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COMMUNICATION

Tungsten and molybdenum catalyst-mediated cyclisation of *N*-propargyl amides†

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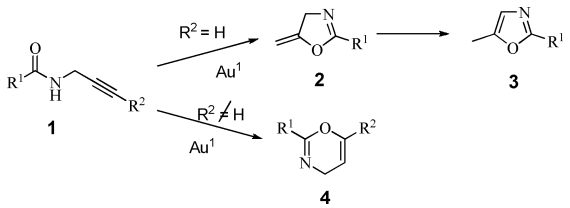
Tungsten and molybdenum catalysts were employed to promote the cyclisation of *N*-propargylic amides to afford the corresponding oxazolines or oxazines *via* 5-*exo-dig* or 6-*endo-dig* mode.

In contrast to the wide application of late transition metal catalysts such as Pd, Au, In and Ru for new bond formation in synthetic organic chemistry,[1] related reactions promoted by early transition-metal complexes such as Mo and W have not been well explored and have scarcely been reported owing to their relatively low activity as efficient catalysts in organic transformations.[2] Nevertheless, it would be interesting and highly desirable to develop the synthetic usefulness of Group *VI* metals in organic transformations due to their characteristic reactivities.

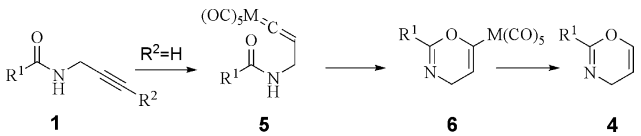
Group *VI* metal carbonyl complexes have attracted a great deal of attention due to their ability for electrophilic activation of alkyne functionality under photochemical conditions.[3] During the last two decades, McDonald *et al.* efficiently employed $Mo(CO)_5{\cdot}(Et_3N)$ as a catalyst to promote the cyclisation of alkynyl alcohols[4] while Iwasawa *et al.* developed the cyclisation of various silyl ethers using $W(CO)_5{\cdot}(THF)$ catalyst and also investigated the detailed mechanism of this kind of cyclisation reaction.[5]

The cyclisations of propargylic amides with Au,[6] Ag,[7] Cu[8] and Pd[9] catalysts are known to give oxazoline derivatives. According to the previous report by Hashmi *et al.*,[10] the mode of the cyclisation depended on the nature of the propargylic amides as shown in Scheme 1. The 6-*endo-dig* ring closure was observed for the alkyl-substituted alkynes, whereas the 5-*exo-dig* ring closure was general for terminal alkynes. In addition, the oxazolines are prone to aromatization and their preparations require mild conditions.

As we were keen on expanding the application of W and Mo catalysts in organic synthesis, we studied the possibility of using Mo and W catalysts for the cyclisation of propargylic amides to prepare oxazolines **2** and/or oxazines **4** *via* the 5-*exo* mode and/or 6-*endo* mode. Since W and Mo catalysts are known to form vinylidene carbene species with alkynes,[11] oxazines **4** could be formed *via* intermediate **5** (Scheme 2). Based on



Scheme 1



Scheme 2

this assumption, we studied the effectiveness of W and Mo catalysts in the cyclisation of propargylic amides. As shown in Table 1, we began our studies with *N*-propynylbenzamide **7** using 20 mol% $W(CO)_3(CH_3CN)_3$.[12] When the reaction was carried out in refluxing toluene, no reaction occurred (entry 1). Similarly, no reaction occurred using Mo catalysts in refluxing THF (entries 3 and 4).[13] When the reaction was carried out using $W(CO)_6$ or $Mo(CO)_6$ in the presence of Et_3N in refluxing toluene, the reaction did not proceed to an observable extent (entries 5 and 6). However, when the similar reaction was carried out under irradiation at 350 nm, the cyclisation proceeded but the oxazoline product was isolated in 40% yield contrary to our expectations (entry 7). In the absence of Et_3N, only trace amounts (<5%) of the desired cyclised product was detected along with the recovery of the starting material (entry 8). It was found that DABCO (1,4-diazabicyclo[2.2.2]octane) turned out to be much more effective than Et_3N and gave better yields (entry 9).[14] In addition, carrying out the reaction in toluene improved the yield further (entry 10). It is noteworthy that Mo catalyst also catalyzed the cyclisation but was less effective than W catalyst (entry 12). Finally, the cyclisation in the presence of DABCO alone in refluxing toluene did not occur (entry 13).

To further improve the yield, when the reaction mixture was treated with trimethylamine *N*-oxide dihydrate for the oxidative treatment of the W complex product,[15] the yield was increased to some extent (84%). Thus, the remaining reactions were carried out using 20 mol% $W(CO)_6$ in the presence of DABCO (1 equiv) in toluene at 350 nm for 12 h and subsequent oxidative treatment with

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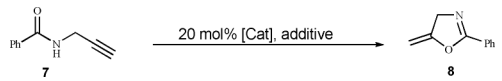
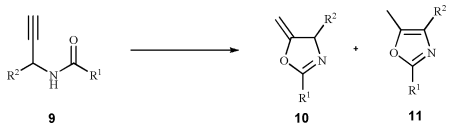
Table 1 $M(CO)_5(L)$-Catalyzed cyclisation of propargyl amide **7**



7 8

Entry	Cat.	Additive	Solvent	Condition	Time (h)	Yield (%)
1	$W(CO)_3(CH_3CN)_3$	—	Toluene	reflux	10	trace
2	$W(CO)_3(CH_3CN)_3$	—	CH_3CN	reflux	10	0
3	$Mo(CO)_3(CH_3CN)_3$	—	THF	reflux	20	0
4	$Mo(CO)_3(DMF)_3$	—	THF	reflux	20	0
5	$W(CO)_6$	Et_3N	Toluene	reflux	12	trace
6	$Mo(CO)_6$	Et_3N	Toluene	reflux	12	trace
7	$W(CO)_6$	Et_3N	THF	350 nm	12	40
8	$W(CO)_6$	—	THF	350 nm	12	trace
9	$W(CO)_6$	DABCO	THF	350 nm	12	63
10	$W(CO)_6$	DABCO	Toluene	350 nm	12	73
11	$W(CO)_6$	DABCO	Toluene	350 nm	24	65
12	$Mo(CO)_6$	DABCO	Toluene	350 nm	12	45
13	—	DABCO	Toluene	reflux	10	0

Table 2 $W(CO)_6$-Catalyzed cyclisation of unsubstituted and monosubstituted propargyl amides[a]



9 10 11

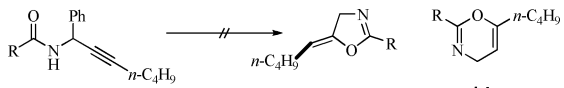
Entry	R^1	R^2	Yield (%) (**10** : **11**)
1	**9a**: Ph	H	80 : 0
2	**9b**: 2-BrPh	H	89 : 0
3	**9c**: 2-MeOPh	H	91 : 0
4	**9d**: n-C_7H_{15}	H	83 : 0
5	**9e**: 4-NO_2Ph	H	0
6	**9f**: Ph	Me	65 : 33
7	**9g**: Bn	Me	20 : 73
8	**9h**: 2-BrPh	Me	72 : 22
9	**9l**: n-C_7H_{15}	Me	67 : 25

[a] 1. $W(CO)_6$ (0.2 equiv), DABCO (1 equiv), toluene (1 mL), N_2, 350 nm, 20 h, r.t.; 2. Trimethylamine *N*-oxide dihydrate, THF.

trimethylamine *N*-oxide. In the present approach, two noteworthy features are (i) 5-*exo*-*dig* ring closure to give an oxazoline without any indication of 6-*endo*-*dig* ring closure and (ii) no further isomerization to an oxazole due to the mildness of the reaction conditions.

With the optimum conditions in hand, the scope and limitations of the present method were investigated (Table 2). When a solution of unsubstituted propargylic amides, $W(CO)_6$ (0.2 equiv) and DABCO (1 equiv) in toluene was irradiated at 350 nm for 20 h, oxazoline products were obtained in high yields (entries 1–4). However, 4-nitro-*N*-propynylbenzamide did not undergo cyclisation, probably due to the strong electron-withdrawing nature of the nitro group (entry 5). Concerning the isomerisation of oxazolines to oxazoles, as we observed previously, oxazoline **10** (R^2 = H) did not undergo isomerization to oxazole **11**.

The cyclisation of monoalkyl substituted propargylic amide **9** (R^2 = Me) afforded a mixture of **10** and **11** (entries 6–9). To complete the isomerization of oxazolines to oxazoles, when a toluene solution of a 65 : 33 mixture of oxazoline **10f** and oxazole **11f** in the presence of DABCO (2 equiv) was stirred at 80 °C for 12 h, the isomerization was incomplete, yielding a 46 : 47 mixture of **10f** and **11f** (entry 6). The complete isomerization could be achieved by treating with DBU at room temperature. For instance, treatment of a 65 : 33 mixture of **10f** and **11f** with DBU (1 equiv) in benzene at room temperature overnight afforded **11f** in 97% yield. In the case of *n*-butyl substituted propargylic amides **12a** and **12b**, contrary to previous reports,[10,16] they did not undergo cyclisation to give **13** and/or **14** under the present conditions and the starting propargylic amides were recovered unchanged.

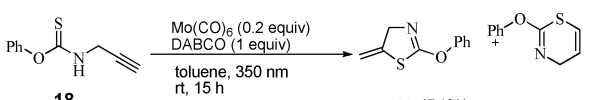


12a: R=Ph
12b: R=CH_2Ph

13 14

We next studied the cyclisation of disubstituted propargylic amides using W and Mo catalysts along with DABCO under standard reaction conditions. As we anticipated at the onset of this research, when **15** was subjected to the standard cyclisation conditions using 20 mol% $W(CO)_6$, oxazine **17** was obtained as a major product along with oxazoline **16** in a ratio of 78 : 17 (entry 1) and the product ratio remained the same for a longer reaction time (24 h). The use of Mo catalyst provided a similar result in favor of oxazine **17** (85 : 10) (entry 2). However, oxazines were not always obtained as a major product and the ratio of oxazolines and oxazines were variable, as shown in Table 3, and seemed to be dependent on the nature of the catalysts and the structure of the propargyl amides.

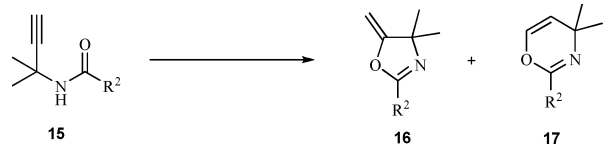
We next studied the cyclisation of thiocarbamate **18** using $W(CO)_6$/$Mo(CO)_6$ and DABCO (Scheme 3). When a toluene solution of **18** with $W(CO)_6$ and DABCO in toluene was irradiated at 350 nm for 15 h, no reaction occurred and the starting material was recovered unchanged. However, using $Mo(CO)_6$–DABCO under similar conditions the cyclisation proceeded cleanly, yielding a 54 : 36 mixture of thiazolidine **19** and thiaoxazine **20**. Furthermore, we also attempted the cyclisation of carbamate **21** and urea



18 **19** (54%) **20** (36%)

Scheme 3

Table 3 $W(CO)_6/Mo(CO)_6$ Catalyzed cyclisation of dimethyl substituted propargyl amides[a]

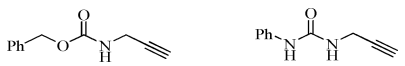


15 **16** **17**

Entry	R^2	Cat.	(**16** : **17**) (%)
1	**15a**: Ph	W	17 : 78
2	Ph	Mo	10 : 85
3	**15b**: 2-BrPh	W	49 : 49
4	2-BrPh	Mo	16 : 82
5	**15c**: Bn	W	69 : 23
6	Bn	Mo	8 : 86
7	**15d**: *n*-C_7H_{15}	W	32 : 63
8	*n*-C_7H_{15}	Mo	68 : 27

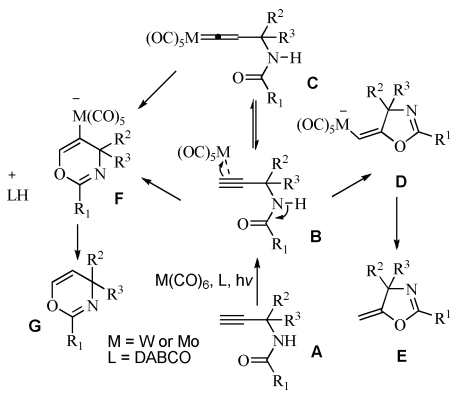
[a] The reaction was carried out using $W(CO)_6/Mo(CO)_6$ (0.2 equiv) and DABCO (1 equiv) at 350 nm in toluene (1 mL) at rt, 15 h.

22 using W and Mo catalysts under various conditions but the cyclisation did not occur.



21 **22**

Mechanistically, the alkynyl functionality of the propargylic amides is activated by coordination with the W and Mo catalysts to generate π–alkyne complex **B**, which is in equilibrium with the vinylidene complex **C** (Scheme 4).[11] Intramolecular nucleophilic attack of the carbonyl oxygen on the amide of intermediate **B** *via* 5-*exo* or 6-*endo* mode followed by the protonation of the corresponding carbene compounds **D** or **F** would produce oxazoline **E** or oxazine **G**.[17]



Scheme 4

In conclusion, we have developed W and Mo catalyst mediated cyclisation of propargylic amides to oxazolines and/or oxazines. The ratio of oxazolines and oxazines depends very much on the structure of the substrates and the nature of the catalysts. Further studies on the W and Mo-mediated cyclisations are currently in progress.

Acknowledgements

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Notes and references

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17 Deuterium exchange experiment in the presence of CH_3OD (20 equiv) using compound **7** indicated approximately 80% deuterium incorporation in two *exo*-methylene hydrogens. The detailed studies will be reported in due course.