The Oligomerization and Co-oligomerization of Active Methylene Compounds and Isocyanides Catalyzed by Octaisocyanidedicobalt[1)]

Yasuhiro YAMAMOTO* and Hiroshi YAMAZAKI

The Institute of Physical and Chemical Research, Wako, Saitama 351

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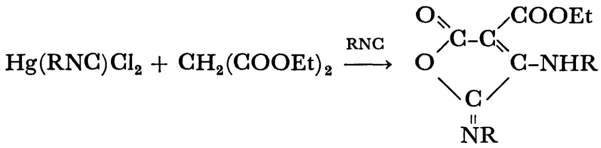
The reactions of RNC with $CH_2R^1R^2$ ($R=2,6\text{-}Me_2C_6H_3$; R^1, R^2=COOMe, COOEt, CN) in the presence of $Co_2(RNC)_8$ or $Co_2(CO)_8$ gave cyclic compounds in a 4:1 molar ratio. $Co_2(RNC)_8$ also catalyzed $CH_2(CN)_2$ to give a pyridine derivative.

Octacarbonyldicobalt has been widely used as a precursor of the catalyst of the hydroformylation of olefins and the carbonylation of various unsaturated organic compounds.[2)] Recently we have reported the synthesis and characterization of $Co_2(RNC)_8$, by analogy with $Co_2(CO)_8$.[3)] From the versatile reactivities of $Co_2(CO)_8$, one can expect catalytic actions similar to those of the corresponding isocyanide complexes. In fact, we established the hydrogenation of acetylene and the co-oligomerization of acetylene or azobenzene with isocyanide, catalyzed by $Co_2(RNC)_8$.[4,5)]

The compounds with an active methylene group, such as the malonic ester, malononitrile, and the cyanoacetic ester, have become keystones for syntheses of a heterocyclic system.[6)] Saegusa *et al.* reported that the reactions of *t*-butyl isocyanide with active methylene compounds gave three substituted olefins in the presence of Cu_2O (Eq. 1).[7)]

$$CH_2XY + t\text{-BuNC} \longrightarrow XYC{=}CHNHBu\text{-}t \qquad (1)$$

Sawai and Takizawa have described producing a 2:1 cyclic adduct consisting of RNC and CH_2XY by the reactions of isocyanide–mercury(II) chloride complex with active methylene compounds in the presence of Et_3N (Eq. 2).[8)]



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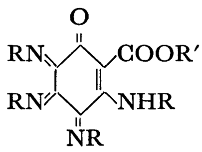
We wish here to report on cyclo-cooligomerization reactions between CH_2XY and RNC and on the oligomerization of an active methylene compound in the presence of a catalytic amount of $Co_2(RNC)_8$.

Results and Discussion

A mixture of $CH_2(COOMe)_2$, $2,6\text{-}Me_2C_6H_3NC$, and $Co_2(2,6\text{-}Me_2C_6H_3NC)_8$ was heated in toluene at 120—125 °C.[9)] The subsequent chromatography of the mixture on alumina gave two compounds: a reddish brown compound **1a**, formulated as $(C_9H_9N)_4(C_4H_4O_3)$ from the mass spectrum, M^+ 624 (624.75), and brown crystals, **2**, with the empirical formula of $(C_6H_6N)_6$. Compound **2** was identical with the compound obtained from the oligomerization of 2,6-xylyl isocyanide with $HgCl_2$ by Sawai and Takizawa.[10)] The infrared spectrum of **1a** showed an absorption at 3403 cm^{-1} due to a NH group, two bands at 1712 and 1688 cm^{-1} due to the carbonyl groups, and two broad bands at 1616 and 1593 cm^{-1} due to the C=N groups. The ^1H NMR spectrum showed four singlets, at δ 1.90, 2.03, 2.19, and 2.39, due to the *o*-methyl groups, a singlet at δ 3.21 due to a methoxycarbonyl group, and a broad signal at δ 4.91 due to a NH group. These spectral characteristics suggest a cyclic imino derivative. The other derivatives **1b** and **1c** were also prepared from the reaction of $CH_2(COOEt)_2$ with 2,6-xylyl isocyanide, or from that of $CH_2(COOMe)_2$ with *o*-tolyl isocyanide in the presence of $Co_2(CO)_8$, respectively. However, a similar reaction with *t*-butyl isocyanide led to the recovery of the starting material without undergoing a cyclic cooligomerization.



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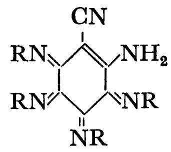

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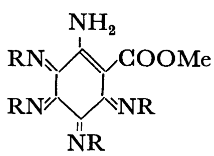
a $R=2,6\text{-}Me_2C_6H_3$, $R'=Me$
b $R=2,6\text{-}Me_2C_6H_3$, $R'=Et$
c $R=4\text{-}MeC_6H_4$ $R'=Me$

When malononitrile was treated with 2,6-xylyl isocyanide at 120—125 °C in the presence of $Co_2(2,6\text{-}Me_2C_6H_3NC)_8$ or $Co_2(CO)_8$, two compounds, **3** and **4**, were isolated as brown and pale yellow crystals respectively. Compound **3** was formulated as a 1:4 adduct of malononitrile and 2,6-xylyl isocyanide. The infrared spectrum showed the presence of the C≡N, C=N, and NH groups. The ^1H NMR spectrum showed four bands, at δ 1.90, 2.01, 2.23, and 2.44, due to the ortho-methyl groups and a broad singlet at δ 4.67 due to the NH group. Compound **4** was a trimer of malononitrile and was identified as 4-cyanomethyl-2,6-diamino-3,5-dicyanopyridine by a comparison of its infrared and UV spectra with those of an authentic sample.[6)] When the reactions were carried out in the absence of isocyanide, a trimerization of malononitrile occurred to give **4**. The results are listed in Table 1. The reaction of 2,6-xylyl isocyanide with methyl cyanoacetate in the presence of $Co_2(2,6\text{-}Me_2C_6H_3NC)_8$ gave a yellow compound consisting with the formula of $(C_9H_9N)_4(NCCH_2COOCH_3)$, **5**. The infrared spec-



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$R=2,6\text{-}Me_2C_6H_3$

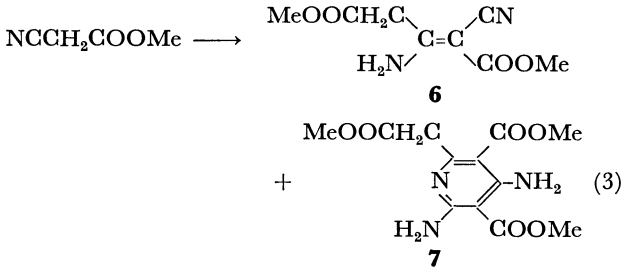
trum showed the presence of the NH and methoxy-

TABLE 1. TRIMERIZATION OF MALONONITRILE

Catalyst[a)]	Temp/°C	Time/h	Yield/%
$Co_2(2,6\text{-}Me_2C_6H_3NC)_8$	r.t.	15	0
$Co_2(2,6\text{-}Me_2C_6H_3NC)_8$	80	2	51
$Co_2(t\text{-}BuNC)_5Co(CO)_4$[b)]	80	2	56
$Co_2(2,6\text{-}Me_2C_6H_3NC)_8$	120	1	65
$Co_2(2,6\text{-}Me_2C_6H_3NC)_8$[c)]	120	1.5	73

a) Catalyst: 0.15 mmol. $CH_2(CN)_2$; *ca.* 13 mmol. b) *t*-BuNC (0.3 mmol) was added. c) 2,6-$Me_2C_6H_3NC$ (0.2 mmol) was added.

carbonyl groups, but the absence of the C≡N group. The ^1H NMR spectrum showed four bands, at δ 2.01 (bs, 2-CH_3), 2.12 (s, CH_3), and 2.23 (s, CH_3) due to the ortho-methyl groups, a singlet at δ 3.83 due to the methoxycarbonyl group, and a broad signal at δ 3.55(2H) due to the NH groups. The treatment of methyl cyanoacetate with $Co_2(2,6\text{-}Me_2C_6H_3NC)_8$ in the absence of 2,6-xylyl isocyanide gave a dimer, **6**, and a trimer, **7**, of methyl cyanoacetate in low yields. The dimer, **6**, was identified as a tetrasubstituted olefin; it is obtained from methyl cyanoacetate and bases. The trimer, **7**, was tentatively identified as a pyridine derivative by a comparison of its UV spectrum with that of **4**.



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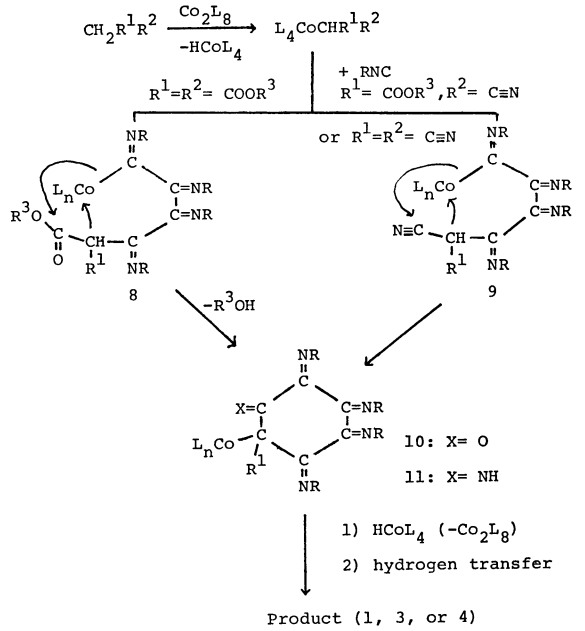
(3)

The initial step of the co-oligomerization is probably the formation of $HCo(RNC)_4$ and $R^1R^2HCCo(RNC)_4$ by a cleavage of the metal-metal bond, followed by a successive insertion of isocyanide molecules into a carbon-metal bond. The step-by-step insertion of isocyanide has been explored in various alkyl metal complexes.[11)] The intermediates, **10** and **11**, are generated by a nucleophilic attack of a tertiary carbon on the cobalt atom, accompanied by ring closure through an elimination of ROH or a transfer of hydrogen onto the cyano group. The resulting tetraimino cyclic intermediates are reduced with the $HCo(RNC)_4$ formed in the initial step. Thus, the reactions are achieved by a transfer of hydrogen to an imino nitrogen. The $Co_2(RNC)_8$ reformed in these reactions again undergoes a cleavage of a metal-metal bond, and the catalytic cycle is complete. Pyridine derivatives are probably formed by a transformation similar to that of the base-promoted reaction of active methylene compounds.[6)]

Experimental

The reactions were carried out under an atmosphere of nitrogen. The melting points are uncorrected. The IR spectra were recorded with a Shimadzu IR-27G spectrometer. The NMR spectra were measured with a JEOL C-60HL



Scheme 1. Possible path for the formation of tetraiminocyclic compounds.

apparatus. The mass spectra were measured on a JEOL Type JPS-1S mass spectrometer with a directinlet system. The isocyanides were prepared according to the literature.[12)] The $Co_2(CO)_8$[13)] and $Co_2(RNC)_8$[3)] were prepared by procedures described in the ilterature.

Reactions of Isocyanides with Active Methylene Compounds. Some representative examples will be described below.

Reaction of 2,6-Xylyl Isocyanide with Dimethyl Malonate. A mixture of 2,6-$Me_2C_6H_3NC$ (0.21 g, 1.6 mmol), $CH_2(COOMe)_2$ (1.3 g, 10 mmol), and $Co_2(2,6\text{-}Me_2C_6H_3NC)_8$ (0.16 g, 0.10 mmol) in toluene (10 ml) was heated at 120—125 °C for 4 h. The solvent was then removed *in vacuo*, and the residue was chromatographed on alumina. Compounds **1a** (0.12 g, 48%) and **2** (0.07 g, 7%) were isolated by using benzene or benzene–CH_2Cl_2 (10:1) respectively as the eluents. **1a** (mp 244—246 °C). Found: C, 76.35; H, 6.43; N, 8.95%. Calcd for $C_{40}H_{40}N_4O_3$: C, 76.89; H, 6.45; N, 8.87%. By using an analogous procedure except for the use of $Co_2(CO)_8$ instead of $Co_2(RNC)_8$, the following compounds were prepared.

1b (51%, mp 247—248 °C). NMR ($CDCl_3$): δ 1.20 (t, 3.5 Hz, Me), 1.87, 2.02, 2.19, 2.38 (s, *o*-Me), 3.71 (q, 3.5 Hz, CH_2), 4.89 (b, NH), and 6.5—7.3 (c, aromatic protons). IR (KBr): 3398 (NH), 1713, 1689, 1676, 1615, and 1591 (C=O and C=N) cm^{-1}. Mass: 638 (668.78). Found: C, 77.04; H, 6.63; N, 8.77%. Calcd for $C_{41}H_{42}N_4O_3$: C, 77.09; H, 6.63; N, 8.77%. **1c** (43%, mp 186—188 °C). IR (KBr): 3498 (NH), 1740, 1693, 1625, and 1598 (C=O and C=N) cm^{-1}. Mass: 568 (568.65). Found: C, 76.32; H, 5.76; N, 9.98%. Calcd for $C_{36}H_{32}N_4O_3$: C, 76.03; H, 5.67; N, 9.85%.

Reaction of 2,6-Xylyl Isocyanide with Malononitrile. A mixture of $Co_2(CO)_8$ (0.035 g, 0.1 mmol) and 2,6-xylyl isocyanide (0.21 g, 1.6 mmol) was stirred in toluene (10 ml) at reflux. After 0.5 h, $CH_2(CN)_2$ (0.7 g, 10.6 mmol) was added to the solution. After the reaction was over (2 h), the resulting solids, **4** (0.03 g, 13%), identified as 4-cyanomethyl-2,6-diamino-3,5-dicyanopyridine, were removed by filtration. The orange-brown solution was chromatographed on alumina, CH_2Cl_2 being used as the eluent. The subsequent removal of the solvent and crystallization

of the residue from benzene–hexane gave **3** (0.1 g, (42%), mp 265 °C) as brown crystals. NMR ($CDCl_3$): δ 1.90, 2.01, 2.23, 2.44 (s, *o*-CH_3), 4.67 (b, NH_2), and 6.5—7.4 (c, aromatic protons). IR (KBr): 3310 (NH), 2195 (C≡N), 1625, 1610, and 1590 (C=N) cm^{-1}. Mass: 590 (590.78). Found: C, 79.27; H, 6.46; N, 14.43%. Calcd for $C_{39}H_{38}N_6$: C, 79.26; H, 6.48; N, 14.23%.

5 (45%, mp 203—204 °C) was obtained from 2,6-Me_2-C_6H_3NC (0.22 g), methyl cyanoacetate (0.5 g), and $Co_2(CO)_8$ (0.04 g). IR (KBr): 3350 (NH), 1755, 1740, 1623, and 1595 (C=O and C=N) cm^{-1}. Mass: 623 (623.77). Found: C, 76.80; H, 6.65; N, 11.09%. Calcd for $C_{40}H_{41}N_5O_2$: C, 77.02; H, 6.46;, N, 10.95%.

Oligomerization of Methyl Cyanoacetate. A mixture of $CH_2(CH)$ (COOMe) (0.5 g, 5.0 mmol) and Co_2[2,6-$Me_2C_6H_3NC]_8$ (0.2 g, 0.17 mmol) in toluene was stirred in toluene (10 ml) at reflux for 2 h. The solvent and the unreacted ester were then removed *in vacuo*. The residue was chromatographed on alumina, CH_2Cl_2–benzene and CH_2Cl_2 being used as the eluents. The dimer, **6** (0.03 g, 12%), from the first band was isolated. The product, **7**, from the second band was a trimer (0.01 g, (6%), mp 114—119 °C). IR (KBr): 3510, 3430 (NH), 1735, 1683, 1632, 1586, and 1538 (C=O and C=N) cm^{-1}. Mass: 297 (297.26). UV (CH_3OH): λ_{max} 244 (ε 8400), 260 (ε 7300), and 324 (ε 2800). Found: C, 48.15; H, 5.03; N, 13.78%. Calcd for $C_{12}H_{15}N_3O_6$: C, 48.48; H, 5.09; N, 14.14%.

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References

1) This paper is Part IV in the series "Organic Synthesis by Low-valent Isocyanide Complexes." Part I; Y. Yamamoto and N. Hagihara, *Bull. Chem. Soc. Jpn.*, **42**, 2077 (1969). Part II; Y. Yamamoto and H. Yamazaki, *Synthesis*, **1976**, 750. Part III; Y. Yamamoto and H. Yamazaki, *J. Org. Chem.*, **42**, 4136 (1977).

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