Cobalt Metallacycles. Part 5.[1] Synthesis of Pyridines from Nitriles and Acetylenes *via* Cobaltacyclopentadienes

By **Yasuo Wakatsuki** * and **Hiroshi Yamazaki,** The Institute of Physical and Chemical Research, Wako-shi, Saitama 351, Japan

The complexes, $[Co(CR^1{:}CR^2{\cdot}CR^3{:}CR^4)(cp)(PPh_3)]$ (cp = η-cyclopentadienyl) react with nitriles to give highly substituted pyridines. When $R^4 = CO_2Me$, nitriles react regioselectively such that the nitrogen atom in the resulting pyridine ring occupies a position away from the carbon to which the CO_2Me is attached. The reaction with 2-methylacrylonitrile gives, beside the pyridine, a cyclohexadiene derivative and its complex. The complex $[Co(cp)-(PhC{:}CPh)(PPh_3)]$ does not react with nitriles to form a nitrogen-containing cobalt metallacycle. The mechanism of the stoicheiometric and catalytic reaction is discussed.

IN Part 1 of this series we reported the preparation and characterization of cobaltacyclopentadiene complexes, $[Co(CR^1{:}CR^2{\cdot}CR^3{:}CR^4)(cp)(PPh_3)]$ (1; cp = η-C_5H_5), having various substituents.[2] It has also been shown that the reaction of (1) with olefins and acetylenes provides a simple way of preparing highly substituted cyclohexadienes and benzenes.[3] Control of substitution in these organic ring compounds has been achieved by using (1) with substituents at the desired positions in the metallacyclopentadiene ring. In certain cases the reaction proceeds catalytically.

As an application of these reactions, we have briefly communicated that the CN triple bond of nitrile can also be incorporated into an organic cyclic compound to give pyridine either stoicheiometrically, by the reaction with (1),[4] or catalytically by the reaction with acetylenes in the presence of (1a; R^1—R^4 = Ph) or the diphenyl-acetylene complex, $[Co(cp)(PhC{:}CPh)(PPh_3)]$ (2a).[5] Later, several workers reported similar formation of pyridines from nitriles and acetylenes using $[Co(cp)-(CO)_2]$,[6] $[Co(cp)(\eta^4\text{-diene})]$,[7] and $[Co(cp)_2]$[8] as the

catalyst. The mechanism of these catalytic reactions has remained obscure, although our preliminary results on the stoicheiometric reaction of (1) with nitriles strongly suggested a cobaltacyclopentadiene intermediate.[4]

In this paper we describe a detailed study of the stoicheiometric reaction of (1) with nitriles, first to demonstrate the synthetic utility of the reaction and secondly to shed light on the mechanism of the reaction, which is closely related to the catalyzed pyridine synthesis from nitriles and acetylenes.

RESULTS AND DISCUSSION

The reactions of (1a)—(1c) with nitriles were conducted at 70 °C in benzene whereas higher temperatures (>120 °C) were necessary when the cobaltacyclopentadiene had methoxycarbonyl as the substituent(s), *i.e.* in the cases of (1d)—(1h) [equation (1)]. The decomposed material precipitated as the reaction proceeded. The desired pyridine was obtained in moderate yield, by column-chromatographic work-up of the reaction mixture to remove triphenylphosphine and the decomposed material. The Table summarizes the highly substituted

[1] Part 4, Y. Wakatsuki and H. Yamazaki, *J. Organometallic Chem.*, 1978, **149**, 385.

[2] H. Yamazaki and Y. Wakatsuki, *J. Organometallic Chem.*, 1977, **139**, 157.

[3] Y. Wakatsuki, T. Kuramitsu, and H. Yamazaki, *Tetrahedron Letters*, 1974, 4549.

[4] Y. Wakatsuki and H. Yamazaki, *J.C.S. Chem. Comm.*, 1973, 280.

[5] Y. Wakatsuki and H. Yamazaki, *Tetrahedron Letters*, 1973, 3383.

[6] K. P. C. Vollhart and R. G. Bergman, *J. Amer. Chem. Soc.*, 1974, **96**, 4996.

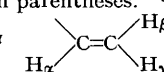[7] H. Bönnemann and R. Brinkman, *Synthesis*, 1975, 600.

[8] Y. Wakatsuki and H. Yamazaki, *Synthesis*, 1976, 26.

pyridines thus obtained. In principle, the present method can be also applied to other cobaltacyclopenta- dienes and nitriles, providing a route to a wide variety of substituted pyridines.

Yields, melting points, analyses, and n.m.r. data for the substituted pyridines:

	Pyridine derivative					Yield (%)	M.p. (θc/°C)	Analysis (%) [a]	^{1}H N.m.r. in CDCl$_3$ [b] (δ/p.p.m.)
	R^1	R^2	R^3	R^4	R^5				
(3a-1)	Ph	Ph	Ph	Ph	Me	33	167	C 90.5 (90.65) H 5.85 (5.85) N 3.45 (3.50)	2.50 (s, CH$_3$)
(3a-2)	Ph	Ph	Ph	Ph	Ph	30	237—240 [c]	C 91.45 (91.45) H 5.55 (5.50) N 2.95 (3.05)	
(3a-3)	Ph	Ph	Ph	Ph	CH=CH$_2$	72	173	C 90.65 (90.9) H 5.75 (5.65) N 3.50 (3.40)	5.36 [dd, Hα, J(HαHβ) 8, J(HαHγ) 4.5] [d]
(3a-4)	Ph	Ph	Ph	Ph	CMe=CH$_2$	20	184	C 90.8 (90.75) H 6.05 (5.95) N 3.25 (3.30)	1.95 (br s, CH$_3$) 4.98 {(m, Hβ and 5.12 { Hγ)
(3b-1)	Ph	Me	Me	Ph	Pr^i	66	154	C 87.7 (87.65) H 7.70 (7.70) N 4.35 (4.65)	1.15 (d, CH J 13) 1.98 (s, CH$_3$), 2.27 (s, CH$_3$) 2.81 (spt, H, J 13)
(3b-2)	Ph	Me	Me	Ph	CH=CH$_2$	53	125	C 88.3 (88.4) H 6.75 (6.70) N 4.85 (4.90)	2.02 (s, CH$_3$), 2.29 (s, CH$_3$) 5.17 [dd, Hα, J(HαHβ), 17, J(HαHγ) 9.5] [d] 6.36 (d, Hγ), 6.39 (d, Hβ)
(3b-3)	Ph	Me	Me	Ph	CMe=CH$_2$	54	122—123	C 88.05 (88.25) H 7.10 (7.05) N 4.60 (4.70)	1.82 (br s, CH$_3$) 2.07 (s, CH$_3$), 2.27 (s, CH$_3$) 4.82 and 4.99 (m, Hβ and Hγ)
(3c) [e]	Ph C$_6$H$_4$Me-p	Ph H	H Ph	C$_6$H$_4$Me-p Ph	Me Me	39	110—118	C 89.35 (89.5) H 6.40 (6.30) N 4.10 (4.20)	2.41 (s, Ph–CH$_3$) 2.49 (s, CH$_3$) 2.63 (s, CH$_3$)
(3d-1)	Ph	CO$_2$Me	CO$_2$Me	Ph	Me	33	107	C 73.35 (73.1) H 5.35 (5.30) N 4.00 (3.90)	2.46 (s, CH$_3$) 3.52 (s, CO$_2$CH$_3$) 3.63 (s, CO$_2$CH$_3$)
(3d-2)	Ph	CO$_2$Me	CO$_2$Me	Ph	Et	53	138	C 73.7 (73.6) H 5.65 (5.65) N 3.70 (3.75)	1.17 (t, J 14.5, CH$_3$) 2.72 (q, CH$_2$) 3.50 (s, CO$_2$CH$_3$), 3.62 (s, CO$_2$CH$_3$)
(3e)	Ph	Ph	CO$_2$Me	CO$_2$Me	Me	33	119—120	C 73.35 (73.7) H 5.30 (5.30) N 3.75 (3.90)	2.82 (s, CH$_3$) 3.54 (s, CO$_2$CH$_3$), 3.93 (s, CO$_2$CH$_3$)
(3f-1)	Ph	CO$_2$Me	Ph	CO$_2$Me	Me	61	f	C 72.85 (73.1) H 5.30 (5.30) N 3.30 (3.90)	2.78 (s, CH$_3$) 3.47 (s, CO$_2$CH$_3$), 3.67 (s, CO$_2$CH$_3$)
(3f-2)	Ph	CO$_2$Me	Ph	CO$_2$Me	Ph	57	162—163	C 76.75 (76.6) H 5.20 (5.00) N 3.25 (3.30)	3.38 (s, CO$_2$CH$_3$)
(3g)	Ph	Ph	Me	CO$_2$Me	Pr^n	57	70—71	C 79.95 (79.95) H 6.80 (6.70) N 3.90 (4.05)	1.02 (t, J 7, CH$_3$), 3.94 (s, CO$_2$CH$_3$) 1.86 (sxt, J 7, CH$_2$) 2.09 (s, CH$_3$), 2.83 (t, J 7, CH$_2$)
(3h)	Me	CO$_2$Me	Me	CO$_2$Me	Me	51	72—73 [g]	C 60.95 (60.75) H 6.35 (6.35) N 5.90 (5.90)	2.24 (s, CH$_3$) 2.50 (s, CH$_3$) 3.92 (s, CO$_2$CH$_3$)

[a] Calculated values are given in parentheses. [b] Phenyl absorptions are omitted; J values in Hz. [c] Lit., 242 °C (W. Dilthey, *J. Prakt. Chem.*, 1922, **104**, 32). [d]

[e] Mixture of two isomers. [f] Viscous oil. [g] Lit., 82 °C (A. Hantzsch, *Ber.*, 1883, **16**, 1947).

Previously we have shown that complexes (1) react with olefins to form cyclohexadienes and/or cyclohexadiene complexes and that the first step of the reaction is displacement of the phosphine ligand in (1) by
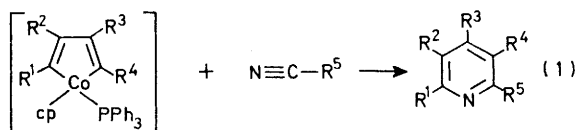
(1a) $R^1 = R^2 = R^3 = R^4 = Ph$
(1b) $R^1 = R^4 = Ph$, $R^2 = R^3 = Me$
(1c) $R^1 = R^2 = Ph$, $R^3 = H$, $R^4 = C_6H_4Me-p$
(1d) $R^1 = R^4 = Ph$, $R^2 = R^3 = CO_2Me$
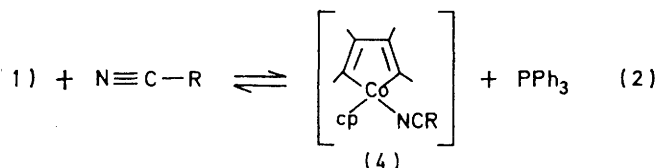(1e) $R^1 = R^2 = Ph$, $R^3 = R^4 = CO_2Me$
(1f) $R^1 = R^3 = Ph$, $R^2 = R^4 = CO_2Me$
(1g) $R^1 = R^2 = Ph$, $R^3 = Me$, $R^4 = CO_2Me$
(1h) $R^1 = R^3 = Me$, $R^2 = R^4 = CO_2Me$

$cp = \eta-C_5H_5$

olefins.[9] In the present reaction with nitriles, a similar equilibrium (2) is conceivable: indeed, addition of free PPh_3 to the reaction (1d) + EtCN ⟶ (3d-2) markedly

retarded the reaction rate. We propose that the next step is insertion of the co-ordinated nitrile into one of the Co–C σ bonds, forming a seven-membered cobalt metallacycle (5).

As expected, when acrylonitrile or 2-methylacrylonitrile were treated with (1), co-ordination and insertion of the olefinic bond competed with those of the nitrile group, cyanocyclohexadiene as well as 2-alkenylpyridine being the products.

Interestingly, when (1) has a CO_2Me group as a substituent at the positions next to the cobalt, i.e. in the cases of (1e)—(1h), only one isomer of the possible two isomeric pyridines resulted from the reaction with nitriles. The structure of the isomer was unequivocally determined in the cases of pyridines derived from

(1f) R = Ph
(1h) R = Me

(3f–2),(3h)
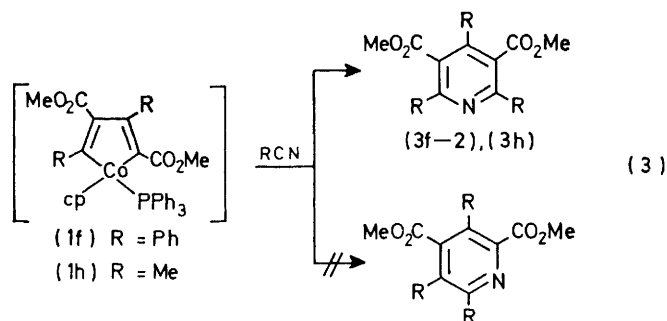
the reactions of (1f) with benzonitrile and (1h) with acetonitrile [equation (3)]. In both cases the n.m.r. spectra

* An atomic model study showed that the steric interaction between the cp ring and R (or R′) is not critical.

showed that the two methoxycarbonyl groups are magnetically equivalent [two of the three C–Me groups of (3h) are also equivalent], indicating incorporation of the CN bond into the cyclopentadiene ring in such a way as to position the N atom away from the C atom to which the CO_2Me group is attached. This rule was employed in assigning the structures of other pyridines, (3e) and (3g), formed by similar reactions.

To accommodate these observations the intermediate seven-membered cobalt metallacycle should have the configuration (5a) or (5b) where R is the substituent originating from the nitrile and $R' = CO_2Me$. In view of the polarity of the cobalt–carbon σ bond ($Co^{\delta+}-C^{\delta-}$) in (1) and that of the CN triple bond ($R-C^{\delta+}\equiv N^{\delta-}$), (5a) could well be favoured over (5b), whereas steric interaction between R and R′ would favour (5b).*

For comparison, the reaction of (1f) with phenylacetylene, which possesses a much less polar triple bond than benzonitrile but has comparable bulkiness, was examined under similar conditions to that of (1f) + PhCN ⟶ (3f-2) [equation (3)]. A good yield of a 1 : 1 mixture of 1,3-bis(methoxycarbonyl)-2,4,6-triphenylbenzene and 1,3-bis(methoxycarbonyl)-2,4,5-triphenylbenzene resulted, suggesting that the polarity of the CN triple bond, and not the steric interaction between the substituents, is the determining factor for the regioselective pyridine formation. Therefore we conclude that (5a) is more likely than (5b).

(5a)   (5b)
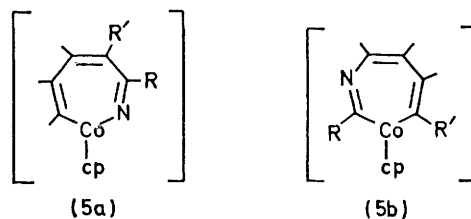
The final step of the pyridine formation would be reductive elimination of the pyridine ring from (5a). In

(6)
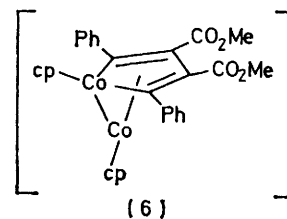
some cases the Co(cp) unit thus liberated was stabilized by co-ordination to unchanged cobaltacyclopentadiene forming the known binuclear framework (6).[10] This observation implies that the η-cyclopentadienyl ring remains co-ordinated to cobalt throughout the reaction.

All the attempts to prepare pyridines via an alternative cobalt metallacycle, i.e. a five-membered metallacycle consisting of one acetylene unit and one nitrile unit (1′), were unsuccessful, e.g. the (diphenylacetylene)cobalt

[9] Y. Wakatsuki and H. Yamazaki, J. Organometallic Chem., 1977, 139, 169.
[10] M. Rosenblum and B. North, J. Amer. Chem. Soc., 1968, 90, 1060.

complex (2a) did not react with nitriles. However, when dimethyl acetylenedicarboxylate or diphenylacetylene was added to a mixture of (2a) and acetonitrile, (3e) and (3a-1), respectively, were formed even at ambient temperature. These results can be interpreted in terms

After 20 h the reaction mixture was concentrated and chromatographed on Al_2O_3 (1.5 × 10 cm). The column was washed with hexane and the eluate was collected with benzene–hexane (1 : 1) (80 cm³). The solvent was evaporated and hexane was added to the residue to give
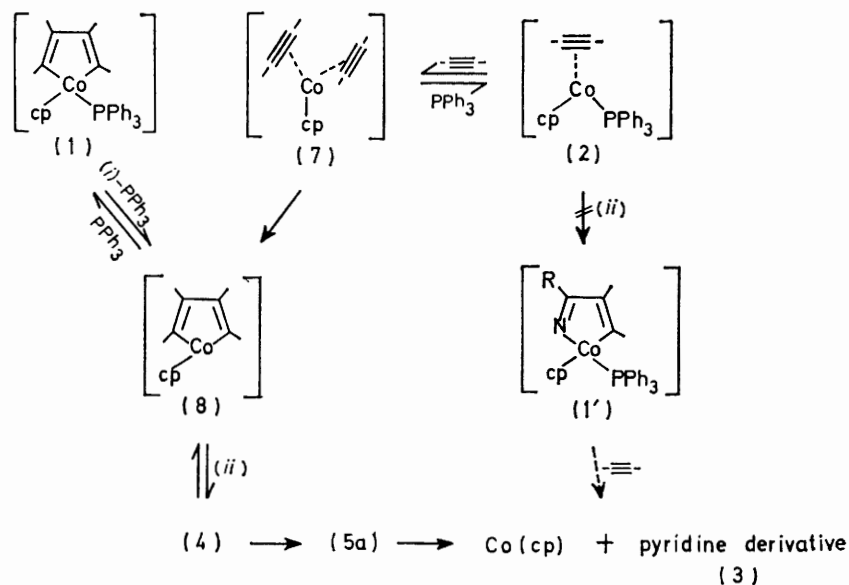
SCHEME (i) Heat; (ii) RCN

of the reactions illustrated in the Scheme.* The reaction sequence (2) ⟶ (7) ⟶ (8) ⟶ (1) has been proposed for the formation of (1) by the reaction of acetylene complexes [Co(cp)(R¹C≡CR²)(PPh₃)] (2) with

$$[Co(cp)(R^1C \equiv CR^2)(PPh_3)] \qquad (2)$$
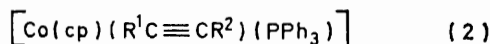
acetylenes, which proceeds at room temperature.[2] In the presence of a large excess of a nitrile, intermediate (8) will react with nitrile to form (4), which leads to pyridine (3) rather than with phosphine to form (1). Heating is required in order to generate the co-ordinatively unsaturated intermediate (8) from (1) by removing phosphine. In the catalyzed process, the Co(cp) unit liberated in the final step of the Scheme will regenerate (7) by co-ordination of acetylene.

EXPERIMENTAL

All the reactions were carried out under an atmosphere of nitrogen. Melting points were uncorrected, and determined on a Mitamura micro-melting-point apparatus. Hydrogen-1 n.m.r. spectra were recorded on Varian HA-100 and JEOL-60 spectrometers in CDCl₃. For column chromatography, Sumitomo KCG-30 activated alumina was used. The preparation and characterization of complexes (1) has been described previously.[2]

Reactions of (1) with Alkyl and Phenyl Cyanides.—As an example, the preparation of (3b-1) is described below. A mixture of (1b) (300 mg) and isobutyronitrile (3 cm³) in benzene (15 cm³) was heated at 70 °C in a sealed tube.

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* A related scheme has been suggested for the ring-opening reactions of cobaltacyclopentadienes.[1]

colourless crystals (86 mg) of 2-isopropyl-4,5-dimethyl-3,6-diphenylpyridine (3b-1) on cooling. Other reactions of (1) with alkyl or phenyl cyanides were accomplished by similar procedures. For chromatographic elution of pyridines having a methoxycarbonyl group, a polar solvent such as dichloromethane was used.

Reaction of (1) with Alkenyl Cyanides.—To a solution of (1a) (371 mg) in benzene (15 cm³) was added 2-methyl acrylonitrile (1 cm³) and the mixture was heated at 70 °C for 60 h. Similar work-up to that described above, including the chromatography, of the resulting reaction mixture gave the following compounds: yellow crystals of (η-cyclopentadienyl)(η⁴-tetraphenylcyclobutadiene)cobalt [40 mg, eluted with benzene–hexane (1 : 2)], colourless crystals of 2-(1-methylvinyl)-3,4,5,6-tetraphenylpyridine (3a-4) [40 mg, eluted with benzene–hexane (1 : 1)], brown crystals of (1a) (20 mg, eluted with benzene), colourless crystals of 5-cyano-5-methyl-1,2,3,4-tetraphenylcyclohexa-1,3-diene (21 mg, 10% yield, eluted with benzene), m.p. 166 °C (Found: C, 90.65; H, 5.95; N, 3.20. Calc. for $C_{28}H_{25}N$: C, 90.75; H, 5.95; N, 3.30%), ¹H n.m.r. δ 1.19 (s, CH₃), 2.10 (s, H), 4.54 (s, H), and 6.8—7.4 p.p.m. (m, C₆H₅), i.r. (KBr disc) ν(CN) at 2 230 cm⁻¹, and finally the red crystalline cobalt complex of the above cyclohexadiene[9] (33 mg, 12% yield, eluted with benzene), m.p. 196—197 °C (Found: C, 81.15; H, 5.65; N, 2.60. Calc. for $C_{33}H_{30}CoN$: C, 81.15; H, 5.50; N, 2.55%), δ 1.19 (s, CH₃), 1.70 (d, H, J 15 Hz), 3.32 (d, H), and 4.86 p.p.m. (s, C₅H₅), i.r. (KBr disc) ν(CN) at 2 230 cm⁻¹.

Similarly, a 4.6% yield of dark brown crystals of (η-cyclopentadienyl)(1—2;3—4-η-5-cyano-2,3,5-trimethyl-1,4-diphenylcyclohexa-1,3-diene)cobalt was isolated as a by-product of (3b-3), m.p. 176—178 °C (decomp.) [Found: C, 76.7; H, 6.35%; M 423 (mass spectrum). Calc. for $C_{27}H_{26}CoN$: C, 76.6; H, 6.20%; M 423.4], δ 0.96 (s, CH₃),

2.13 (d, H, J 14 Hz), 2.32 (s, CH$_3$), 2.38 (s, CH$_3$), 2.57 (d, H), and 4.70 p.p.m. (s, C$_5$H$_5$), i.r. (KBr disc) ν(CN) at 2 230 cm^{-1}.

The reaction of acrylonitrile was examined under similar conditions. Only trace amounts of cyclohexadiene derivatives were isolated.

Isolation of μ-[2,3-*Bis(methoxycarbonyl)*-1,4-*diphenylbutadiene*-1,4-*diyl*-C^{1}C^4:1—2;3—4-η]-*bis*[(η-*cyclopentadienyl*)-*cobalt*] (6).—To a benzene solution (15 cm^3) of (1d) (247 mg) was added propionitrile (1 cm^3) and the mixture was heated at 130 °C for 3.5 h. After concentration, the reaction mixture was chromatographed on Al$_2$O$_3$ (1.5 × 10 cm). Triphenylphosphine was eluted with benzene–hexane (1 : 1). The colourless fraction eluted with dichloromethane was collected from which the pyridine (3d-2) was obtained. A second dark brown fraction, also eluted with dichloromethane, was collected and the solvent was evaporated. Addition of hexane to the residue afforded dark brown crystals of (6) in 16% yield, decomposes without melting 215—220 °C [Found: C, 63.45; H, 4.60%; M 568 (mass spectrum). Calc. for C$_{30}$H$_{26}$Co$_2$O$_4$: C, 63.4; H, 4.60%; M 568.4], δ 4.56 (s, CO$_2$CH$_3$), 5.32 (s, C$_5$H$_5$), and 6.27 p.p.m. (s, C$_5$H$_5$).

Effect of PPh$_3$ *on the Reaction of* (1) *with Nitriles.*—From the reaction mixture described above [(1d) + EtCN] no (1d) was recovered. The reaction was repeated under the same conditions, but with addition of 46 mg [0.5 mol of (1d)] or 92 mg of PPh$_3$ [equimolar amount of (1d)]. From the former reaction system 16 mg (6.5%) of (1d) was recovered, whereas 36 mg (15%) of (1d) was recovered from the latter.

Formation of Pyridine from the Monoacetylene Complex (2). —Dimethyl acetylenedicarboxylate (0.5 g, in 5 cm^3 of benzene) was added dropwise to a cooled mixture of [Co(cp)-(PhC⋮CPh)(PPh$_3$)] (2a) (564 mg) and acetonitrile (10 cm^3) in benzene (20 cm^3). The mixture was allowed to stand at room temperature for 5 h. After concentration, the reaction mixture was chromatographed on Al$_2$O$_3$. Triphenylphosphine and excess of acetylene were eluted with benzene. The fraction eluted with benzene–dichloromethane (1 : 1) was collected. Evaporation of the solvent followed by addition of hexane yielded 3,4-bis(methoxycarbonyl)-2-methyl-5,6-diphenylpyridine (3e) in 44% yield. Similarly, from (2a) (564 mg) and diphenylacetylene (890 mg) in the presence of acetylene, 2-methyl-3,4,5,6-tetraphenylpyridine (3a-1) was obtained in 31% yield.