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SYNTHESIS OF 2-OXO- AND 2-IMINO-1,2-DIHYDROPYRIDINES BY COBALT-CATALYZED CYCLOCOTRIMERIZATION OF ACETYLENES WITH ISOCYANATES AND CARBODIIMIDES.

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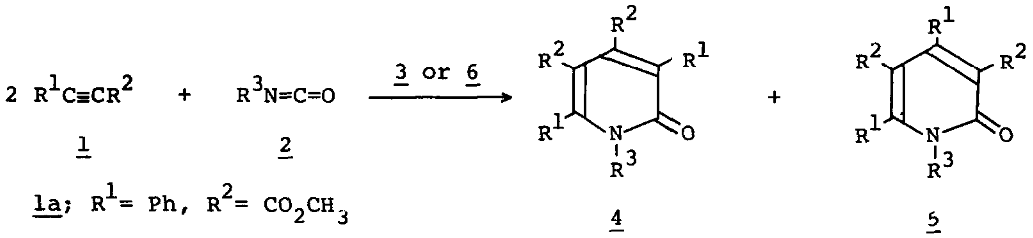
Recently, the cobalt-catalyzed synthesis of pyridines from acetylenes and nitriles was reported by our group[1] and Bönnemann et al.[2]. In this connection, the catalytic cyclocotrimerization of acetylenes with hetero-unsaturated compounds other than nitriles is of great interest in a sence of providing a new facile synthetic method of heterocyclic compounds. We now wish to report a cobalt-catalyzed synthesis of 2-oxo- or 2-imino-1,2-dihydropyridines from acetylenes and isocyanates or carbodiimides.

When a solution of methyl phenylpropiolate (1a, 6.25mmol), phenyl isocyanate (2a, 3.36mmol) and η-cyclopentadienyltriphenylphosphine-2,5-diphenyl-3,4-bis-(methoxycarbonyl)cobaltacyclopentadiene (3a, 0.28mmol) in benzene (10 ml) was heated in a sealed tube at 135° for 19 hr, a reddish brown solution was obtained. From the reaction mixture, dimethyl 1,3,6-triphenyl-2-oxo-1,2-dihydropyridine-4,5-dicarboxylate (4a)[3] and dimethyl 1,4,6-triphenyl-2-oxo-1,2-dihydropyridine-3,5-dicarboxylate (5a)[3] were isolated in 40 and 26 % yields, respectively, based on the acetylene employed. Di(η-cyclopentadienyl)cobalt (6) was also found to be an effective catalyst in this reaction.

In the presence of these catalysts, several acetylenes and isocyanates gave a variety of 2-oxo-1,2-dihydropyridines as summarized in the Table 1. Unsymmetrical acetylenes afforded only two isomers among four possible forms, similar to the case of forming pyridines by the reaction with nitriles. For example, the reaction of phenylacetylene (1b) with methyl isocyanate (2b) gave 1-methyl-3,6/4,6-diphenyl-2-oxo-1,2-dihydropyridine (4b and 5b).



1a; R^1= Ph, R^2= CO_2CH_3

1b; R^1= Ph, R^2= H

1c; R^1= CH_3, R^2= H

1d, R^1= n-C_4H_9, R^2= H

1e; R^1= Ph, R^2= Ph

1f; R^1= Ph, R^2= CH_3

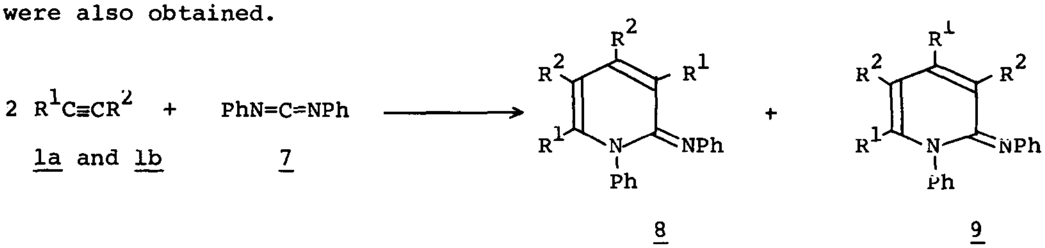
1g; R^1= H, R^2= H

2a; R^3= Ph

2b; R^3= CH_3

2c; R^3= n-C_4H_9

Similarly, the cyclocotrimerization of acetylenes with diphenylcarbodiimode (7) gave 2-imino-1,2-dihydropyridines. In the reaction of 1a with 7, dimethyl 1,3,6-triphenyl-2-(phenylimino)-1,2-dihydropyridine-4,5-dicarboxylate (8a) and dimethyl 1,4,6-triphenyl-2-(phenylimino)-1,2-dihydropyridine-3,5-dicarboxylate (9a) were obtained in 23 and 32 % yields, respectively. From 1b and 7, 1,3,6- and 1,4,6-triphenyl-2-(phenylimino)-1,2-dihydropyridine (8b and 9b) were also obtained.



Attempt to obtain a 2-thioxo-1,2-dihydropyridine by the reaction of acetylenes with isothiocyanates was unsuccessful, because the desulfurization of isothiocyanate occurred preferentially.

Among terminal acetylenes methyl propiolate (1h) resulted in different products. The reaction of 1h (24 mmol) with methyl isocyanate (50 mmol) in the presence of 6 (0.26 mmol) at 150° afforded two crystalline products, 10a (colorless, m.p. 96.5-97.5°, M^+ 198) and 10b (colorless, m.p. 103-104°, M^+ 198), in 34 and 17% yields, respectively.

Table 1. Cyclocotrimerization of acetylenes with isocyanates and carbodiimides.

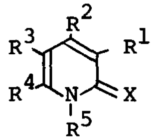
$R^1C{\equiv}CR^2$ (ml)	$R^3N{=}C{=}X$ (ml)	Cat. (mg)	Temp. (°C)	Time (hr)	Products (mg)		Catalytic activity[a] (%)
1a (1)	2a (0.4)	3a (200)	135	19	4a[3](540)	5a[3](360)	730
1a (1)	2a (0.4)	6 (60)	135	19	4a (280)	5a (250)	443
1a (1)	2b (1)	3a (200)	135	8	4b[3](300)	5b[3](260)	523
1a (1)	2b (1)	6 (75)	135	8	4b (510)	5b (350)	565
1a (2)	2b (0.5)	6 (38)	160	8	4b (580)	5b (340)	1210
1a (2)	2c (0.8)	6 (75)	160	8	4c (405)	5c[3](205)	375
1b (2)	2b (2)	6 (190)	150	8	4d (560)	5d[3](395)	365
1c (2)	2b (2)	6 (40)	135	6	4e (190)[b]	5e (165)[b]	970
1d (1)	2b (1)	6 (55)	135	8	4f (255)[b]	5f (50)[b]	470
1e (1.8g)	2a (0.7)	3b[c](250)	135	18	4g[3](300)		180
1f (2)	2b (2)	6 (40)	135	7	4h[3](75)	–	125
1g (10atm)	2b (5)	6 (378)	140	4	4i (461)		210
1a (1.2)	7 (0.6)	6 (80)	150	7	8a (353)	9a (489)	400
1b (1.2)	7 (0.8)	6 (180)	150	6	8b (181)	9b (610)	200

a. Mol of the products/ mol of catalyst.

b. The structures and the yields of the products were estimated by N.M.R..

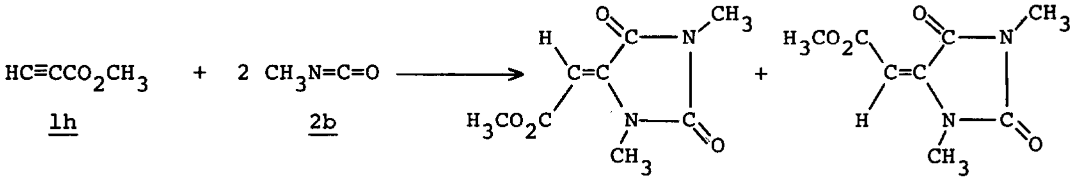
c. 3b: η-Cyclopentadienyltriphenylphosphine-2,3,4,5-tetraphenylcobaltacyclopentadiene.

Table 2. New compounds of 2-oxo- and 2-imino-1,2-dihydropyridines



	R^1	R^2	R^3	R^4	R^5	X	Color	M.p. (°C)
4c	Ph	CO_2CH_3	CO_2CH_3	Ph	n-C_4H_9	O	colorless	104-106
4d	Ph	H	H	Ph	CH_3	O	colorless	157-158
8a	Ph	CO_2CH_3	CO_2CH_3	Ph	Ph	NPh	red	219-220
8b	Ph	H	H	Ph	Ph	NPh	red	160-162
9a	CO_2CH_3	Ph	CO_2CH_3	Ph	Ph	NPh	orange	211-212
9b	H	Ph	H	Ph	Ph	NPh	orange	154-155

The structures of 10a and 10b were assigned to Z- and E-4-(methoxycarbonylmethylene)-1,3-dimethylhydantoin, based on the spectral data and the following chemical evidence. Thus, both 10a and 10b were converted to dimethylparabanic acid by the oxidation with $KMnO_4$, and to 4-(methoxycarbonylmethyl)-1,3-dimethylhydantoin (colorless oil, b.p. 120°/3mmHg, M^+ 200) by the hydrogenation on Pd-C.



10a 10b

Similar formation of hydantoins has been observed in the reaction of phenylacetylene with isocyanates in the presence of stoichiometric amounts of pentacarbonyl iron[5]. But in this case, the reaction of phenylacetylene with isocyanates gave only 2-oxo-1,2-dihydropyridines. The formation of 10 needs the transfer of the acetylenic hydrogen of 1h. Different behavior between 1h other terminal acetylenes in this catalytic system may be attributed to difference of their ability for the oxidative addition to the catalytic site.

References and notes

1. Y. Wakatsuki and H. Yamazaki, Tetrahedron Lett., 3383 (1973); Synthesis, 26 (1976).
2. H. Bönnemann, R. Brinkmann and H. Schenklum, Synthesis, 575 (1974).
3. The compound 4a and 5a are prepared by the stoichiometric reaction of the corresponding cobaltacyclopentadiene derivatives (3) with 2a.
   P. Hong and H. Yamazaki, Synthesis, in press.
4. In these reactions, isocyanurates and benzenes were obtained as by-products. Use of large excess of an isocyanate should be avoided, because the isocyanurate make the isolation of 2-oxo-1,2-dihydropyridines difficult.
5. Y. Ohshiro, K. Kinugasa, T. Minami and T. Agawa, J. Org. Chem., 35, 2136 (1970).