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Rhodium-Catalyzed Intramolecular Alkyne-carbodiimide Pauson–Khand-Type Reaction

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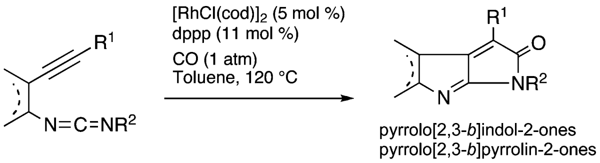
ABSTRACT



An efficient, Rh-catalyzed intramolecular Pauson–Khand-type carbonylation of alkyne-carbodiimides leading to 4,5-dihydro-1*H*-pyrrolo[2,3-*b*]pyrrolin-2-ones and 1*H*-pyrrolo[2,3-*b*]indol-2-ones is described.

As part of our ongoing interest in designing new synthetic strategies for nitrogen heterocycles, we have developed facile and efficient methods involving ring-forming reactions such as electrocyclizations, intramolecular hetero Diels−Alder reactions, hetero Michael additions, etc., of functionalized carbodiimides and ketenimines as the key synthetic step.[1] It is well documented that [2+2+1]-cocyclization of an alkyne, an alkene, and carbon monoxide promoted by transition metals, which is known as the Pauson−Khand reaction (when Co$_2$(CO)$_8$ is used) or the Pauson−Khand-type reaction (when other metal complexes are used), is a powerful and elegant synthetic method for cyclopentenones and their derivatives.[2] The hetero Pauson−Khand reaction has also been developed in which a carbonyl or imine functionality instead of an alkene or alkyne π-component is incorporated as a hetero-alkene counterpart.[3] Allenes are versatile building blocks in organic synthesis,[4] and recently, the synthetic utility of such cyclocarbonylation reactions has been greatly enhanced through the use of an allene functionality instead of alkenes.[5] However, there had been no reports on Pauson−Khand-type

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(4) (a) Zimmer, R.; Dinesh, C. U.; Nandanan, E.; Khan, F. A. *Chem. Rev.* **2000**, *100*, 3067. (b) *The Chemistry of Ketenes, Allenes, and Related Compounds*; Patai, S., Ed.; John Wiley & Sons: New York, 1980; Part 1 & 2. (c) *Modern Allene Chemistry*; Krause, N., Hashmi, A. S. K., Eds.; Wiley-VCH: Weinheim, 2004. (d) Bates, R. W.; Satcharoen, V. *Chem. Soc. Rev.* **2002**, *31*, 12.

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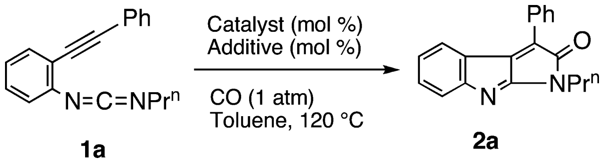
reactions involving heterocumulene as a 2π-component,[6] until our recent report of the heterocumulenic Pauson−Khand-type reaction appeared.[7] The reaction involved alkyne-carbodiimides as both 2π-components in the intramolecular [2+2+1]-cyclocarbonylation. Unfortunately, however, it required stoichiometric amounts of $Mo(CO)_6$ in the presence of DMSO as a promoter upon heating in toluene to obtain good to fair yields of the Pauson−Khand products, pyrrolo-[2,3-*b*]pyrrolinones and pyrrolo[2,3-*b*]indolones.[7] Our attention has now focused on the development of a catalytic version of the heterocumulenic Pauson−Khand-type reaction. Here, we present the *rhodium-catalyzed* heterocumulenic Pauson−Khand-type reaction of alkyne-carbodiimides for the first time.[8]

First, screening of metal catalysts[2] in combination with an additive (ligand) was performed in the Pauson−Khand-type reaction of *N*-[(*o*-phenylethynyl)]phenyl-*N′*-propylcarbodiimide (**1a**) under an atmospheric pressure of carbon monoxide in toluene at ca. 120 °C. Selected results are listed in Table 1. The use of a stoichiometric amount of $Mo(CO)_6$ (100 mol %)[3d,7] in the presence of 5 equiv of DMSO afforded Pauson−Khand product **2a** in 55% yield (entry 1). However, catalytic use (5 mol %) of the same Mo complex and DMSO (25 mol %) under the same conditions required a longer reaction time (8 h) and was less effective, as it gave 16% yield of **2a** (entry 2). The reactions employing 5 mol % of $Cr(CO)_6$, $W(CO)_6$, $Ru_3(CO)_{12}$,[3e,g] and $Co_2(CO)_8$ resulted in much lower or no yield of **2a** (entries 3−6), whereas $Co_2(CO)_8$ (5 mol %) combined with $P(OPh)_3$ (20 mol %) provided **2a** in somewhat better yield (entry 7). When $[RhCl(CO)dppp]_2$ (5 mol %) (generated in situ by mixing $[RhCl(cod)]_2$ and 1,3-bis(diphenylphosphino)propane (dppp, 11 mol %) as the ligand) was used,[9] the best results were obtained, with 77% yield of **2a** (entry 10). The efficiency of the catalytic system was found to be largely dependent on the combination of the complex with its ligand. It is clear that dppp is superior to the other phosphine ligands, $P(OPh)_3$, 1,2-bis(diphenylphosphino)ethane (dppe), and 1,4-bis(diphenylphosphino)butane (dppb) for this substrate (entry 10 vs entries 8, 9, and 12).[10] The amount of the catalyst, $[RhCl(CO)dppp]_2$, could be reduced to 2.5 mol %, while maintaining a fairly good yield (58%) of **2a** (entry 11).

Table 1. Screening of Catalysts and Additives in Pauson−Khand-Type Reactions of **1a** to Give **2a**



1a **2a**

entry	catalyst	(mol %)	additive	(mol %)	time (h)	yield (%)[a]
1	$Mo(CO)_6$	(100)	DMSO	(500)	1	55
2	$Mo(CO)_6$	(5)	DMSO	(25)	8	16
3	$Cr(CO)_6$	(5)	DMSO	(25)	7	0
4	$W(CO)_6$	(5)	DMSO	(25)	13	0
5	$Ru_3(CO)_{12}$	(5)	DMSO	(25)	7	0
6[b]	$Co_2(CO)_8$	(5)	DMSO	(25)	8	12
7[b]	$Co_2(CO)_8$	(5)	$P(OPh)_3$	(20)	10	28
8[c]	$[RhCl(cod)]_2$	(5)	PPh_3	(22)	7	6
9[c]	$[RhCl(cod)]_2$	(5)	dppe[d]	(11)	6	17
10[c]	$[RhCl(cod)]_2$	(5)	dppp[e]	(11)	1.5	77
11[c]	$[RhCl(cod)]_2$	(2.5)	dppp[e]	(5.5)	2	58
12[c]	$[RhCl(cod)]_2$	(5)	dppb[f]	(11)	4	29

[a] Yield of isolated product **2a**. [b] Dimethoxyethane was used as solvent. [c] cod = 1,5-cyclooctadiene. [d] 1,2-Bis(diphenylphosphino)ethane. [e] 1,3-Bis(diphenylphosphino)propane. [f] 1,4-Bis(diphenylphosphino)butane.

Given the best result (entry 10, Table 1) in the model reaction of **1a**, we thus applied this catalytic system under the optimized conditions to substrates **1** bearing a variety of substituents (R^1, R^2) on the terminal alkyne and the nitrogen atom. The results are shown in Table 2. The alkyl- and aryl-substituted carbodiimides **1** produced moderate to good yields of **2**, whereas in the cases of carbodiimides **1b**,**g** having a substituent of R^2 = cyclohexyl, Pauson−Khand products **2b**,**g** were obtained in lower yields. This is probably due to

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(5) For a review on allenic Pauson−Khand reactions, see: Alcaide, B.; Almendros, P. *Eur. J. Org. Chem.* **2004**, 3377. For selected recent reports on allenic Pauson−Khand reactions, see (allene-ene): (a) Wender, P. A.; Croatt, M. P.; Deschamps, N. M. *Angew. Chem., Int. Ed.* **2006**, *45*, 2459. (allene-yne): (b) Mukai, C.; Hirose, T.; Teramoto, S.; Kitagaki, S. *Tetrahedron* **2005**, *61*, 10983. (c) Mukai, C.; Inagaki, F.; Yoshida, T.; Yoshitani, K.; Hara, Y.; Kitagaki, S. *J. Org. Chem.* **2005**, *70*, 7159. (d) Mukai, C.; Inagaki, F.; Yoshida, T.; Kitagaki, S. *Tetrahedron Lett.* **2004**, *45*, 4117. (e) Shibata, T.; Kadowaki, S.; Hirase M.; Takagi, K. *Synlett* **2003**, 573. (f) Narasaka, K.; Shibata, T. *Chem. Lett.* **1994**, 315. (allenic, first report): (g) Shibata, T.; Koga, Y.; Narasaka, K. *Bull. Chem. Soc. Jpn.* **1994**, *68*, 911. (h) Brummond, K. M.; Chen, H.; Fisher, K. D.; Kerekes, A. D.; Rickards, B.; Still, P. C.; Geib, S. J. *Org. Lett.* **2002**, *4*, 1931. (i) Brummond, K. M.; Kerekes, A. D.; Wan, H. *J. Org. Chem.* **2002**, *67*, 5156. (j) Anorbe, L.; Poblador, A.; Dominguez, G.; Perez-Castells, J. *Tetrahedron Lett.* **2004**, *45*, 4441. (k) Alcaide, B.; Almendros, P.; Allagoncillo, C. *Chem.−Eur. J.* **2002**, *8*, 1719. (l) Cao, H.; Flippen-Anderson, J.; Cook, J. M. *J. Am. Chem. Soc.* **2003**, *125*, 3230. (m) Pagenkopf, B. L.; Belanger, D. B.; O'Mahony, D. J. R.; Livinghouse, T. *Synthesis* **2000**, 1009. (inter allene-yne): (n) Antras, F.; Ahmar, M.; Cazes, B. *Tetrahedron Lett.* **2001**, *42*, 8153. (o) Antras, F.; Ahmar, M.; Cazes, B. *Tetrahedron Lett.* **2001**, *42*, 8157. (allene-carbonyl): (p) Yu, C.-M.; Hong, Y.-T. *J. Org. Chem.* **2004**, *69*, 8506.[3e] (q) Kang, S.-K.; Kim, K.-J.; Hong, Y.-T. *Angew. Chem.* **2002**, *114*, 1654.[3h]

(6) To our knowledge, there are only three reports. (a) One is as early as 1970 of the cocycloaddition reaction of diphenylcarbodiimide or phenyl isocyanate, diphenylacetylene, and $Fe(CO)_5$, which afforded indeed a Pauson−Khand-type product in a reasonable yield: Ohshiro, Y.; Kinugasa, K.; Minami, T.; Agawa, T. *J. Org. Chem.* **1970**, *35*, 2136. (b) Hoberg, H.; Oster, B. W. *J. Organomet. Chem.* **1982**, *234*, C35. (c) Very recently, Ru-catalyzed intermolecular Pauson−Khand-type cocyclization of isocyanates has been reported. Kondo, T.; Nomura, M.; Ura, Y.; Wada, K.; Mitsudo, T. *J. Am. Chem. Soc.* **2006**, *128*, 14816.

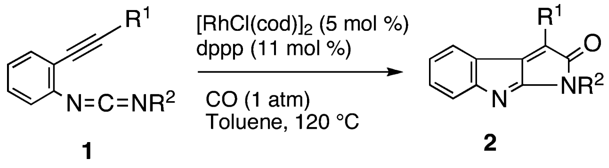
(7) Saito, T.; Shiotani, M.; Otani, T.; Hasaba, S. *Heterocycles* **2003**, *60*, 1045. The catalytic version of this research was presented at: 85th Annual Meeting of the Chemical Society of Japan, Yokohama, March, 2005; Abstract 1B2−25. 35th Congress of Heterocyclic Chemistry, Osaka, October, 2005; Abstract 2C-08. The International Chemical Congress of Pacific Basin Societies, Honolulu, Hawaii, December, 2005; Abstract ORGN 1696.

(8) Very recently, Mukai et al. reported a synthesis of the indole alkaloid, (±)-physostigmine, through the first *catalytic* heterocumulenic Pauson−Khand reaction of alkynylcarbodiimides for the construction of a pyrrolo-[2,3-*b*]indol-2-one skeleton as the key step, where 10−20 mol % of $Co_2(CO)_8$ and a tetramethylthiourea promoter (60−120 mol %) were successfully applied. Mukai, C.; Yoshida, T.; Sorimachi, M.; Odani, A. *Org. Lett.* **2006**, *8*, 83.

(9) (a) Jeong, N.; Lee, S.; Sung, B.-K. *Organometallics* **1998**, *17*, 3642. (b) Jeong, N.; Seo, S. D.; Shin, J. Y. *J. Am. Chem. Soc.* **2000**, *122*, 10220.

(10) For a Pauson−Khand reaction using a Rh(I) complex catalyst, see: Koga, Y.; Kobayashi, T.; Narasaka, K. *Chem. Lett.* **1998**, 249. Mukai, C.; Nomura, I.; Yamanishi, K.; Hanaoka, M. *Org. Lett.* **2002**, *4*, 1755. Refs 5b−d.

Table 2. Catalytic Pauson−Khand-Type Reaction of **1** to Give **2**[a]



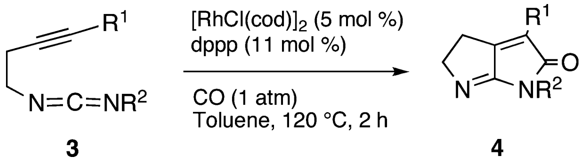
entry	**1**	R^1	R^2	time (h)	**2**	yield (%)[b]
1	**1a**	Ph	*n*-Pr	1.5	**2a**	77
2	**1b**	Ph	*c*-Hex	1.5	**2b**	27
3	**1c**	Ph	Ph	1.5	**2c**	50
4	**1d**	Ph	*p*-MeC$_6$H$_4$	1.5	**2d**	50
5	**1e**	Ph	*p*-ClC$_6$H$_4$	1.5	**2e**	57
6	**1f**	Me$_3$Si	*n*-Pr	2.0	**2f**	60
7	**1g**	Me$_3$Si	*c*-Hex	2.5	**2g**	20
8	**1h**	Me$_3$Si	Ph	1.5	**2h**	85
9	**1i**	Me$_3$Si	*p*-MeC$_6$H$_4$	1.5	**2i**	77
10	**1j**	Me$_3$Si	*p*-ClC$_6$H$_4$	1.5	**2j**	77

[a] **1** (0.23 mmol), 0.16 M, at 120 °C of bath temp. [b] Yield of isolated **2**.

steric hindrance caused by the bulky cyclohexyl group in the cyclization process.

To study the generality of the catalytic carbodiimide Pauson−Khand reaction, this Rh catalyst was next applied to the reaction of ethylene-tethered alkyne-carbodiimides **3** (Table 3). The use of 5 mol % of [RhCl(CO)dppp]$_2$ catalyst generated in situ also proved to be effective for the Pauson−Khand-type reaction of *N*-(3-alkynyl)-*N*′-arylcarbodiimides **3b**−**g** to furnish 4,5-dihydro-1*H*-pyrrolo[2,3-*b*]pyrrolin-2-ones (**4b**−**g**) in acceptable yields, whereas the reaction of *N*-(3-pentynyl)-*N*′-propylcarbodiimide **3a** did not give any cyclized products. The reason for the latter results can be ascribed to the fact that dialkylcarbodiimides bearing less bulky substituents (as in **3a**) are apt to dimerize or deteriorate under such harsh reaction conditions.[11]

Table 3. Catalytic Pauson−Khand-Type Reaction of **3** to Give **4**[a]



entry	**3**	R^1	R^2	**4**	yield (%)[b]
1	**3a**	Me	*n*-Pr	**4a**	0
2	**3b**	Me	Ph	**4b**	43
3	**3c**	Me	*p*-MeC$_6$H$_4$	**4c**	44
4	**3d**	Me	*p*-ClC$_6$H$_4$	**4d**	47
5	**3e**	Et	Ph	**4e**	46
6	**3f**	Et	*p*-MeC$_6$H$_4$	**4f**	46
7	**3g**	Et	*p*-ClC$_6$H$_4$	**4g**	47

[a] **3** (0.53 mmol), 0.15 M, at 120 °C of bath temp. [b] Yield of isolated **4**.

In conclusion, the first examples of Rh-catalyzed Pauson−Khand-type reactions of alkyne-carbodiimides are reported, thus providing a facile and efficient route to the Pauson−Khand products, pyrrolo-indolones and pyrrolo-pyrrolinones.

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Supporting Information Available: A typical experimental procedure for synthesis of **2a** and characterization data of new compounds **1a**,**b**, **1d**−**g**, **1i**,**j**, **2a**−**j**, **3a**−**g**, and **4b**−**g**, and ^{1}H NMR and ^{13}C NMR spectra of compounds **1a**,**b**, **1d**−**g**, **1i**,**j**, **2a**−**j**, **3a**−**g**, and **4b**−**g**. This material is available free of charge via the Internet at http://pubs.acs.org.

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[11] Kurzer, F.; Douraghi-Zadeh, K. *Chem. Rev.* **1967**, *67*, 107.