First Cobalt(I)-catalysed Heterocyclotrimerization of Ethyne with Nitriles to Pyridines in Water under Mild Conditions

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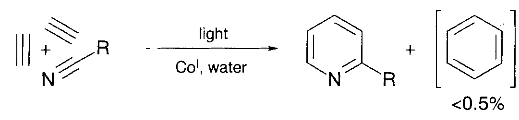
In water the synthesis of substituted pyridines with cobalt(I)-complexes is carried out at room temperature and normal pressure with very high product selectivity in the presence of light.

The thermally driven cobalt(I)-catalysed cotrimerization of alkynes and nitriles has been described by Yamazaki and Wakatsuki,[1] Bönnemann and Brijoux,[2] and Vollhardt.[3] However, with ethyne, the problems arising from these syntheses and disfavouring industrial application are the required high temperatures and pressures and the rather high side-yield of benzene.

In 1989 our group observed that these somewhat drastic conditions with ethyne are unnecessary if the reaction is activated in the presence of light.[4] Even sunlight was found to be suitable. The visible region of 350–480 nm was then established to have the required light quantum energy. As a consequence, a broad spectrum of pyridine derivatives, substituted at the α-carbon, have been made available by these means in a one-step reaction under ambient conditions.



Scheme 1

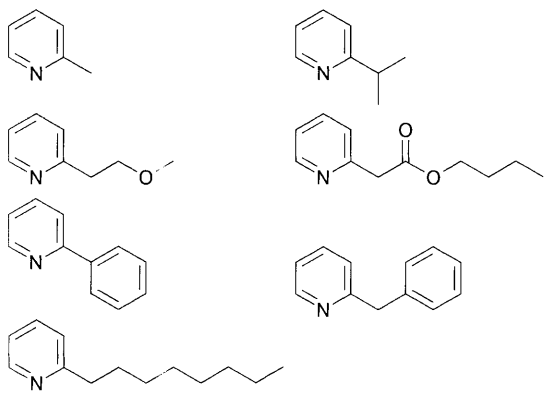


Fig. 1

Bönnemann and Brijoux have, by sophisticated studies, proposed a mechanism of the thermally performed cotrimerization, whose main feature consists of the intermediacy of a metallacyclopentadiene species, formed by the reaction of two molecules of alkyne with a cobalt(I) centre.[2] Reaction of this with ethyne or nitrile results in the competitive formation of benzene and pyridine. While in the thermal reaction high pressures and concentrations are beneficial for the formation of the metallacyclic intermediate(s), they are likely to provide a higher side-yield of undesired benzene.

Our previous investigations indicate that the mechanism of the photolytically initiated reaction should be similar to the thermal process.[6] However, light quantum energy appears to accelerate some of the steps which are rate-determining in the thermal reaction (probably the formation of the metallacycle) and thus accounts for the mild conditions by which product selectivities are enhanced. Further optimization of selectivities is possible by a careful choice of solvent and temperature, respectively. We finally tried water.

In *supercritical* water of 374 °C the 'dark' reaction of hex-1-yne and acetonitrile results in a yield of 15% of pyridine isomers, as Jerome and Parsons recently reported.[7]

Employing light of *ca.* 400 nm we found, that [in the presence of a cobalt(I) catalyst] the heterotrimerizations of ethyne with nitriles in water could be conducted under ambient conditions (see Scheme 1).[8]† Here, by gas chromatography, we detected always less than 0.5% of the homotrimerization product benzene.‡ (Using common organic solvents we usually found 5–30% of benzene).

Pyridines, synthesized by this manner in water, are shown in Fig. 1; there appears to be no limitation of the scope of the water-reaction.

The addition of micelle-forming surfactants has some influence upon the reactions in water. Water-soluble as well as insoluble nitriles generally are suitable for the reaction with ethyne. However, in case of water-soluble nitriles, satisfactory results were only obtained in the presence of surfactants.

Table 1 Reaction of selected nitriles with ethyne in water

Nitrile (mmol)	Yield of pyridine (%)	Yield of benzene (%)[a]	Catalyst (mmol)	Surfactant (mmol)	t/*h*
PhCN (24.3)	41	0.2	**1** (0.0077)	—	3
Bu^{n}OCOCH$_2$CN (17.5)	50	0.2	**1** (0.006)	—	3
PhCN (24.3)	74.5	0.5	**1** (0.08)	—	3
PhCN (24.3)	51	0.02	**1** (0.02)	Brij 56[b] (0.2)	4
PhCN (24.3)	62	0.37	**3** (0.049)	—	3
PhCN (24.3)	67	0.37	**3** (0.075)	Brij 56 (0.2)	4
PhCH$_2$CN (43.4)	67	0.44	**2** (0.054)	—	3
PhCH$_2$CN (21.7)	62	0.1	**1** (0.047)	Brij 56 (0.2)	4
C$_9$H$_{19}$CN (20.75)	73	0.5	**1** (0.065)	—	3
MeCN (20.1)	18	—	**1** (0.07)	Brij 56 (0.2)	4
MeOCH$_2$CH$_2$CN (27.6)	20	—	**1** (0.0775)	Brij 56 (0.2)	4
C$_9$H$_{19}$CN (1)	38[a]	0.3	**1** (0.01)	Tween 20[c] (0.1)	8

[a] Detected by GC and GC–MS. [b] Decaoxyethylenehexadecyl ether. [c] Polyoxyethylenesorbitanmonolaurate.

Micelle-forming surfactants, *e.g.* Brij 56, were, on the other hand, found to be somewhat disadvantageous in cases where water-insoluble nitriles are involved; with usually the best results accomplished in the absence of surfactants (Table 1).

Our first studies of these catalytic reactions with cyclopentadienyl(cycloocta-1,5-diene)cobalt(I) [Co(η^5-C_5H_5)(cod)] **1** and other derivatives such as acetylcyclopentadienyl(cycloocta-1,5-diene)cobalt(I) [Co(η^5-C_5H_4MeCO)(cod)] **2** and cycloocta-1,5-diene-(indenyl)cobalt(I) [Co(η^5-C_9H_7)(cod)] **3** also showed good performances as indicated in Table 1.

It may be considered surprising that this organometallic and catalytic reaction proceeds well in the presence of a medium such as water. We assume the catalyst forms an emulsion with the nitrile while water precludes the fast approach of hydrophobic ethyne, allowing only small quantities to come close to the coordination sphere of cobalt(I). The low solubility (and hence steady-state solution concentration) of ethyne may well account for the observed product selectivity.

Further reactivity studies in water, with and without surfactants, are currently under way. Since the photocatalytic synthesis of functionalised pyridines is performed by unsophisticated means, requiring only sunlight and water (the latter may be recycled), and the formation of by-products is avoided, we believe it to be an elegant and environmentally friendly advance.

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Footnotes

† All operations were performed under an atmosphere of prepurified argon using standard Schlenck techniques. Ethyne of 99.5% purity (Linde) was generally used as received. Catalysts were prepared according to literature procedures.[9] Nitriles were purchased commercially from Fluka, stored over activated molecular sieve (3 Å) and distilled. *Example of the experimental procedures*; (*a*) 2-phenylpyridines: a thermostatted (25 °C) reaction vessel, equipped with a Teflon-coated magnetic spin bar, is loaded with 2.5 ml (24.3 mmol) benzonitrile and 1.8 mg (7.7 μmol) of [Co(η^5-C_5H_5)(cod)]. To the solution, 10 ml of oxygen-free water was added and the vessel connected with an ethyne measuring and delivering device, maintaining a constant pressure of ethyne. Alternatively, ethyne may simply be bubbled through the solution. The mixture is irradiated by two 460 W Phillips HPM 12 lamps (*ca.* 400 nm) for 3 h. The yield of 2-phenylpyridine is 9.96 mmol (41%), as isolated by vacuum distillation. Benzene content (*ca.* 0.2%) was detectable only by means of gas chromatography; (*b*) 2-(2-methoxyethyl)pyridine: the same procedure is employed with a mixture of 230 mg (0.2 mmol) decaoxyethylenehexadecyl ether (Brij 56), dissolved at 40 °C in 10 ml of oxygen-free water, and 2.5 ml (27.6 mmol) 3-methoxypropionitrile, in which 18 mg (77.5 μmol) of [Co(η^5-C_5H_5)(cod)] has been dissolved. After 4 h of irradiation a yield of 0.76 g (5.5 mmol, 20%) of 2-(2-methoxyethyl)pyridine was obtained.

‡ GLC analyses were performed on an HP 5890 II chromatography column 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 cm^3 min^{-1}).

References

1 H. Yamazaki and Y. Wakatsuki, *Tetrahedron Lett.*, 1973, **36**, 3383.

2 H. Bönnemann and W. Brijoux, *Adv. Heterocycl. Chem.*, 1990, **48**, 177.

3 K. P. C. Vollhardt, *Angew. Chem., Int. Ed. Engl.*, 1984, **23**, 539; *Angew. Chem.*, 1984, **96**, 525.

4 W. Schulz, H. Pracejus and G. Oehme, *Tetrahedron Lett.*, 1989, **30**, 1229.

5 B. Heller, J. Reihsig, W. Schulz and G. Oehme, *Appl. Organomet. Chem.*, 1993, **7**, 641; F. Karabet, B. Heller, K. Kortus and G.Oehme, submitted for publication; B. Heller, W. Schulz, G. Oehme and D. Heller, DE 41 422 47, 1991.

6 B. Heller, D. Heller and G. Oehme, to be published.

7 K. S. Jerome and E. J. Parsons, *Organometallics*, 1993, **12**, 2991.

8 B. Heller and G. Oehme, DE 43 451 27, 1993.

9 H. Bönnemann, B. Bogdanovič, R. Brinckmann, B. Spliedhoff and D. He, *J. Organomet. Chem.*, 1993, **451**, 23.