Synthesis of 2-Oxo-1,2-dihydropyridines by the Reaction of Cobaltacylopentadiene Complexes with Isocyanates

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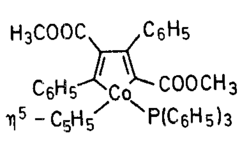
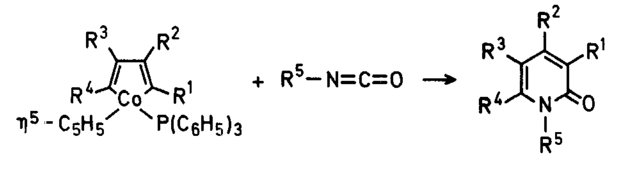
Metallocyclopentadiene complexes are useful as starting materials for preparing cyclic organic compounds[1,2,3]. As part of studies on the synthetic use of cobaltacyclopentadiene complexes (**1**)[1], which are easily obtained by the reaction of η^5-cyclopentadienylbis[triphenylphosphine]cobalt with two molecules of acetylenes, we wish to describe the reaction of **1** with isocyanates **2** to provide a facile synthetic route to 2-oxo-1,2-dihydropyridines **3**.

When a mixture of complex **1a** ($R^1=R^4=C_6H_5$, $R^2=R^3=COOCH_3$), phenyl isocyanate (**2a**), and benzene in a sealed tube was heated at 130° for 2 h, a colorless crystalline product (**3a**, $C_{27}H_{21}NO_5$) was obtained in a 66% yield. The N.M.R. spectrum shows the presence of two kinds of methoxycarbonyl groups at $\delta=3.36$ and 3.55 ppm, and the I.R. spectrum indicates a strong band at 1665 cm^{-1}, suggestive of the conjugated six-membered ring lactam[4], along with carbonyl streching bands for methoxycarbonyl groups. From these spectral data and the elemental analysis, we assigned to **3a** the structure dimethyl 1,3,6-triphenyl-2-oxo-1,2-dihydropyridine-4,5-dicarboxylate.



1d

Under similar conditions methyl isocyanate (**2b**) also reacted with **1a** to give dimethyl 1-methyl-3,6-diphenyl-2-oxo-1,2-dihydropyridine-4,5-dicarboxylate (**3b**). Similarly, several cobaltacyclopentadiene complexes (**1b–d**) and isocyanates have been successfully employed for preparing 2-oxo-1,2-dihydropyridines **3**. The results are shown in the Table.

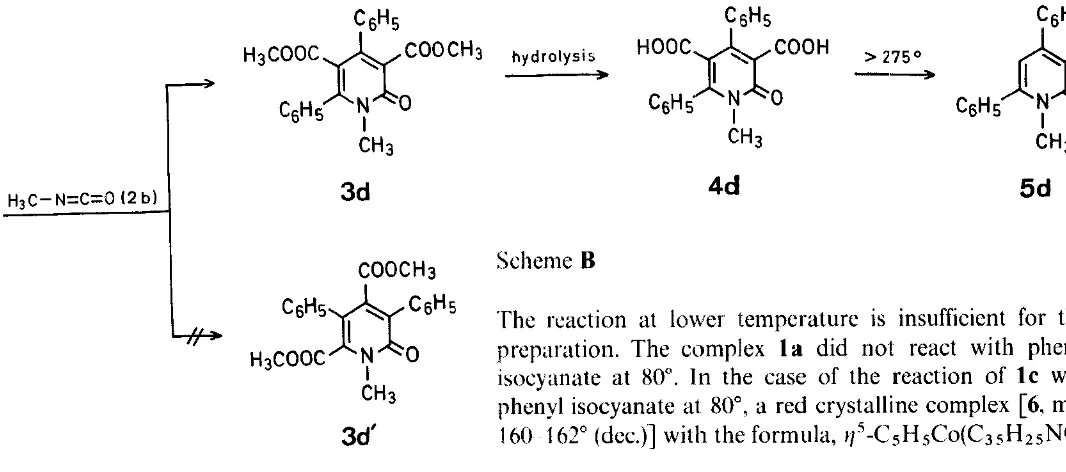


1a-d **2a-c** **3a-j**

1	R^1	R^2	R^3	R^4	2	R^5
a	C_6H_5	$COOCH_3$	$COOCH_3$	C_6H_5	a	C_6H_5
b	$COOCH_3$	C_6H_5	$COOCH_3$	C_6H_5	b	CH_3
c	C_6H_5	C_6H_5	C_6H_5	C_6H_5	c	n-C_4H_9
d	C_6H_5	CH_3	CH_3	C_6H_5		

Scheme A

In the reaction of an unsymmetrical cobaltacyclopentadiene complex **1b** ($R^1=R^3=COOCH_3$, $R^2=R^4=C_6H_5$), the formation of two types of 2-oxo-1,2-dihydropyridines, **3d** and **3d'**, are possible, according to the direction of addition of isocyanates (see Scheme **B**). However, the reaction proceeds regioselectively to afford only one product of the type **3d** (similar results are obtained with phenyl and n-butyl isocyanates). The structure was assigned on the basis of the following evidence. The N.M.R. spectrum of **3d** shows three peaks at $\delta=3.06$, 3.30, and 3.59 ppm due to methyl groups. The peak at 3.30 is assignable to N—CH_3, according to comparison with those of methoxycarbonyl in **3c** (3.10 and 3.61) and **3e** (3.13 and 3.59). This peak exists at a similar position to N—CH_3 in **3b** (3.28), **3g** (3.38), and **3j** (3.22), having a phenyl group at the 6-position. To further ascertain the structure here under consideration, **3d** was hydrolyzed to the acid **4d** which was decarboxylated under heating above 275° to 1-methyl-4,6-diphenyl-2-oxo-1,2-dihydropyridine (**5d**)[5].



Scheme **B**

The reaction at lower temperature is insufficient for this preparation. The complex **1a** did not react with phenyl isocyanate at 80°. In the case of the reaction of **1c** with phenyl isocyanate at 80°, a red crystalline complex [**6**, m.p. 160-162° (dec.)] with the formula, η^5-$C_5H_5Co(C_{35}H_{25}NO)$,

Table. 2-Oxo-1,2-dihydropyridines (**3**) from Cobaltacyclopentadiene Complexes (**1a–d**) and Isocyanates (**2a–c**)

	R^1	R^2	R^3	R^4	R^5	Yield [%]	m.p. (Lit. m.p.)	Molecular formula[a]	I.R. (KBr) $\nu_{C=O}$ [cm^{-1}]	^{1}H-N.M.R. (CDCl$_3$) δ [ppm]
3a	C_6H_5	$COOCH_3$	$COOCH_3$	C_6H_5	C_6H_5	66	224–225° (219–221°)[6]	$C_{27}H_{21}NO_5$ (439.5)	1745, 1725, 1665	3.36 (s, 3H), 3.55 (s, 3H), 6.90–7.50 (m, 15H)
3b	C_6H_5	$COOCH_3$	$COOCH_3$	C_6H_5	CH_3	70	112–113°	$C_{22}H_{19}NO_5$ (377.4)	1735, 1725, 1651	3.28 (s, 3H), 3.37 (s, 3H), 3.52 (s, 3H), 7.2–7.6 (m, 10H)
3c	$COOCH_3$	C_6H_5	$COOCH_3$	C_6H_5	C_6H_5	53	240–241°	$C_{27}H_{21}NO_5$ (439.5)	1735, 1655	3.10 (s, 3H), 3.61 (s, 3H), 7.0–7.45 (m, 15H)
3d	$COOCH_3$	C_6H_5	$COOCH_3$	C_6H_5	CH_3	37	133–134°	$C_{22}H_{19}NO_5$ (377.4)	1740, 1640	3.06 (s, 3H), 3.30 (s, 3H), 3.59 (s, 3H), 7.2–7.5 (m, 10H)
3e	$COOCH_3$	C_6H_5	$COOCH_3$	C_6H_5	n-C_4H_9	45	134–136°	$C_{25}H_{25}NO_5$ (419.5)	1740, 1720	0.73 (t, 3H), 1.13 (sext, 2H), 1.60 (quint, 2H), 3.03 (s, 3H), 3.59 (s, 3H), 3.79 (t, 2H), 7.2–7.5 (m, 10H)
3f	C_6H_5	C_6H_5	C_6H_5	C_6H_5	C_6H_5	72	231–232°	$C_{35}H_{25}NO$ (475.6)	1645	
3g	C_6H_5	C_6H_5	C_6H_5	C_6H_5	CH_3	75	232–234°	$C_{30}H_{23}NO$ (413.5)	1635	3.38 (s, 3H), 6.6–7.4 (m, 20H)
3h	C_6H_5	C_6H_5	C_6H_5	C_6H_5	n-C_4H_9	87	206–207°	$C_{33}H_{29}NO$ (455.6)	1631	0.71 (t, 3H), 1.15 (sext, 2H), 1.70 (quint, 2H), 3.89 (t, 2H), 6.60–7.20 (m, 20H)
3i	C_6H_5	CH_3	CH_3	C_6H_5	C_6H_5	81	249–252°	$C_{25}H_{21}NO$ (351.4)	1645	1.87 (s, 3H), 2.13 (s, 3H), 7.0–7.4 (m, 15H)
3j	C_6H_5	CH_3	CH_3	C_6H_5	CH_3	58	200–201° (203–203.5°)[7]	$C_{20}H_{19}NO$ (289.4)	1635	1.79 (s, 3H), 2.03 (s, 3H), 3.22 (s, 3H), 7.2–7.6 (m, 10H)

[a] Satisfactory mass spectra and elemental analysis (C ±0.40%, H ±0.30%, N ±0.15%) were obtained for all compounds.

was obtained in a 49% yield. The oxidation with ceric ammonium nitrate and the thermolysis of **6** gave pentaphenyl-2-oxo-1,2-dihydropyridine (**3f**). Therefore, the structure of **6** may be assigned as a pyridine-cobalt complex in which the diene part in the 2-oxo-1,2-dihydropyridine is coordinated to a cobalt atom, and is thought to be an intermediate for the formation of pyridones in the reaction (Scheme A).

We have also found that 2-oxo-1,2-dihydropyridines could be prepared by the co-trimerization of acetylenes and isocyanates in the presence of the complex **1**. Further study on this catalytic reaction is in progress.

Dimethyl 1,3,6-Triphenyl-2-oxo-1,2-dihydropyridine-4,5-dicarboxylate (3a):

The mixture of **1a** (353 mg, 0.5 mmol), phenyl isocyanate (1 ml), and benzene (10 ml) in an ampoule was heated at 130° for 2 h. After removal of the solvent in vacuo, the residue was chromatographed on alumina. Elution with benzene/ethyl acetate (10:1) gave a crystalline product **3a**; yield: 145 mg (66%); recrystallization from benzene/hexane; m.p. 224–225° (Lit.[6] 219–221°).

$C_{27}H_{21}NO_5$	calc.	C 73.79	H 4.82	N 3.19
(439.5)	found	73.74	4.76	3.24

1-n-Butyl-3,4,5,6-tetraphenyl-2-oxo-1,2-dihydropyridine (3h):

The mixture of **1c** (371 mg, 0.5 mmol), n-butyl isocyanate (0.5 ml), and benzene (10 ml) in an ampoule was heated at 135° for 2 h. After removal of the solvent, the greenish brown residue was submitted to chromatography on alumina, benzene/ethyl acetate (10:1) being used as eluent. A light yellow fraction was collected, and evaporated to give colorless crystals; yield: 197 mg (87%); recrystallization from benzene/hexane; m.p. 206–207°.

$C_{33}H_{29}NO$	calc.	C 87.00	H 6.42	N 3.07
(455.6)	found	86.94	6.47	3.03

1-Methyl-4,6-diphenyl-2-oxo-1,2-dihydropyridine-3,5-dicarboxylic acid (4d) and 1-Methyl-4,6-diphenyl-2-oxo-1,2-dihydropyridine (5d):

To a solution of potassium hydroxide (3 g) in methanol (10 ml), **3d** (280 mg, 0.74 mmol) was added, and the solution was refluxed for 7 h on the steam bath. The reaction mixture was then cooled, and the methanol was evaporated. When the residue was acidified with dilute hydrochloric acid, colorless solid was precipitated. The solid was washed with water and was dried under vacuo; yield: 210 mg (82%); recrystallization from methanol/water; m.p. 275° (dec).

$C_{20}H_{15}NO_5$	calc.	C 68.76	H 4.33	N 4.01
(349.3)	found	68.70	4.37	4.08

The acid **4** (100 mg) was placed in a small test tube which was immersed in a sand bath and then slowly heated under a stream of nitrogen. By the time 300° was reached, the material was yellow and bubbling. Upon cooling a pale yellow solid was obtained, and this was chromatographed on alumina. Elution with benzene/ethyl acetate (3:2) gave **5**; yield: 46 mg (63%); recrystallization from benzene/hexane; m.p. 91–92° (Lit.[5] 92°).

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[1] Y. Wakatsuki, T. Kuramitsu, H. Yamazaki, *Tetrahedron Lett.* **1974**, 4549.

[2] E. H. Braye, W. Hübel, *Chem. Ind.* (London) **1959**, 1250.

[3] E. Müller, *Synthesis* **1974**, 761.
See also A. P. Kozikowski, H. F. Wetter, *Synthesis* **1976**, 561.

[4] L. J. Bellamy, *Advances in Infrared Group Frequencies*, Methuen and Co., London, 1968, p. 165.

[5] I. E-S. El-Kholy, F. K. Rafla, M. M. Mishrikey, *J. Chem. Soc.* [C] **1970**, 1578.

[6] K. T. Potts, J. Baum, E. Houghton, *J. Org. Chem.* **39**, 3631 (1974).

[7] N. Ishibe, J. Masui, *J. Am. Chem. Soc.* **96**, 1152 (1974).