ELSEVIER

Journal of Molecular Catalysis A: Chemical 136 (1998) 219–233

JOURNAL OF MOLECULAR CATALYSIS A: CHEMICAL

Control of selectivity in the cobalt(I)-catalysed cocyclisation of alkynes with nitriles

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Received 3 November 1997; accepted 15 January 1998

Abstract

The selectivity of photochemical synthesis of pyridines based on alkynes (e.g., ethyne, propyne, butyne, dimethylbutyne) and nitriles (e.g., benzo-, aceto-, trimethoxybenzonitrile, *n*-butylcyanoacetate, *tert*-butylcyanide) with cobalt(I) complexes ([YCo(cod)]; Y = η^5-cyclopentadienyl, η^5-indenyl, η^5-tetraphenylcyclopentadienyl, η^5-acetylcyclopentadienyl, η^3- cyclooctenyl, η^6-1-phenylborinato; cod = cycloocta-1,5-diene) can be controlled. Thus, very high chemoselectivities are obtained at low alkyne concentrations. For gaseous reactants the appropriate concentrations can be adjusted by choosing the correct partial pressures. One also can take advantage of the temperature dependent solubility of gases in different solvents. In water, for example, the product distribution can be shifted in favour of the formation of pyridines. The regioselectivity can be advantageously influenced by the properties of the ligands in the precatalyst and by the application of bulky nitriles and alkynes. Instead of artificial light sunlight can also be employed as a radiation source without loss of selectivity.

Keywords: Photochemical activation; Catalysis; Cobalt(I) complexes; Heterocyclotrimerisation; Pyridines; Nitriles; Alkynes

1. Introduction

Besides the classical thermal method [1–7] the photochemical cocyclisation of alkynes (two moles) with nitriles (one mole) became also a powerful tool for the synthesis of mono- or higher (up to penta-) substituted pyridines. While the thermal cocyclisation ('dark reaction') requires high pressure and high temperature, especially in reactions with gaseous alkynes like ethyne, the irradiation with light of wavelengths ranging from 350 to 500 nm allows to synthesise differently substituted pyridines in a large variety at ambient temperature and normal pressure. Based on this methodology many nitriles (e.g., alkyl-, aryl-, alkoxyalkyl-, aminoalkyl- or vinylcyanides) and differently substituted alkynes can be used [8–10]. Scheme 1 shows examples of pyridines which can be obtained with this method.

In contrast to the 'dark reaction' [11], the nitrile reacts in the photochemical synthesis exclusively to the desired pyridine [12]. This is illustrated in Fig. 1 for the formation of 2-phenylpyridine from ethyne and benzonitrile using

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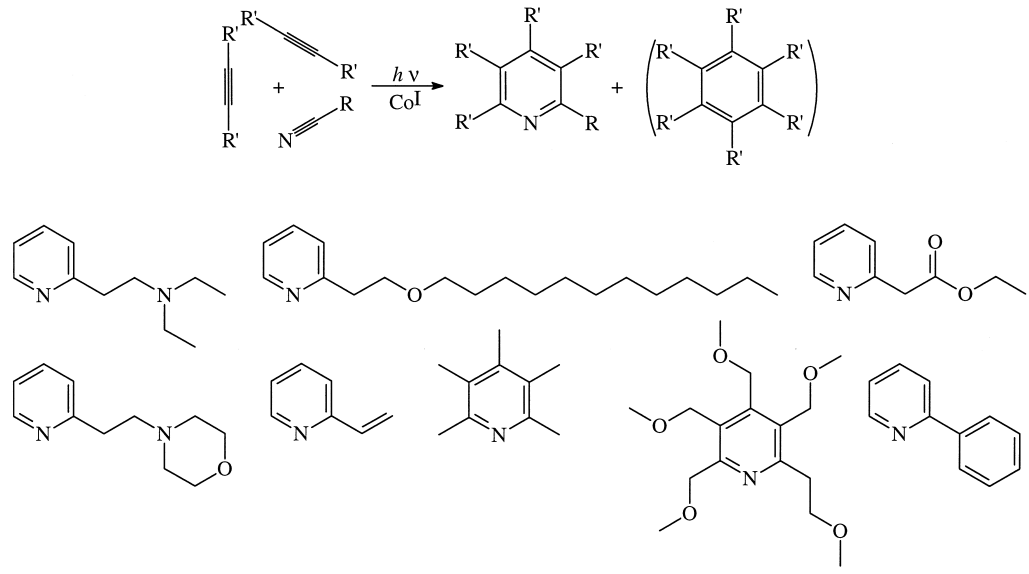
1381-1169/98/$ - see front matter
PII: S1381-1169(98)00058-2



Scheme 1.

[CpCo(cod)] (η^5-cyclopentadienyl-η^4-cycloocta-1,5-diene-cobalt(I)) as precatalyst. The concentration of benzonitrile is plotted vs. the concentration of 2-phenylpyridine (Fig. 1). The slope of the resulting straight line is -1 as expected from the balance (Eq. (1)).

$$[N] = [N]_0 - [P] \quad (1)$$

where [P] = pyridine concentration, [N] = nitrile concentration. The validity of Eq. (1) has also been verified for other nitriles. By-products containing nitrogen were not detected.

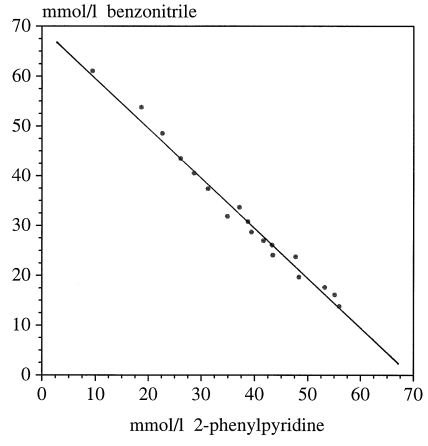


Fig. 1. Plot of the concentration of benzonitrile vs. the concentration of 2-phenylpyridine due to Eq. (1).

In organic solvents such as toluene, hexane or even in neat nitrile turnover numbers (TON) [1] up to 60 000 excellent degrees of nitrile conversions (up to 100%) and consequently high yields of pyridines can be achieved, using optimised reaction conditions. Unfortunately, a considerable amount of by-product resulting from the undesired homocyclisation of three alkynes is formed, similar to the thermal synthesis.

Investigations of the mechanism [12] of the photochemical pyridine synthesis clearly indicated that the sequence of reactions is closely related to that suggested by Bönnemann [13,14] for the thermal reaction. Obviously, by the action of light free coordination sites on cobalt are created and a central building block—presuma-

[1] The observed cocyclisations are accompanied by deactivation of the catalyst in both the thermally [11] and photochemically [12] driven variant and more or less depending on the reaction conditions applied. This change of the catalyst concentration causes the determination of the TON to became inaccurate.

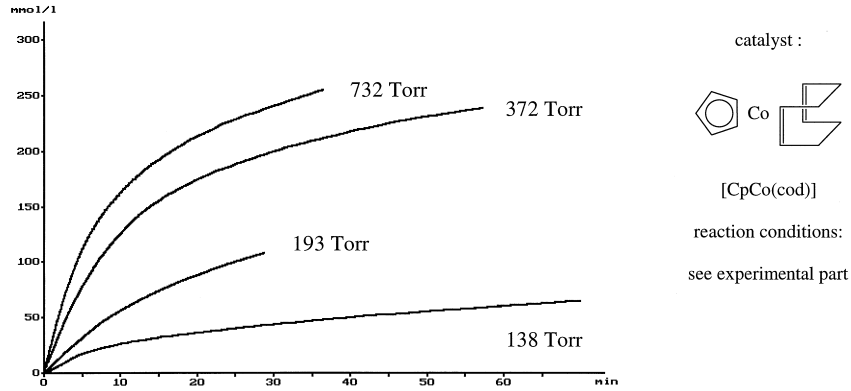


Fig. 2. Consumption of ethyne by variation of the partial pressure of ethyne.

bly a metallacycle [2]—is generated. This intermediate reacts either with one equivalent of nitrile or alkyne thus forming either the hetero- or the homocyclisation product (a pyridine or a benzene derivative), respectively. These parallel reactions which start from the same intermediate are rate determining in the photochemical synthesis. On the contrary, in the thermal synthesis Bönnemann et al. [3–5] found in the rate determining step two alkyne molecules bound to the metal. In order to provide a high concentration of the emerging intermediate, a high concentration of the alkyne has to be ensured in the 'dark reaction'. Under photochemical conditions not the formation, but the subsequent reaction of the common intermediate is rate determining. According to Ref. [12] there is a direct proportionality between the concentrations of the alkyne (e.g., ethyne) and the carbocycle (e.g., benzene). Thus, a direct control of the product ratio (pyridine/benzene) and consequently the chemoselectivity should be possible. In this contribution, we will give evidence for this hypothesis.

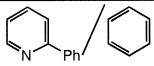
Low concentrations of gaseous alkynes in the reaction solution under isobaric conditions can be adjusted either by diminishing the partial pressure of the alkyne or by taking the temperature dependent solubility of alkynes in different solvents into consideration. The results obtained in water or organic solvents and under reduced pressure will be discussed. Among the substrates utilised, substituted alkynes have also been included, to elucidate the regioselectivity of the reaction. Finally, possibilities to scale-up the reaction (preserving selectivity), taking advantage of sunlight as a source of energy, will be presented.

2. Results and discussion

In order to study whether the synthesis under photochemical conditions can be carried out successfully even under reduced partial pressure of ethyne, different ethyne/argon mixtures were reacted with benzonitrile. The course of the reaction was followed using an apparatus for the measurement of the gas consumption as described in Section 4. The device allows the determination of the consumption of ethyne un-

[2] In general a metallacycle being the reactive intermediate is postulated either for the Co(I)-catalysed hetero- or the homocyclisation [1–7]. Corresponding ligand stabilised systems were found in Refs. [15,16]. Moreover, in the case of the homocyclisation also a cyclobutadiene species is discussed being observed in the cobalt catalysis as inactive 'break off' [17] and active intermediate, respectively [18] or relating to the nickel catalysed cyclotrimerisation as an active intermediate [19]. The binuclear species found by Wilke [20–22] and tom Dieck et al. [23,24] being an intermediate in the Ni catalysed homocyclisation (tetramerisation) is to be considered here too.

Table 1
Influence of the variation of the partial pressure of ethyne on the chemoselectivity in the cocyclisation with benzonitrile*

partial pressure of ethyne (Torr)**	732	627	510	372	193	138	101
	1.5	2.7	3.1	5.7	10.4	20.3	44,5

* Values calculated from the molar ratio of products were obtained by GLC analysis after quenching of the reaction. A detailed description is given in the experimental section for the reactions by variation of the partial pressure of ethyne.
** The vapour pressure of the solvent has been taken into account.

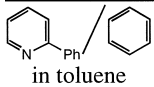
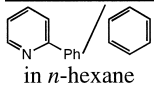
der isobaric conditions at varying partial pressure as exemplified in Ref. [25]. Fig. 2 shows the consumption of ethyne using different partial pressures in the cocyclisation with benzonitrile.

It should be noted that interpreting only the individual curves showing the total consumption of ethyne is not sufficient, since the amount of ethyne consumed is made up from the amount of pyridine (2 moles ethyne + 1 mole nitrile) and benzene (3 moles ethyne) formed. Thus, in Table 1, the gaschromatographically determined mole ratio of both products in the quenched reaction mixture is depicted.

With decreasing concentration of ethyne, the rate of the formation of pyridine diminishes somewhat. The reason is that the steady state concentration of the key intermediate depends on the concentration of ethyne. At the same time the generation of benzene is reduced drastically. Thus, by simply lowering the partial pressure, pyridines bearing substituents in 2-position could be produced with high selectivity from gaseous alkynes. Accordingly, the chemoselectivity in reactions with non-gaseous alkynes could be controlled by adjusting the molar ratio of the substrates. In all cases, when the alkyne was used in an understoichiometric ratio in relation to the nitrile, the pyridines were formed with high chemoselectivities. Therefore, a slow and dropwise addition of the alkyne was advantageous. A typical procedure is given in Section 4 (formation of 2,3,4,5,6-pentamethylpyridine from acetonitrile and but-2-yne).

A low concentration of the gaseous reactants could be achieved not only by diminished pressure but also by the proper choice of the solvent and the temperature. Results obtained with various organic solvents at different temperatures clearly show that the amount of homocyclisa-

Table 2
Influence of the variation of temperature in toluene and *n*-hexane on the chemoselectivity in the cocyclisation of benzonitrile with ethyne[a]

temperature	10°C	15°C	25°C	35°C	45°C
 in toluene	0.8	1.0	1.3	1.6	1.9
 in *n*-hexane	1.1	2.0	2.1	2.8	4.9

[a] Values calculated from the molar ratio of products were obtained by GLC analysis after quenching of the reaction. A detailed description is given in the experimental section for the reactions in organic solvents by variation of temperature.

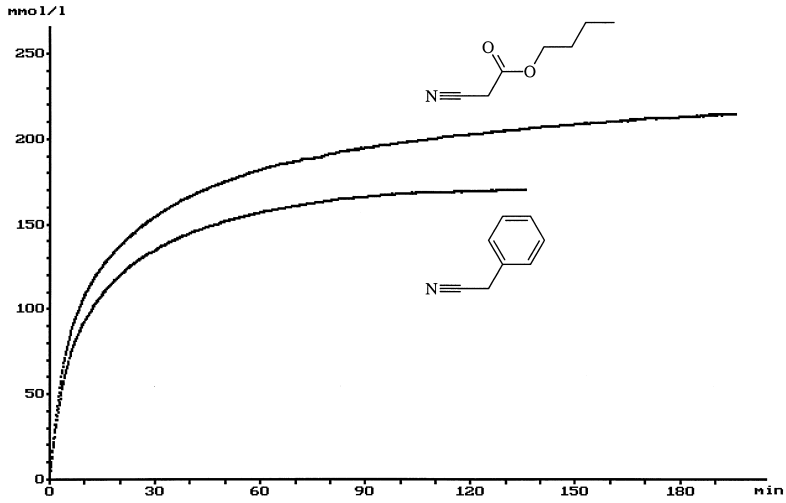


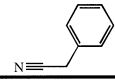
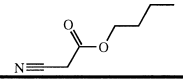
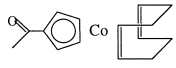
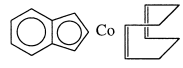
Fig. 3. Influence of different nitriles and precatalyst on the ethyne consumption in water (see also Table 3).

tion product can be controlled in a similarly efficient way (again the model reaction of ethyne with benzonitrile to 2-phenylpyridine, [CpCo-(cod)] as precatalyst was investigated).

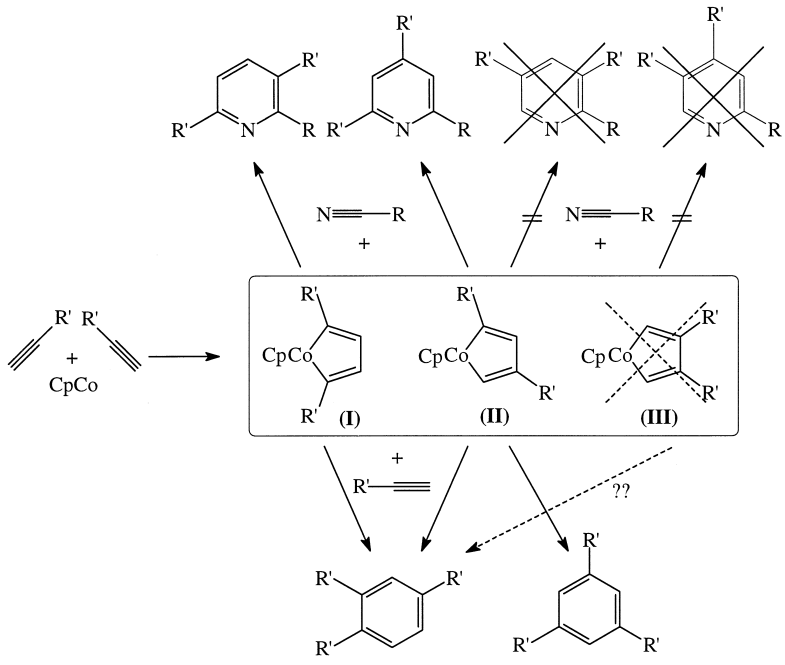
As the gas solubility generally decreases with increasing temperature, the concentration of ethyne, and thus the amount of the undesired cyclisation product, is diminished (see Table 2). The solubility of ethyne in the temperature range studied is smaller in *n*-hexane than in toluene. The mole fraction (X_b) of the gas solubility at 1.031 bar partial pressure of ethyne in *n*-hexane at 25°C has a value of 0.013 [26], whereas in toluene it is 0.0183 [27]. Thus, at a certain temperature the amount of the homocyclisation product formed is higher in toluene than in *n*-hexane.

Similar investigations with other solvents (ethanol, methanol, acetone) showed the same dependence on the gas solubility (ethyne con-

Table 3
Cocyclisation in water with different precatalysts[a]

nitrile		
precatalyst		
conversion of nitrile	67 %	79 %
yield of pyridine	67 %	79 %
yield of benzene	0.4 %	0.8 %

[a] Values were obtained by GLC analysis after quenching of the reaction. A detailed description is given in Section 4 for the reactions in water.



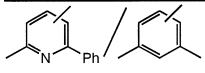
Scheme 2.

centration in solution). As the catalyst is less stable in these solvents, much lower turnovers were consequently observed.

Jerome and Parsons [28] cocyclised hexyne and acetonitrile in supercritical water at 374°C in the presence of $[CpCo(CO)_2]$ (η^5-cyclopentadienyl-dicarbonyl-cobalt(I)) affording the corresponding pyridine isomers in a yield of 15%. We were the first to show that the Co(I)-catalysed synthesis of pyridines can also be run in water at 25°C and under atmospheric pressure by concomitant irradiation with light of wavelengths between 360 and 500 nm [29]. The reaction proceeded particularly successfully with nitriles, which are insoluble in water. As is detailed in Ref. [29], besides aryl- and alkyl-, alkoxy-substituted nitriles can also be used for cocyclisation with ethyne. [CpCo(cod)] as well as other precatalysts substituted at the Cp ring can be used. Fig. 3 and Table 3 illustrate two relevant examples for the cocyclisation in water.

As described in Section 4 for the reaction of butyl cyanoacetate with ethyne, we observed a decrease of the conversion when a surfactant was added. The surfactant led to a more or less pronounced clouding which caused scattering and reflection of the radiated light. Therefore, the amount of light reaching the reaction centre got smaller. Obviously, a micellar catalysis did not take place.

Table 4
Influence of salt addition on the chemoselectivity in the cocyclisation of benzonitrile with propyne[a]

salt addition (saturated solution)	-	$MgSO_4$	NaCl	$(NH_4)_2SO_4$
	4.55	8.1	24	99

[a] Values were obtained by GLC analysis after quenching of the reaction. A detailed description is given in Section 4 for the reactions in aqueous solutions by addition of salt.

The addition of 1–5 vol.% of an organic solvent (e.g., toluene) was advantageous when water was used as solvent, especially when water soluble nitriles were applied. For example, 2-methoxy-propionitrile does not cyclise with ethyne to the corresponding pyridine in neat water. In contrast dissolution of the precatalyst in toluene prior to the reaction gave yields up to 20%. An appropriate example is given in Section 4. The degree of the conversion of nitriles insoluble in water could be slightly increased by adding traces of toluene to the aqueous phase resulting in a higher stability of the catalyst. Under these conditions the selectivity remained constant, while in neat toluene a serious loss of selectivity was observed (for an example, see Table 7 in Section 4).

In accordance with the results obtained under reduced ethyne pressure, the amount of benzene formed in water with or without addition of surfactants or traces of toluene is less than 1% with respect to the alkyne converted. This can be explained by the low solubility and thus low concentration of ethyne in water. It is remarkable that this reaction employing organometallic compounds can be carried out in water under such mild conditions. We suggest that tiny drops (fine emulsion) formed by the nitrile hosting the precatalyst represent the actual place of reaction. The only function of water is to provide for the optimal amount of ethyne.

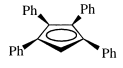
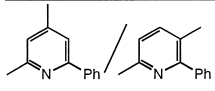
Beside the variation of the nitrile, we also investigated the influence of the substituents at the –C≡C– bond upon the reaction in water. The chemoselectivity of the synthesis was quite good, provided the alkyne concentration was low in comparison to the nitrile. When gaseous propyne was employed, which is better soluble in the used solvents than ethyne, the appropriate diminution of solubility could be achieved by the addition of different salts [30]. Table 4 shows that in a saturated salt solution selectivities of 99% could be obtained.

Considering the monosubstituted acetylenes like propyne (Scheme 2) beside the problem of chemoselectivity (ratio of hetero- to carbocycle), the question of regioselectivity (ratio of positional isomers of pyridine) has to be addressed.

If the mechanism discussed above holds equally for the photochemical synthesis, the regioselectivity should be controllable by the substitution pattern of the intermediate key complex, which we suggest to be a metallacycle (see footnote 2). Due to the pyridine isomers observed, one can conclude that only two ((**I**) and (**II**) in Scheme 2) of the three possible isomers of the metallacycle are formed in the thermally induced [13,14] as well as in the photochemical reaction.

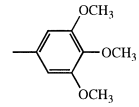
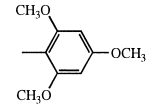
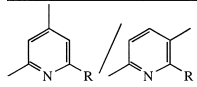
The regioselectivity of the different pyridines obtained depends on several factors. As shown in Table 5 the choice of the ligand Y in precatalysts of the type [YCo(cod)] considerably influenced the ratio of the isomers formed. Thus, with indenyl ligands only 52% of the symmetrically substituted pyridine was obtained (molar

Table 5
Influence of the precatalyst on the cocyclisation of benzonitrile with propyne[a]

Y-ligand in YCo					
	2.6	2.1	1.8	1.4	1.1

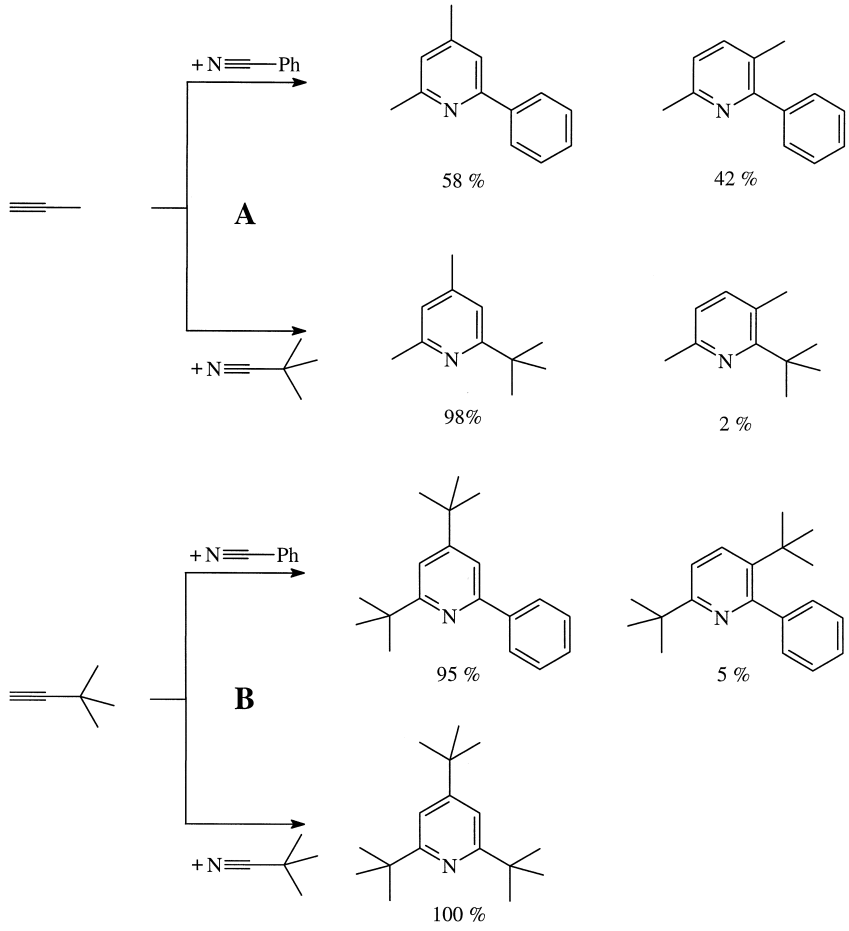
[a] Values calculated from the molar ratio of products were obtained by GLC analysis after quenching of the reaction. A detailed description is given in Section 4 for the standard conditions.

Table 6
Influence of substituents at the nitrile on the regioselectivity in the cocyclisation with propyne[a]

substituent **R** at the nitrile	—CH_3				
	1.3	1.4	1.3	6.2	49.1

[a] Values calculated from the molar ratio of products were obtained by GLC analysis after quenching of the reaction. A detailed description is given in Section 4 for the standard conditions.

ratio: 1.1). The amount increased (72%; molar ratio: 2.6) when the tetraphenyl substituted cyclopentadienyl ligand was used. Obviously, in this series those two half-sandwich complexes feature superior regioselectivities (here the ratio of symmetrically to unsymmetrically substituted



Scheme 3.

pyridine) which combine highest steric demand with strong π-electron accepting capability.

To clarify the contributions of steric and electronic effects on the regioselectivity a broader variation of ligands is highly desirable in forthcoming investigations.

Apart from this, up to now it is not clear whether the ligand Y in the complex [YCo(cod)] supports the formation of one of the alternative metallacycles (**I**) or (**II**) (Scheme 2) or whether it influences the rate of the subsequent reaction of these intermediates to pyridines.

Since the regioselectivity neither could be remarkably influenced by the choice of the reaction medium (e.g., organic solvents, water with or without addition of surfactants and inorganic salts, respectively) nor by variation of the temperature (-10°C to 45°C), we attempted to enrich one of the isomers by the appropriate choice of substituents in the nitrile or in the alkyne.

We investigated the influence of nitrile substituents upon the cocyclisation of differently substituted nitriles and propyne with [CpCo(cod)] as precatalyst. The results obtained are given in Table 6. As can be seen clearly, bulky substituents like the *tert*-butyl-group affected the regioselectivity so strongly that the ratio of isomers was shifted to 49.1.

In Scheme 3, the effect exerted by the substituents in the nitrile as well as in the alkyne is shown. Pathway **A** exemplifies the influence of the nitrile. Thus, in the reaction of propyne with benzonitrile both pyridine isomers are obtained, the product ratio being as expected. When the phenyl substituent was replaced by a *tert*-butyl-group the product ratio changed extremely; now the 2,4,6-product was formed with 98%. Pathway **B** gives two examples of the reaction of an alkyne bearing bulky substituents. The reaction of 3,3-dimethyl-but-1-yne with the 'simple' benzonitrile led to a change in the regioselectivity, indicating the dominance of the alkyne substituents. Combining the former with *tert*-butylcyanide being a bulky nitrile the 2,4,6-isomer was exclusively formed.

Similar results were obtained in the photochemical reaction of 3-methyl-but-1-yne-3-ol with benzonitrile and *tert*-butylcyanide. While with benzonitrile 'only' 84% of the 2,4,6-substituted isomer were formed, with *tert*-butylcyanide 100% could be achieved.

The influence of a bulky substituent in the alkyne can be explained with the assumption of the preferred formation of intermediate (**II**) (Scheme 2). On the other hand in case of bulky nitriles two reasons for the superior regioselectivity may be relevant. Either the selectivity is caused by the hindered attack on the metallacycle (**I**) or by the instability of the pyridines formed.

It is reasonable to assume that during the reaction of the nitrile with the intermediates (**I**) or (**II**) the insertion into the sterically crowded Co–C(R′)-bond compared with the insertion in the less crowded Co–C(H)-bond is hampered when a bulky substituent in the nitrile (R) is present. The Co–C(H)-bond exists only in the metallacycle (**II**), which gives rise exclusively to the 2,4,6-substituted pyridine. If the stability of the pyridines was responsible for the observed selectivity, the formation of the 2,3,6-isomer should be disfavoured because of the steric repulsion between the *ortho* substituents. This explanation presumes reversibility of the last step in the catalytic cycle. The absence of the unsymmetric isomer, as shown in the reaction of *tert*-butylcyanide with 3,3-dimethyl-but-1-yne as well as the full conversion of the nitrile [3] indicate that an equilibrium is not established and therefore reversibility of the reaction does not occur.

The photochemical pyridine synthesis could also be performed with high chemoselectivity with the light of the sun. Our first investigations on the model reaction of ethyne with benzonitrile giving 2-phenylpyridine in water with [CpCo(cod)] showed high conversions and con-

[3] In cases of incomplete conversion, further addition of catalyst led to quantitative conversion.

vincingly demonstrated the efficiency of this alternative [31,32]. The high selectivities achieved in lab scale reactions were also obtained in an upscaled reaction using sunlight. Only traces of undesired by-products were observed. Nitrile and ethyne gave selectively 2-phenylpyridine. Benzene was formed in 1%. The reaction of 6.82 mole of benzonitrile with ethyne in 40 l water in 4.5 h gave the corresponding pyridine in 25% yield. The addition of 1–2 vol.% toluene (e.g., 40-l water, 500-ml toluene) led to more than 40% conversion. A deactivation of the catalyst was not observed. The catalyst is highly suitable for solar chemical experiments. The reaction conditions were not optimised and therefore it should be possible to improve the yields under solar conditions too.

3. Summary

The presented heterocyclisation of alkynes with nitriles to substituted pyridines shows exemplarily that a shift of the rate determining step occurring in the change from the thermal 'dark reaction' to the photochemical synthesis gives the opportunity to control the chemoselectivity.

The photochemical synthesis could be performed with low alkyne concentrations (e.g., in water with or without addition of salts, under reduced partial pressure of a gaseous alkyne or by the slow addition of a liquid alkyne), which favoured the formation of pyridines (chemoselectivity), due to the direct proportionality between the concentration of alkyne and the concentration of the undesired benzene derivatives.

The regioselectivity of the reaction could also be influenced by the proper choice of the ligands in the precatalyst and by bulky substituents in the substrates.

Instead of artificial light sunlight could also be used as irradiation source without loss of selectivity. In conclusion, we have succeeded in developing a new highly selective synthesis of substituted pyridines, which can be carried out easily both on the lab scale as well as on larger scales for the production of great amounts of a multitude of pyridines. Moreover, the photochemical synthesis can also be run in water promoted by sunlight, and thus meets the highest ecologic requirements.

4. Experimental

4.1. Spectroscopic measurements:

GLC analyses were performed on a HP 5890 II chromatograph with OV 101 coated fused silica capillaries of 12 m length (temperature program: 10 min at 35°C isothermally, then 10°C min^{-1} up to 200°C); argon as carrier gas, 1 ml min^{-1}. Reaction products were separated by preparative GLC using a HP 5890 II combined with a cooled injection system and multi column switching program (Fa. GERSTEL-Mülheim, Germany). Column: FFAP and HP1 each 30 m length, ∅ (internal diameter) 0.53 mm, film thickness: 5.0 μm; temperature program: 10 min isotherm at 60°C, heating rate 10°C min^{-1} up to 240°C, carrier gas hydrogen, gas stream 8 ml min^{-1}.

^{1}H NMR spectra were measured with a BRUKER AC 250 MHz or 400 MHz spectrometer.

IR spectra were recorded on a HP GLC-FTIR 5965B instrument (column HP5, 25 m length, temperature program: 2 min at 50°C isothermally, then 20°C min^{-1} up to 260°C).

Mass spectra were measured with a HP MS-GLC 59827A mass spectrometer (GLC: HP 5890 II, column: HP1, 25 m length or HP5, 25 m length).

4.2. Gas measuring device

The system works in principle as follows. The pressure drop in the gas phase of the reaction vessel, caused by the chemical reaction, is detected by a photodiode in a pressure gauge. Through a magnetic valve with argon as counterpressure the closed gas phase over the solu-

tion is pressurised with mercury in the gas buret. A high dynamic of the device is guaranteed by a computer controlled regulator which contains fuzzy-logic components. Finally, the gas consumption as function of the time is registrated as computer file over the electrical resistance of a platinum wire (0.1 mm diameter) in the gas buret.

4.3. Chemicals

All operations were performed under an atmosphere of argon (Linde 5.0) and strict exclusion of air. Ethyne of 99.5% purity (Linde) and propyne of 99% purity (Air Liquide) were used without further purification. Nitriles, alkyne compounds and organic solvents, which were purchased from Fluka, were rigorously dried and distilled.

The precatalysts [CpCo(cod)] (η^5-cyclopentadienyl-η^4-cycloocta-1,5-diene-cobalt(I)) [33–35], [(ind)Co(cod)] (η^5-indenyl-η^4-cycloocta-1,5-diene-cobalt(I)) [35] and [(coe)Co(cod)] (η^3-cyclooctenyl-η^4-cycloocta-1,5-diene-cobalt(I)) [36,37] were prepared according to literature procedures. [(Ph-BC_5H_5)Co(cod)] (η^6-1-phenylborinato-η^4-cycloocta-1,5-diene-cobalt(I))—supplied from Prof. Dr. G.E. Herberich (RWTH Aachen); [(Cp^{Ph4})Co(cod)] (η^5-tetraphenylcyclopentadienyl-η^4-cycloocta-1,5-diene-cobalt(I)) and [(Cp^{Ac})Co(cod)] (η^5-acetylcyclopentadienyl-η^4-cycloocta-1,5-diene-cobalt(I))—supplied from Dr. H.-U. Jürgens (University of Rostock).

4.3.1. Example of experimental procedure of cocyclisation ('standard conditions')

4.3.1.1. Reaction with gaseous alkyne compound

2-Phenylpyridine. A thermostatted (25°C) reaction vessel, equipped with a Teflon-coated magnetic spin bar, was connected to a computer-linked automatic and thermostatted gas buret as described basically above and in Refs. [12,25] and symmetrically positioned between two 460 W Philips HPM 12 lamps. The vessel was loaded with 13 ml of toluene, 1 ml of a toluene solution containing 1.031 mmol of benzonitrile and 1.031 mmol of *n*-octane (inner standard), and 1 ml of a catalyst/toluene solution containing 0.01031 mmol of [CpCo(cod)] using gas-tight Hamilton-syringes. The mixture was stirred and saturated with ethyne while protected against light. Then the lamps were switched on and, after their warm-up (4 min), the vessel was exposed to the irradiation. In general, all cocyclisations were performed under isobaric conditions. The time dependence of the reaction progress was observed by using the apparatus for measurement of the ethyne consumption and GLC analysis after interrupting the reaction. Quenching was done by switching off the lamps and exposing the reaction mixture to air. After a reaction time of 2 h 95% of the starting nitrile had been converted to 2-phenylpyridine (0.979 mmol).

Variation in Table 5, nitrile: benzonitrile; alkyne: propyne; solvent: toluene; temperature: 25°C; time: 2 h; precatalyst: [(Cp^{Ph4})Co(cod)], [(Ph-BC_5H_5)Co(cod)], [(coe)Co(cod)], [CpCo(cod)], [(ind)Co(cod)].

Variation in Table 6, nitrile: aceto-, benzo-, 3,4,5-trimethoxybenzo-, 2,4,6-trimethoxybenzonitrile, *tert*-butylcyanide; alkyne: propyne; precatalyst: [CpCo(cod)]; solvent: toluene; temperature: 25°C; time: 2 h.

The yields in Table 5 as well as in Table 6 were determined by GLC. Pyridines obtained were isolated by preparative gas chromatography and identified using commonly applied analytic methods (^{1}H NMR, GLC-IR, GLC-MS). All characteristic data were in accordance with those reported in the literature (in Table 5: 3,6-dimethyl-2-phenyl-pyridine [38]; 4,6-dimethyl-2-phenyl-pyridine [39]; in Table 6: 2-*tert*-butyl-4,6-dimethyl-pyridine [40]). Data of newly synthesised pyridines in Table 6 are listed below.

3,6-Dimethyl-2-(3,4,5-trimethoxyphenyl)pyridine. ^{1}H NMR: ($CDCl_3$, 297 K); $\delta = 2.30$ (s, 3H, *m*-CH_3); 2.55 (s, 3H, *o*-CH_3); 3.85 (s, 3H,

OCH_3); 3.90 (s, 6H, OCH_3); 6.70 (s, 2H); 7.02 (d, 1H, H-4); 7.45 (d, 1H, H-5) ppm.

GLC-IR: 3001, 2943 ν(C-H); 1574, 1495, 1462, 1403 ν(C=C); 1228, 1120 ν(C–O–C); 1016, 812 δ(C–H: vicinal of pyridine ring) cm^{-1}.

MS (I_{rel}): $m/z = 273$ (M^+); 272 (M^+–H); 258 (M^+–CH_3); 242 (M^+–OCH_3).

4,6-Dimethyl-2-(3,4,5-trimethoxyphenyl)pyridine. ^{1}H NMR: ($CDCl_3$, 297 K); $\delta = 2.35$ (s, 3H, *p*-CH_3); 2.59 (s, 6H, *o*-CH_3); 3.86 (s, 3H, OCH_3); 3.93 (s, 6H, OCH_3); 6.90 (s, 1H, H-3); 7.19 (s, 2H); 7.26 (s, 1H, H-5) ppm.

GLC-IR: 3001, 2943 ν(C–H); 1570, 1496, 1466, 1421, 1351 ν(C=C); 1228, 1117 ν(C–O–C); 1016, 839 δ(C–H: isolated of pyridine ring) cm^{-1}.

MS (I_{rel}): $m/z = 273$ (M^+); 258 (M^+–CH_3); 242 (M^+–OCH_3).

3,6-Dimethyl-2-(2,4,6-trimethoxyphenyl)pyridine. ^{1}H NMR: ($CDCl_3$, 297 K); $\delta = 2.35$ (s, 3H, *m*-CH_3); 2.55 (s, 3H, *o*-CH_3); 3.71 (s, 6H, OCH_3); 3.87 (s, 3H, OCH_3); 6.19 (s, 2H); 6.86 (d, 1H, H-4); 7.33 (d, 1H, H-5) ppm.

GLC-IR: 3004, 2942 ν(C–H); 1603, 1591, 1459, 1410 ν(C=C); 1207, 1149, 1123 ν(C–O–C); 1040, 812 δ(C–H: vicinal of pyridine ring) cm^{-1}.

MS (I_{rel}): $m/z = 273$ (M^+); 272 (M^+–H); 258 (M^+–CH_3); 242 (M^+–OCH_3).

4,6-Dimethyl-2-(2,4,6-trimethoxyphenyl)pyridine. ^{1}H NMR: ($CDCl_3$, 297 K); $\delta = 2.37$ (s, 3H, *p*-CH_3); 2.60 (s, 6H, *o*-CH_3); 3.85 (s, 6H, OCH_3); 3.98 (s, 3H, OCH_3); 6.89 (s, 1H, H-3); 7.22 (s, 1H, H-5); 7.32 (s, 2H) ppm.

GLC-IR: 3003, 2942, 2845 ν(C–H); 1607, 1464, 1410 ν(C=C); 1208, 1120 ν(C–O–C); 1050, 844 δ(C–H: isolated of pyridine ring) cm^{-1}.

MS (I_{rel}): $m/z = 273$ (M^+); 272 (M^+–H); 258 (M^+–CH_3); 242 (M^+–OCH_3).

2-(tert-Butyl)-3,6-dimethyl-pyridine. This isomer could not be isolated due to the small amounts formed in the reaction (ca. 1.8%). However, the GLC/MS-spectrum clearly corresponded to that characterising the 2,4,6-isomer.

MS (I_{rel}): $m/z = 163$ (M^+); 162 (M^+–H); 148 (M^+–CH_3); 107 (M^+–C_4H_9).

4.3.1.2. Reaction with liquid and solid alkyne and nitrile compounds, respectively

2,3,4,5,6-Pentamethylpyridine [39]. A similar procedure as described in Section 4.3.1.1 was employed applying a mixture of 20 mmol acetonitrile and 10 ml of a catalyst/toluene solution containing 0.1031 mmol of [CpCo(cod)]. In distinction to Section 4.3.1.1 as alkyne 40 mmol but-2-yne dissolved in 16 ml toluene were added dropwise in 5 portions. [Start 6 ml (15 mmol), after 30 min: 4 ml (10 mmol), after 60 min: 3 ml (7.5 mmol), after 90 min: 2 ml (5 mmol), after 120 min: 1 ml (2.5 mmol)]—After addition of the first portion irradiation was started while stirring continued.

Yield: 19 mmol 2,3,4,5,6-pentamethylpyridine.

Variation in Scheme 3 and in the concerned paragraph below, nitrile: benzonitrile, *tert*-butylcyanide; alkyne: propyne, 3,3-dimethyl-but-1-yne, 3-methyl-but-1-yne-3-ol; precatalyst: [CpCo(cod)]; solvent: toluene; temperature: 25°C; time: 2.5 h.

The yields were determined by GLC. Pyridines obtained were isolated by preparative gaschromatography and identified using commonly applied analytic methods (^{1}H NMR, GLC-IR, GLC-MS). All characteristic data were in accordance with those reported in the literature (4,6-di-(*tert*-butyl)-2-phenyl-pyridine [41]). Data of newly synthesised pyridines are listed below.

2,5-Bis-(1-hydroxy-1-methyl-ethyl)-6-phenyl-pyridine). GLC-IR: 3642, 3470 ν(OH); 3072, 2937 ν(C–H); 1598, 1560 ν(C=C); 1405, 1367 (–$C(CH_3)_2$); 1174 (C–O); 959, 808 δ(C–H: vicinal of pyridine ring) cm^{-1}.

MS (I_{rel}): $m/z = 271$ (M^+); 256 (M^+–CH_3); 241 (M^+–$2CH_3$); 213(M^+–$C(CH_3)_2OH^+$), 59 ($C(CH_3)_2OH^+$).

2,4-Bis-(1-hydroxy-1-methyl-ethyl)-6-phenyl-pyridine. GLC-IR: 3617, 3467 ν(OH); 3070, 2937 ν(C–H); 1581, 1557 ν(C=C); 1383, 1369

($-C(CH_3)_2$); 1167 (C–O); 954, 842 δ(C–H: isolated of pyridine ring) cm^{-1}.

MS (I_{rel}): $m/z = 271$ (M^+); 256 (M^+-CH_3); 238; 207; 180; 59 ($C(CH_3)_2OH^+$).

2,4-Bis-(1-hydroxy-1-methyl-ethyl)-6-(tert-butyl)-pyridine. ^1H NMR: ($CDCl_3$, 297 K); $\delta =$ 1.28 (s, 9H, $-C(CH_3)_3$); 1.45 (s, 6H, $-C(CH_3)_2OH$); 1.50 (s, 6H, $-C(CH_3)_2OH$); 7.15 (s, 1H); 7.25 (s, 1H) ppm.

GLC-IR: 3641, 3454 ν(OH); 3084, 2977 ν(C–H); 1599, 1565 ν(C=C); 1366 ($-C(CH_3)_2$); 1174 (C–O); 839 δ(C–H: isolated of pyridine ring) cm^{-1}.

MS (I_{rel}): $m/z = 251$ (M^+); 236 (M^+-CH_3); 218; 192 ($M^+-C_3H_6OH$).

4.3.2. Reactions by variation of the partial pressure of ethyne

The reactions were performed under 'standard conditions' with toluene as solvent. The partial pressure of ethyne was varied. The vapour pressure of toluene at 25°C being 28 Torr was taken into account. It should be noted that isobaric conditions had been maintained. A detailed description of the working method including it's test can be found in Ref. [25]. The employed technique allowed the adjustment of defined mixtures of gases (here: ethyne/argon) in the actual reaction vessel. The latter was connected with the gas consumption apparatus which supplied exclusively the reaction gas consumed (here ethyne).

Variation in Table 1 and Fig. 2, nitrile: benzonitrile; alkyne: ethyne; precatalyst: [CpCo(cod)]; solvent: toluene; temperature: 25°C; time: 1 h (only for Table 1; for further review, see Fig. 2).

Values obtained by GLC analysis after quenching of the reaction (inner standard: *n*-octane).

4.3.3. Reactions in organic solvents by variation of the temperature

The reactions were performed under 'standard conditions'. Solvent and temperature (10–45°C) were varied. The desired temperature in the whole device was adjusted by using a thermostat.

Variation in Table 2, nitrile: benzonitrile; alkyne: ethyne; precatalyst: [CpCo(cod)]; time: 2 h; solvent: toluene, hexane; temperature: 10°C, 15°C, 25°C, 35°C, 45°C.

Values obtained by GLC analysis after quenching of the reaction (inner standard: *n*-octane).

4.3.4. Reactions in water:

A thermostatted (25°C) reaction vessel, equipped with a Teflon-coated magnetic spin bar, was loaded with 17.5 mmol *n*-C_4H_9OC-OCH_2CN [*n*-butylcyanoacetate] and 0.006 mmmol [(ind)Co(cod)]. To the solution 10 ml of oxygen-free water were added. The vessel was connected with an ethyne measuring and delivering device, maintaining the gas pressure constant. Alternatively, ethyne could simply be bubbled through the solution. The mixture was irradiated by two 460 W Phillips HPM 12 lamps

Table 7
Influence of the addition of different surfactants and toluene, respectively, on the cocyclisation of *n*-butylcyanoacetate and ethyne in water

Addition of surfactants or traces of organic solvent	Conversion of nitrile (%)	Yield of benzene (%)
None	90	1
Brij 56® (decaoxyethylene-hexadecyl ether)	83	0.8
Tween 20 (polyoxyethylenesorbitan monolaurate)	79	0.7
DDaPs (3-(*N*-dodecyl-*N*,*N*-dimethylammonio)-propane-1-sulfonate)	84	0.9
SDS (sodium dodecylsulfate)	30	–
CTABr (cetyl-trimethyl-ammonium bromide)	85	0.6
$CTAHSO_4$ (cetyl-trimethyl-ammonium hydrogensulfate)	50	0.5
Toluene (2 vol.% of the amount of water utilised)	95	1

for 3 h. The pyridine was isolated by vacuum distillation (yield: 15 mmol). Benzene content (ca. 0.8%) was detectable only by means of GLC.

Variation in Table 3 and Fig. 3, nitrile: *n*-butylcyanoacetate, benzylcyanide; alkyne: ethyne; solvent: water; temperature: 25°C; precatalyst: [(ind)Co(cod)]; [Cp^{Ac}Co(cod)]; time: 3 h (only for Table 1, for further review, see Fig. 2).

Values obtained by GLC analysis after quenching of the reaction. The obtained pyridines were isolated by preparative GLC or by vacuum distillation and identified using common analysis methods (^{1}H NMR, GLC-IR, GLC-MS).

4.3.5. Reactions in aqueous solutions by addition of traces of organic solvents, surfactants or salts

The same procedure was employed as described for the reaction in water. To the mixture were added 1–5 vol.% of an organic solvent (e.g., toluene) or a surfactant (e.g., Brij 56; ratio of Co/surf. 1:20) or a salt (e.g., 7.5 g $(NH_4)_2SO_4$ dissolved in 10 ml oxygen free water affording a saturated solution). An example of the experimental procedure is given by means of the formation of 2-(2-methoxyethyl)-pyridine. Some characteristic results of the photochemical cotrimerisation of ethyne and *n*-butyl cyanoacetate in aqueous solution in the presence of surfactants or toluene are listed in Table 7.

Variation in Table 4, nitrile: benzonitrile; alkyne: propyne; precatalyst: [CpCo(cod)]; temperature: 25°C; solvent: water; time: 4 h, addition of salt: $MgSO_4$, NaCl, $(NH_4)_2SO_4$ or organic solvents (e.g., toluene) or of surfactants (e.g., Brij 56®, Tween 20, DDaPs, SDS, CTABr, $CTAHSO_4$).

Values obtained by GLC analysis after quenching of the reaction (inner standard: *n*-octane).

2-(2-Methoxyethyl)-pyridine. A thermostatted (25°C) reaction vessel, equipped with a Teflon-coated magnetic spin bar, is loaded with 20 ml oxygen-free water. A mixture consisting of 1 ml of toluene, 23.1 mmol of 2-methoxypropionitrile and 0.086 mmol of [CpCo(cod)] was placed in the reactor. The vessel was connected with an ethyne measuring and delivering device maintaining the gas pressure constant. Alternatively, ethyne could simply be bubbled through the solution. The mixture was stirred and irradiated by two 460 W Phillips HPM 12 lamps for 4 h. The pyridine was detected by GLC (yield: 4.6 mmol) and isolated by preparative GLC. The yield of benzene was only detected by GLC (> 1%).

Acknowledgements

We thank Prof. Dr. U. Rosenthal and PD Dr. A. Börner for helpful discussions. We are grateful to Mrs. M. Heyken for technical assistance, Ing. K. Kortus for GLC, Ing. H. Baudisch for GLC-MS, Dr. Michalik and Dr. W. Baumann for NMR, Dr. H. Fuhrmann for preparative GLC and Ing. C. Fuhrmann for GLC-IR measurements. Acknowledgement is given to Prof. Dr. G.E. Herberich (RWTH Aachen) and Dr. H.-U. Jürgens (University of Rostock) for the generous gift of some catalysts.

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