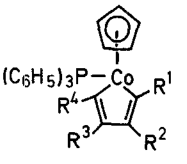
Cobaltocene Catalyzed Synthesis of Pyridines

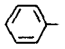
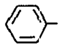
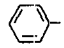
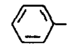
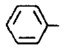
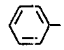
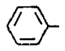
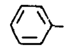
Yasuo Wakatsuki, Hiroshi Yamazaki

The Institute of Physical and Chemical Research, Wako-shi, Saitama 351, Japan

We have recently shown that two molecules of acetylene and one molecule of a nitrile co-cyclotrimerize to give pyridines in the presence of a catalytic amount of cyclopentadienyltriphenylphosphinecobaltatetraphenylcyclopentadiene (**1a**) or cyclopentadienyl(diphenylacetylene)-triphenylphosphinecobalt[1].



1

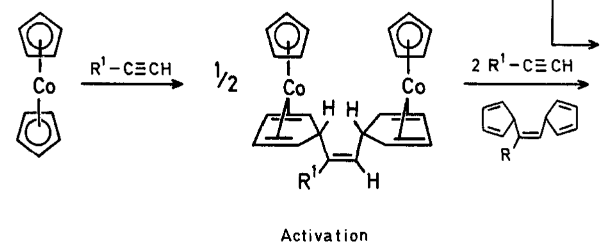
	R^1	R^2	R^3	R^4
a				
b		H_3COOC		H_3COOC
c		H_3COOC	H_3COOC	

Later, Bönnemann and coworkers carried out similar reactions using a Co(I) catalyst, which had been prepared *in situ* from cobalt salts and reductants[2].

Although complex **1a** is a good catalyst, being very stable in air and functioning well under mild conditions, its preparation is troublesome[3]. On searching for more easily obtainable catalysts, we have found that cobaltocene (di-π-cyclopentadienylcobalt) serves this purpose well. We now wish to report this improved method for the synthesis of pyridines from acetylenes and nitriles.

Most of the reactions were carried out at 150° in benzene or toluene: lower temperatures generally resulted in lower yields.

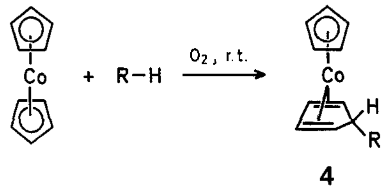
Unsubstituted acetylene (initial pressure at room temp. 8–9 atm) reacted with nitriles (ca. 140 mmol) in an autoclave for 7 hours in the presence of cobaltocene (2 mmol) to give 2-substituted pyridines. Unlike the reactions of substituted acetylenes, only a trace amount of benzene was formed as a by-product. Table 1 summarizes the reaction conditions and the result.



Similarly, mono-substituted acetylenes reacted with nitriles in a sealed ampoule to give a mixture of 2,4,6- and 2,3,6-trisubstituted pyridines (**2** and **3**, respectively). No other isomers of pyridine were detected, but small amounts of benzene derivatives were formed as by-products. Some of the results are shown in Table 2.

As shown in Table 2, the bulkiness of the substituent on the acetylene or the nitrile retards the catalytic activity. In the case of unsubstituted acetylene, however, the catalytic activity was lower than methyl- or ethylacetylene due to some unknown interfering effect.

Cyclopentadienylcyclopentadienecobalt (**4**) is also an active catalyst[4]. It can be prepared readily by bubbling oxygen at room temperature through a solution of cobaltocene and a nitrile or chloroform (R—H)[5].



4

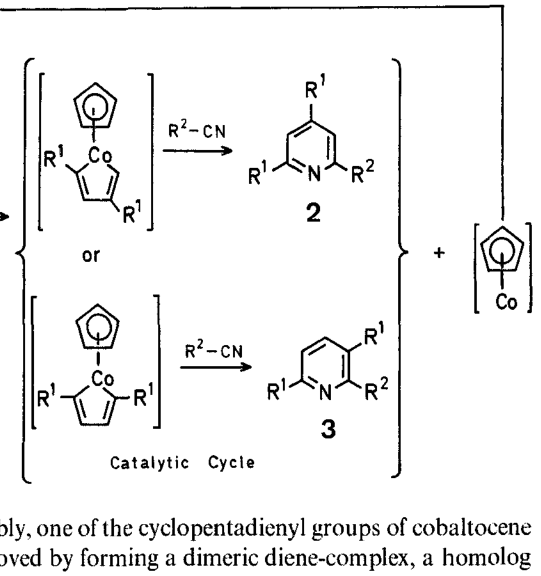
R = $-CH_2CN$, $-CH(CN)CH_3$, $-C(CN)=CH_2$, $-CH(CN)CH_2OCH_3$, $-CCl_3$

Thus, the reaction of cyclopentadienyl(cyanomethylcyclopentadiene)cobalt (**4**, R = CH_2CN) under conditions similar to those indicated in Table 1 yielded 2-picoline with a catalytic activity of 75.

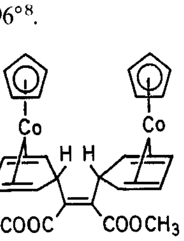
Under the same conditions as those given in Table 2, di-substituted acetylenes did not react at all with nitriles. However, in the reaction of diphenylacetylene with acetonitrile at 120° in the presence of cobaltocene and an equimolar amount of triphenylphosphine, a small amount of **1a** (1% yield based on the initial cobaltocene) was obtained along with cyclopentadienyltetraphenylcyclobutadienecobalt and 2-methyltetraphenylpyridine (44% and 34% yield, based on cobaltocene). Since **1a** is known to react with acetonitrile to give 2-methyltetraphenylpyridine[7], it is probable that **1a** is the intermediate in this pyridine formation.

Moreover, methyl phenyl acetylenecarboxylate reacted with cobaltocene and equimolar amount of triphenylphosphine at 100° for 17 hours to give **1b** and **1c** in 35% and 27% yield, respectively.

For these reasons, we suggest that cyclopentadienylcobaltacyclopentadiene, which has previously been proposed in the pyridine synthesis catalyzed by **1a**[1], is also the key intermediate in the present catalytic reaction.



Probably, one of the cyclopentadienyl groups of cobaltocene is removed by forming a dimeric diene-complex, a homolog of **4**, since cobaltocene reacts with dimethyl acetylenedicarboxylate at room temperature to give a 48% yield of a similar complex (**5**), red crystals that decompose at 193–196°[8].



5

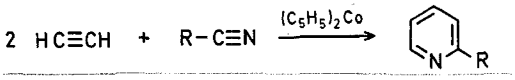
2-Phenylpyridine:

Cobaltocene (378 mg, 2 mmol) was placed in an autoclave (volume 200 ml) and the vessel was filled with nitrogen. Toluene (20 ml) and benzonitrile (14.5 ml, ~140 mmol) were introduced via syringes through a hole at the head of the autoclave. After the vessel was flushed with acetylene 5 times, the acetylene to be reacted was introduced up to a pressure of 9 atm while the autoclave was mechanically shaken at room temperature. The autoclave was heated to 150°. Within 2 hours, the pressure dropped to 3 atm and more acetylene was added (13 atm at 150°). After 7 hours the reaction mixture was fractionally distilled. 2-Phenylpyridine was distilled out at 90°/1.5 torr; yield: 15.8 g, 102 mmol (73% based on benzonitrile).

2-Methyl-4,6-diethylpyridine and 2-Methyl-3,6-diethylpyridine:

To a mixture of toluene (15 ml) and acetonitrile (15 ml) in an ampoule, ethylacetylene (5 ml, ~62 mmol) was introduced by cooling the ampoule. The ampuole was then attached to a vacuum line and throughly degassed. The mixture was distilled into another ampoule which was also attached to the vacuum line and contained cobaltocene (38 mg, 0.2 mmol). The ampoule was sealed and heated to 150°. After 11 hours the reaction mixture was distilled. The fraction (6.80 g) which distilled out at 90–100°/20 torr contained 87% of pyridines and 13% of triethylbenzene as determined by G.L.C. (conditions: 1.5% OV-17 on Shimalite w; 170°). Triethylbenzene was removed by preparative G.L.C. (conditions: 1.5% OV-17 on Shimalite w; 170°). The G.L.C. and N.M.R. spec-

Table 1. The Reaction of Unsubstituted Acetylene with Nitriles[a]



Nitrile R	ml	Solvent	Product and amount	Yield (%)[e]	b.p.	n_D^{20}	Catalytic Activity[f]
CH_3	7.5	benzene	2-methylpyridine (7.91 g)[b]	60	127–129°	1.4985	43
C_2H_5	10	benzene	2-ethylpyridine (9.37 g)[c]	62	144–145°	1.4970	44
n-C_3H_7	13	benzene	2-*n*-propylpyridine (10.8 g)[c]	60	164–165°	1.4921	45
i-C_3H_7	13	benzene	2-*i*-propylpyridine (7.58 g)[c]	43	155–157°	1.4910	31
$H_2C{=}CH$	10	benzene[g]	2-vinylpyridine (5.00 g)[b]	31	~80°/30 torr	1.5488	48
C_6H_5	14.5	toluene	2-phenylpyridine (15.8 g)[b]	73	90°/15 torr	1.6230	51
$C_6H_5CH_2$	15	toluene	2-benzylpyridine (4.25 g)[d]	19	—	—	13

[a] Reaction conditions: solvent (20 ml), cobaltocene (378 mg, 2 mmol); reaction temperature: 150°, reaction time 7 h.

[b] The product is identified by comparison of the I.R. spectrum with that of an authentic sample.

[c] The product is identified by the mass and ^{1}H-N.M.R. spectra.

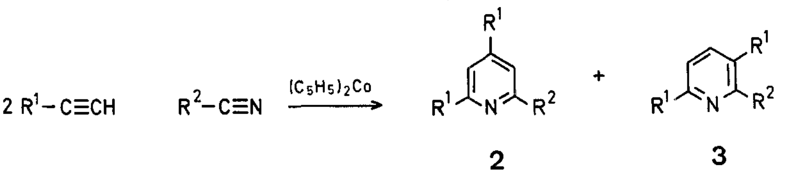
[d] The amount of product is estimated by G.L.C. of the fraction boiling at 80–100°/1.5 torr which is contaminated by benzyl nitrile; picrate m.p. 140° (Lit. 140°).

[e] Yield based on nitrile.

[f] Catalytic Activity: $\frac{\text{mol of pyridine formed}}{\text{mol of catalyst used}}$.

[g] One mmol of cobaltocene used; the reaction was carried out at 110° to lessen the loss of product by polymerisation.

Table 2. The Reaction of Mono-substituted Acetylenes with Nitriles[a]



Acetylene R^1	ml	Nitrile R^2	ml	Products Total Yield in g	Composition[b] % of **2**	% of **3**	% Benzenes	Catalytic Activity[c]
CH_3	5.0	CH_3	15	4.92	48	45	7	188
C_2H_5	5.0	CH_3	15	6.80	57	30	13	200
n-C_3H_7	4.75	CH_3	10	2.86	47	42	11	72
n-C_4H_9	4.65	CH_3	10	0.80	48	40	12	15
C_2H_5	5.0	*n*-C_3H_7	10	4.30	46	28	26	90

[a] Reaction conditions: toluene (15 ml), cobaltocene (38 mg, 0.2 mmol); reaction temperature 150°; reaction time 11 h.

[b] The molar composition of the products was estimated by G.L.C. (conditions: 1.5% OV-17 on Shimalite W; 135–170°) and/or N.M.R.

[c] Catalytic activity: $\frac{\text{mol of } \mathbf{2}+\mathbf{3} \text{ produced}}{\text{mol of catalyst used}}$.

trum showed the remaining pyridine mixture contained *2-methyl-4,6-diethylpyridine* and *2-methyl-3,6-diethylpyridine* in a ratio of 1.9/1.

$C_{10}H_{15}N$	calc.	C 80.48	H 10.13	N 9.39
(149.2)	found	80.44	10.17	9.12

Mass spectrum: $m/e = 149$ ($M^{\oplus}$).

We are grateful to the Ministry of Education of Japan for a Scientific Research Grant-in-aid.

Received: September 4, 1975

---

[1] Y. Wakatsuki, H. Yamazaki, *Tetrahedron Lett.* **1973**, 3383.

[2] H. Bönnemann, R. Brinkmann, H. Schenkluhn, *Synthesis* **1974**, 575.

[3] Y. Wakatsuki, T. Kuramitsu, H. Yamazaki, *Tetrahedron Lett.* **1974**, 4549.
H. Yamazaki, N. Hagihara, *Bull. Chem. Soc. Japan* **44**, 2260 (1971).

[4] Bönnemann and Brinkmann have used closely related compound, $(C_5H_5)Co$(cycloocta-1,5-diene), as catalyst for dipyridyl synthesis from dinitriles and acetylene[6].

[5] H. Kojima, S. Takahashi, H. Yamazaki, N. Hagihara, *Bull. Chem. Soc. Japan* **43**, 2272 (1970).

[6] H. Bönnemann, R. Brinkmann, private communication; *Synthesis* **1975**, 600.

[7] Y. Wakatsuki, H. Yamazaki, *J. Chem. Soc. Chem. Commun.* **1973**, 280.

[8] H. Kojima, H. Yamazaki, unpublished data.