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A NOVEL HETEROCUMULENIC PAUSON-KHAND REACTION OF ALKYNYLCARBODIIMIDES: A FACILE AND EFFICIENT SYNTHESIS OF HETEROCYCLIC RING-FUSED PYRROLINONES

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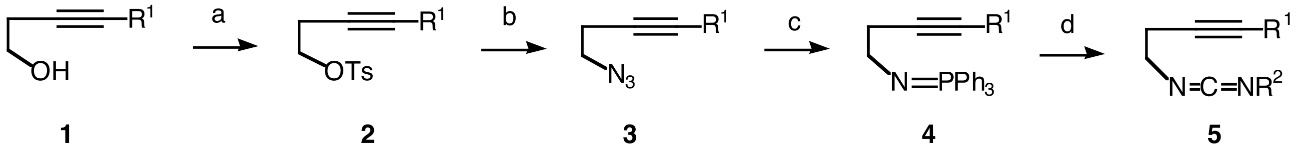
Abstract – The first examples of the heterocumulenic Pauson-Khand reaction are described. Alkynylcarbodiimides undergo an intramolecular Pauson-Khand cycloaddition upon heating in the presence of $Mo(CO)_6$ and DMSO to afford 4,5-dihydro-1*H*-pyrrolo[2,3-*b*]pyrrolin-2-ones and 1*H*-pyrrolo[2,3-*b*]indol-2-ones.

The Pauson-Khand (P-K) reaction is a three-component reaction, formulated as a formal [2+2+1] cycloaddition of an alkyne, an alkene, and carbon monooxide leading to a cyclopentenone,[1] and has been exploited extensively.[2] Recently, allenes have also been utilized successfully in the P-K reaction to give 4- and/or 5-alkylidenecyclopentenones.[3] Curiously, however, no examples of the use of a heterocumulenic system in place of the allene component in either inter- or intramolecular P-K reaction have been reported so far, despite the fact that it would constitute a novel and potent method for straightforward construction of five-membered heterocycles or, in some cases, carbocycles in light of the wide applicability and versatility imparted by this metal carbonyls-assisted cycloaddition. In this context, we have succeeded in performing a heterocumulenic P-K cycloaddition which incorporates a carbodiimide functionality and an internal alkyne moiety together with metal carbonyls. We report here for the first time the heterocumulenic P-K reaction.[4] The present P-K reaction also offers a novel and efficient synthetic method for 4,5-dihydro-1*H*-pyrrolo[2,3-*b*]pyrrolin-2-ones and 1*H*-pyrrolo[2,3-*b*]indol-2-ones.

In order to examine the feasibility of the heterocumulenic P-K reaction, we initially selected simple alkynylcarbodiimides (**5**) as the key substrates. The carbodiimides (**5**) were readily prepared from commercially available alkynols (**1**) by (a) tosylation, (b) nucleophilic substitution by an azide group, (c) Staudinger reaction of azides (**3**) with triphenylphosphine, and by (d) aza-Wittig reaction of iminophosphoranes (**4**) with isocyanates (Scheme 1).



Scheme 1. *Reagents and conditions*: (a) TsCl, Et_3N, CH_2Cl_2, 0 °C □ rt, 3 h, (b) NaN_3, DMF, rt, 3-12 h (82-86 %, two steps), (c) Ph_3P, benzene, 80 °C, 2 h, (d) R^2NCO, benzene, rt, 1 h (27-54 %, two steps).

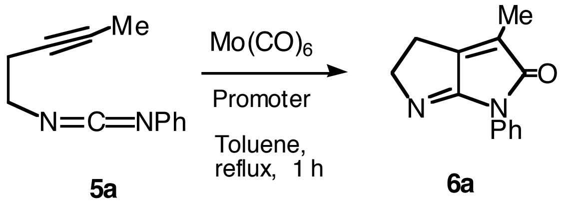


Table 1. Efficiency of promoters in the Pauson-Khand reaction of **5a**[a]

Entry	Promoter	Yield of **6a** (%)[b]
1	None	0
2	NMO	Trace
3	MeCN	21
4	DMF	51
5	DMSO	60

a) The reactions were carried out using 1.1 equiv. $Mo(CO)_6$ and 5 equiv. promoters.
b) Isolated yield.

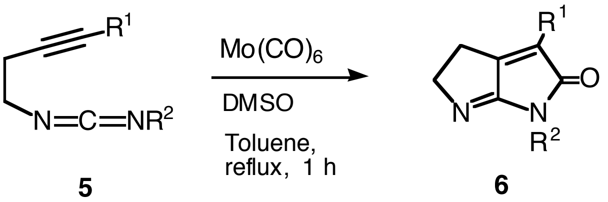


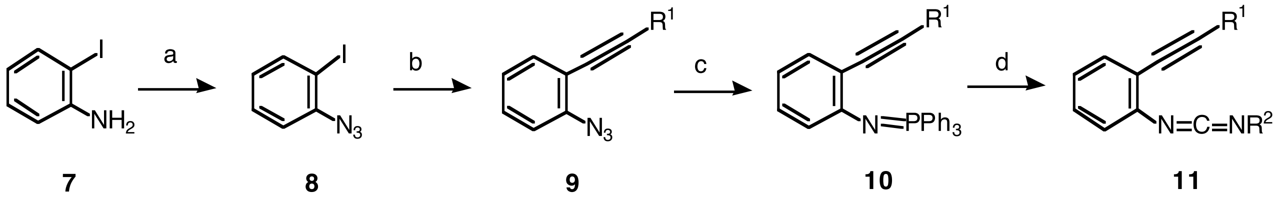
Table 2. Heterocumulenic Pauson-Khand reaction of alkynylcarbodiimides (**5**) to give pyrrolopyrrolones (**6**)[a]

Entry	R^1	R^2	Yield of **6** (%)[b]
a	Me	Ph	60
b	Me	*p*-Tol	53
c	Me	*p*-ClC_6H_4	57
d	Et	Ph	42
e	Et	*p*-Tol	47
f	Et	*p*-ClC_6H_4	49

a) The reactions were carried out using 1.1 equiv $Mo(CO)_6$ and 5 equiv. DMSO.
b) Isolated yield.

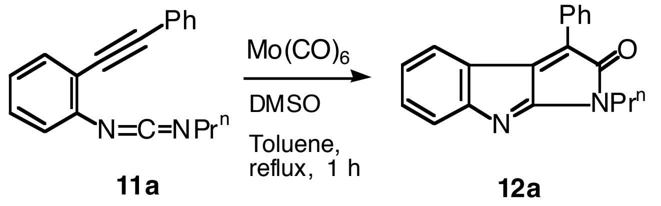
With alkynylcarbodimides (**5**) in hand, we attempted the P-K reaction of **5a** first using dicobaltoctacarbonyl. Disappointingly, all attempts to carry out the P-K reaction under various conditions such as thermal and/or promoter [*N*-methylmorpholine oxide (NMO),[5] DMSO[6]]-assisted conditions were unsuccessful.[†] However, the reactions using molybdenumhexacarbonyl[2] in the presence of some promoters indeed proceeded to yield the expected P-K product, 4,5-dihydro-1*H*-pyrrolo[2,3-b]pyrrolin-2-one (**6a**).[7] The representative results are shown in Table 1. Among the promoters tested under refluxing toluene for 1 h, dimethyl sulfoxide[8] was found to provide the best yield of **6a** (60 %, Entry 5). The $Mo(CO)_6$-mediated P-K reaction procedure with the aid of DMSO under the same reaction conditions was also applied to some other alkynylcarbodiimides (**5b-f**). The P-K reactions worked well to give 1*H*-pyrrolo[2,3-*b*]pyrrolin-2-ones (**6b-f**) (Table 2),[≠] suggesting that this P-K methodology seems to be promising for the synthesis of variously substituted 4,5-dihydro-1*H*-pyrrolo[2,3-*b*]pyrrolin-2-ones.

In order to probe the generality of this carbodiimide-P-K methodology, we next investigated the reaction of alkynylcarbodiimides (**11**) in which both carbodiimide and alkyne functionalities were each connected with an *ortho*-phenylene group. Scheme 2 illustrates the preparation of alkynylcarbodiimides (**11**) from commercially available *o*-iodoaniline (**7**) *via* (a) diazotization and azide-replacement, (b) Heck coupling with an alkyne, followed by (c) Staudinger reaction with triphenylphosphine and (d) aza-Wittig reaction



Scheme 2. *Reagents and conditions*: (a) i, $NaNO_2$-aq.HCl, 5-10 °C, ii, NaN_3, H_2O, 5 °C, 2 h (84 %), (b) $HCCR^1$, $PdCl_2(PPh_3)_2$, CuI, Et_3N, CH_2Cl_2, rt, 1 h (99 %), (c) Ph_3P, benzene, rt, 1.5 h (71-95 %), (d) R^2NCO, benzene, rt, 3-12 h (60-76 %).

with isocyanates. Treatment of carbodiimide (**11a**) with $Mo(CO)_6$ *in the presence of a promoter* under the same conditions above afforded 3-phenyl-1-propyl-1*H*-pyrrolo[2,3-*b*]indol-2-ones (**12a**) as the expected P-K product (Table 3). Pentamethylene sulfide actually promoted the P-K reaction but was less effective with either $Mo(CO)_6$ or $Co_2(CO)_8$ contrary to our expectation (Entry 5).[9] Again, DMSO was found to be a good promoter in this reaction. The results of the DMSO-promoted $Mo(CO)_6$-P-K reactions of **11a-f** are summarized in Table 4.[≠] Although the $Mo(CO)_6$-mediated P-K reaction of **11** having an unsubstituted acetylene (R^1 = H) failed to afford compound (**12**) (R^1 = H), the trimethylsilyl group in **12d-f** could be removed to provide 3-unsubstituted 1*H*-pyrrolo[2,3-*b*]indol-2-ones (**12**).



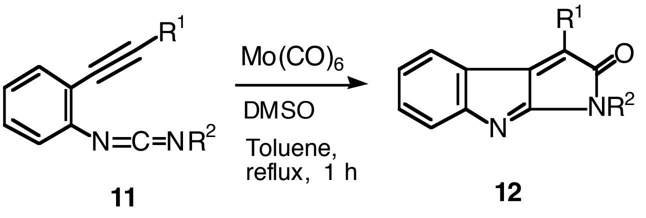


Table 3. Efficiency of promoters in the Pauson-Khand reaction of **11a**[a]

Entry	Promoter	Yield of **12a** (%)[b]
1	None	0
2	NMO	51
3	DMF	44
4	DMSO	55
5	$(CH_2)_5S$	28

a) The reactions were carried out using 1.1 equiv. $Mo(CO)_6$ and 5 equiv. promoters.
b) Isolated yield.

Table 4. Heterocumulenic Pauson-Khand reaction of alkynylcarbodiimides (**11**) to give pyrroloindolones (**12**)[a]

Entry	R^1	R^2	Yield of **12** (%)[b]
a	Ph	n-Pr	55
b	Ph	Ph	45
c	Ph	*p*-Tol	48
d	Me_3Si	n-Pr	50
e	Me_3Si	Ph	60
f	Me_3Si	*p*-Tol	70

a) The reactions were carried out using 1.1 equiv. $Mo(CO)_6$ and 5 equiv. DMSO.
b) Isolated yield.

In conclusion, we have developed a heterocucmulenic Pauson-Khand reaction for the first time. The synthetic usefulness of this methodology was demonstrated in the facile and efficient synthesis of 4,5-dihydro-1*H*-pyrrolo[2,3-*b*]pyrrolin-2-ones and 1*H*-pyrrolo[2,3-*b*]indol-2-ones by using alkynyl-carbodiimides as the substrates in the intramolecular cycloaddition.

Further studies on the heterocucmulenic Pauson-Khand methodology to provide a variety of heterocycles are under way.

† Complexation of the alkyne moiety of **5a**/**11a** with dicobaltoctacarbonyl seems to be successful, but attempts to promote the cycloaddition resulted in decomposition

≠ The reaction in refluxing toluene gave the P-K products (**6**/**12**) albeit in relatively low yields (42-70 %) accompanying polymerization or deterioration of **5**/**11**, while in refluxing benzene (at about 80 ˚C) the reaction hardly occurred.

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