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Reaction of Tantalum–Alkyne Complexes with Isocyanates Leading to (*E*)-α,β-Unsaturated Amides. Stereoselective Functionalization of Carbon–Carbon Triple Bonds

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Treatment of alkynes with low-valent tantalum derived from $TaCl_5$ and zinc produces tantalum–alkyne complexes (not isolated), which react with phenylisocyanate (or butylisocyanate) to give (*E*)-α,β-unsaturated amides stereoselectively.

Insertion of unsaturated compounds into metallacycles provides a general approach to metal-mediated carbon–carbon bond formations.[1] We recently found facile preparation of tantalum–alkyne complexes and utilized the complexes for the synthesis of (*E*)-allylic alcohols by treatment with carbonyl compounds.[2a] To explore the applicability of the tantalum–alkyne complexes, we chose isocyanates as an unsaturated compound.[3,4b]

Treatment of a tantalum–6–dodecyne complex (**2**), derived from 6–dodecyne and a $TaCl_5$–Zn system,[2b] with phenylisocyanate in a mixed solvent of DME–benzene–THF at 25 °C gave a complex mixture; only 9% yield of the desired (*E*)-*N*-phenyl-2-pentyl-2-octenamide (**1**) could be obtained after workup. However, filtration of the reaction mixture containing tantalum–alkyne complexes under an argon atmosphere before addition of isocyanates improved the reaction markedly and **1** was produced in 80% yield (see typical procedure). Deuterated amide ***d*-1** was obtained in 82% yield (100% deuterated) by quenching the reaction mixture of **3** (or **4**) with alkaline D_2O.

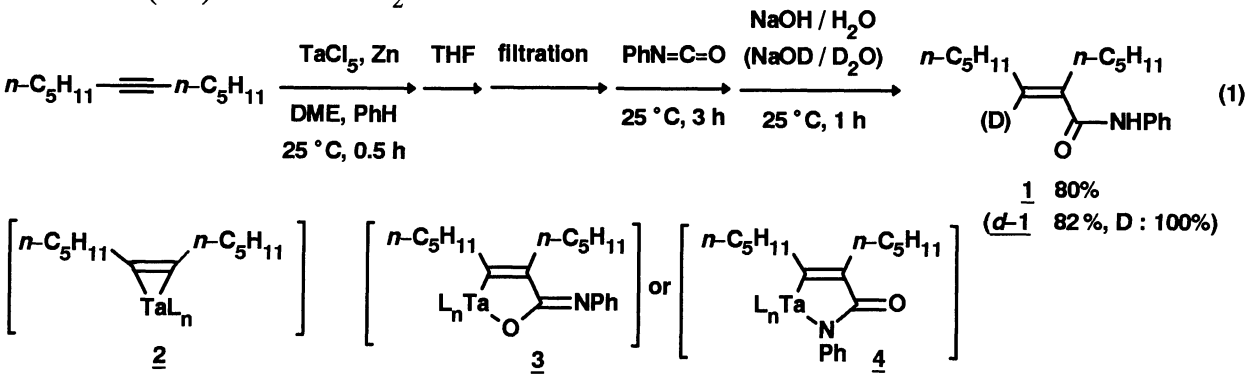
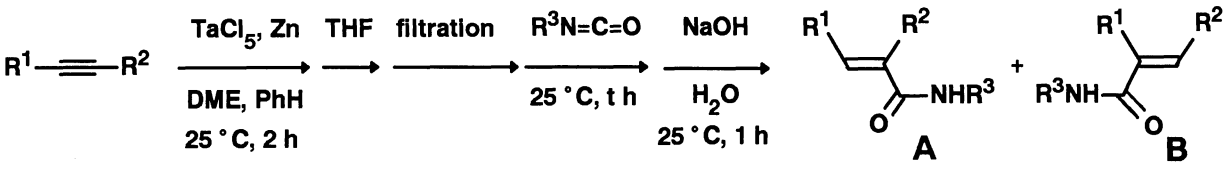


Table 1. Reactions between Alkynes and Isocyanates by Means of $TaCl_5$ and Zinc[a)]



Run	R^1	R^2	R^3	R^3NCO /equiv.	Time /h	Yield[b)] /%	A / B[c)]
1	n-C_5H_{11}	n-C_5H_{11}	Ph	1.2	3	80 [**1**]	-
2			Bu	1.2	3	72	-
3			t-Bu	1.2	20	6 (79)	-
4			Me_3Si	1.2	20	<1 (63)	-
5			Ts	1.2	20	48 (29)	-
6	c-C_6H_{11}	n-C_6H_{13}	Ph	2.0	3	69	55 / 45
7			Bu	2.0	3	62	73 / 27
8	Ph	n-C_6H_{13}	Ph	4.0	3	51	60 / 40
9			Bu	4.0	3	74	72 / 28
10	Me_3Si	n-$C_{10}H_{21}$	Ph	4.0	3	60	84 / 16
11			Bu	1.2	3	33	82 / 18
12	MeS	n-$C_{10}H_{21}$	Ph	2.0	0.2	58	>99 / <1
13			Bu	2.0	0.2	90	>99 / <1

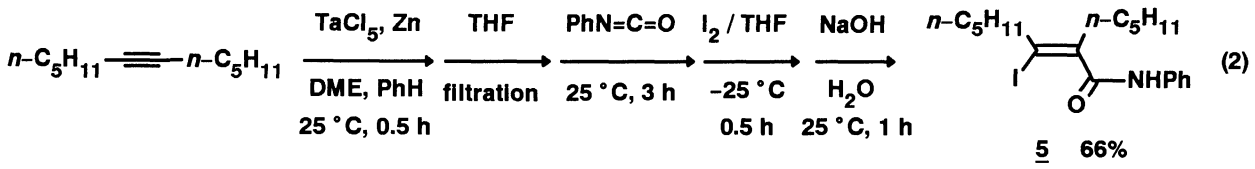
a) The reactions were conducted in 1.0 mmol scale. Two mole of $TaCl_5$ and 3 mol of zinc were employed per mole of an alkyne. b) Isolated yields. Yields of unreacted 6-dodecene are shown in parenthesis. c) The regioisomer ratios (**A/B**) were determined by ^1H NMR.

The results of the reactions between tantalum-alkyne complexes and isocyanates are summarized in Table 1. Reactions between the tantalum-alkyne complexes and butylisocyanate took place at 25 °C and *N*-butylamides were produced in good to excellent yields. In contrast, *t*-butyl- and trimethylsilylisocyanates were almost unreactive due to the bulkiness of the substituents (runs 3 and 4). Reaction with *p*-toluenesulfonylisocyanate proceeded slowly under the reaction conditions and the corresponding amide was obtained in 48% yield (run 5).

Tantalum-alkyne complexes derived from unsymmetrical alkynes produces two regioisomeric amides. Regioselectivities of the reactions between tantalum-alkyne complexes and isocyanates have the same tendency as those between the complexes and aldehydes. Insertion of isocyanates took place at the less hindered side of the tantalum-alkyne complexes (runs 6-11). In the case of a methylthio-substituted alkyne,

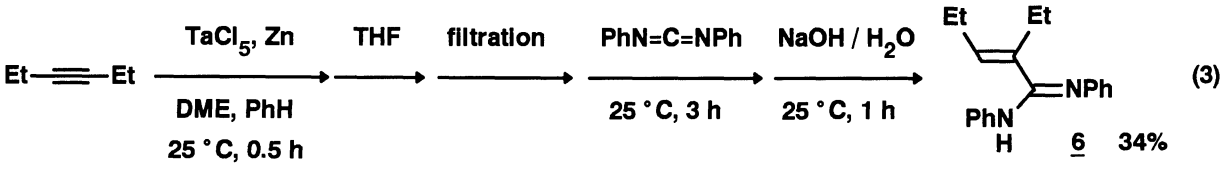
the regioisomer **A** was produced exclusively because of the electronic nature of the substituents (runs 12 and 13).[2c)]

Reaction of the tantalum–6–dodecyne complex **2** with phenylisocyanate, followed by iodinolysis with 5 equiv. of iodine at –25 °C produced (*Z*)–β–iodo–α,β–unsaturated amide **5** in 66% yield stereoselectively (Eq. 2).



Although clarification of the effect of filtration is still continuing, the following are worth noting. (1) When the removed solid by filtration was put back to the reacted mixture of tantalum–alkyne complexes and isocyanates, many byproducts appeared and the yield of the desired adduct **1** fell to 22%. (2) Addition of the following compounds into the filtered tantalum–6–dodecyne solution, derived by treatment of 6–dodecyne with 1.2 equiv. of tantalum and 1.8 equiv. of zinc,[5)] before reaction with phenylisocyanate gave **1** in the following yields in parenthesis: zinc, 1.8 equiv. (23%); low–valent tantalum solution, 1 equiv. (46%); zinc chloride, 1.8 equiv. (64%); none (63%). α,β–Unsaturated amide **1** was obtained in 48% yield under the same conditions without filtration. These results suggest that excess amount of zinc or low–valent tantalum promotes further reactions which consume the initial adduct **3** (or **4**).

Reaction of the tantalum–6–dodecyne complex with phenylthioisocynate resulted in recovery of (*Z*)–6–dodecene in 81% yield.[4a)] In contrast, tantalum–3–hexyne complex reacted with diphenylcarbodiimide to give (*E*)–α,β–unsaturated amidine **6** in 34% yield (Eq. 3).[4c)]



Typical Experimental Procedure: Zinc (0.20 g, 3.0 mmol) was added at 25 °C to a stirring pale yellow solution of $TaCl_5$ (0.72 g, 2.0 mmol) in DME–benzene (1:1, 10 mL) under an argon atmosphere and the mixture was stirred at 25 °C for 40 min. The color of the mixture turned to greenish dark blue with slightly exothermic process. To the mixture was added at 25 °C a solution of 6–dodecyne (0.17 g, 1.0 mmol) in DME–benzene (1:1, 2 mL) and the whole mixture was stirred at 25 °C for 30 min. THF (5 mL) was added to the mixture. After being stirred at 25 °C for 15 min, the mixture was filtered under an argon atmosphere and the removed solid was washed with THF (2x3 mL). To the combined filtrates was added phenylisocyanate (0.14 g, 1.2 mmol) and the resulting mixture was stirred at 25 °C for 3 h. Aqueous NaOH solution (15%, 2

mL) was added and the mixture was stirred at 25 °C for additional 1 h. The deposited white solid was removed by filtration with Hyflo-Super Cel^R and washed well with ethyl acetate (3x5 mL). Organic extracts were dried over $MgSO_4$ and concentrated. Purification by column chromatography on silica gel (ethyl acetate-hexane, 1:20) gave 0.23 g (80% yield) of (*E*)-*N*-phenyl-2-pentyl-2-octenamide (**1**) as a colorless liquid,[6] which solidified gradually on standing.

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References

1) For some representative reactions with metal-alkyne complexes, see: a) Zr: S. L. Buchwald, R. T. Lum, and J. C. Dewan, *J. Am. Chem. Soc.*, **108**, 7441 (1986); S. L. Buchwald, B. T. Watson, and J. C. Huffman, *ibid.*, **109**, 2544 (1987); S. L. Buchwald and R. B. Nielsen, *Chem. Rev.*, **88**, 1047 (1988); T. Takahashi, D. R. Swanson, and E. Negishi, *Chem. Lett.*, **1987**, 623; b) Nb: J. B. Hartung, Jr. and S. F. Pedersen, *J. Am. Chem. Soc.*, **111**, 5468 (1989); Y. Kataoka, J. Miyai, M. Tezuka, K. Takai, K. Oshima, and K. Utimoto, *Tetrahedron Lett.*, **31**, 369 (1990); c) Ta: J. R. Strickler, M. A. Bruck, P. A. Wexler, and D. E. Wigley, *Organometallics* **9**, 266 (1990).

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5) To eliminate the effect of the excess amount of low-valent tantalum, the amount of $TaCl_5$ and zinc was reduced to 1.2 and 1.8 equiv., respectively.

6) (*E*)-*N*-Phenyl-2-pentyl-2-octenamide: Mp 54-56 °C, Bp. 130-132 °C (bath temp, 0.20 Torr); ^1H NMR ($CDCl_3$): δ 0.88 (t, *J*=6.3 Hz, 3H), 0.90 (t, *J*=6.3 Hz, 3H), 1.2-1.6 (m, 12H), 2.16 (dt, *J*=7.3, 7.3 Hz, 2H), 2.37 (t, *J*=7.3 Hz, 2H), 6.26 (t, *J*=7.3 Hz, 1H), 7.07 (dd, *J*=7.6, 7.6 Hz, 1H), 7.29 (dd, *J*=7.6, 7.6 Hz, 2H), 7.57 (d, *J*=7.6 Hz, 2H), 7.7-7.8 (m, 1H); ^{13}C NMR ($CDCl_3$): δ 13.9, 22.4, 27.1, 28.1, 28.7, 31.5, 31.7, 119.9, 123.8, 128.7, 135.4, 137.7, 138.3, 168.0. Found: C, 79.62; H, 10.44; N, 4.84%. Calcd for $C_{19}H_{29}ON$: C, 79.39; H, 10.17; N, 4.87%.

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