.1 Hz, 3 H), 3.10 (d, J = 16.9 Hz, 1 H), 3.39 (q, J = 7.4 Hz, 2 H), 3.48 (d, J = 16.9 Hz, 1 H), 3.61–3.69 (m, 2 H), 3.71–3.75 (m, 2 H), 3.86 (s, 3 H), 3.87–3.96 (m, 1 H), 4.06–4.17 (m, 2 H), 4.21 (qd, J = 7.2, 0.5 Hz, 2 H), 4.47 (br. s, 1 H), 7.15–7.22 (m, 2 H), 7.24–7.38 (m, 8 H), 7.38 (s, 1 H), 7.42–7.47 (m, 4 H), 7.79–7.85 (m, 1 H), 7.92 (d, J = 9.1 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.0, 14.1, 37.0, 38.7, 40.8, 56.7, 59.6, 59.7, 59.8, 61.9, 78.0, 113.7, 116.0, 123.8, 124.9, 126.7, 127.1, 127.67 (2 ×), 127.72 (2 ×), 128.0, 128.5 (4 C), 129.3, 130.3, 133.1, 135.1, 142.4, 150.6, 151.3, 154.2, 161.2, 171.4, 171.5 ppm. HRMS (EI): m/z calcd. for $C_{41}H_{40}N_2O_5$: 640.2932; found: 640.2927.

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