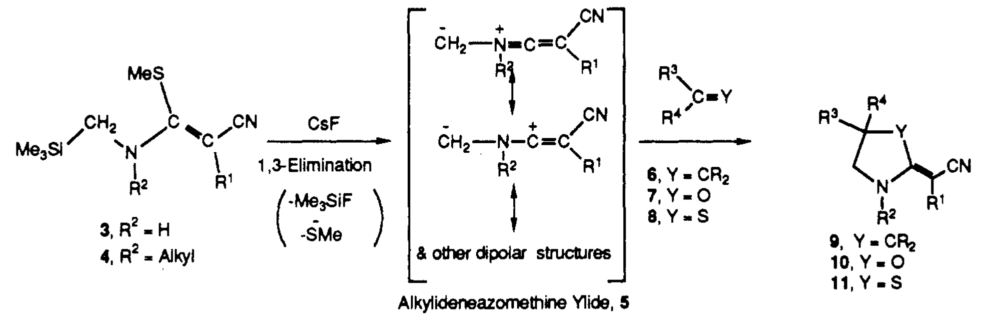
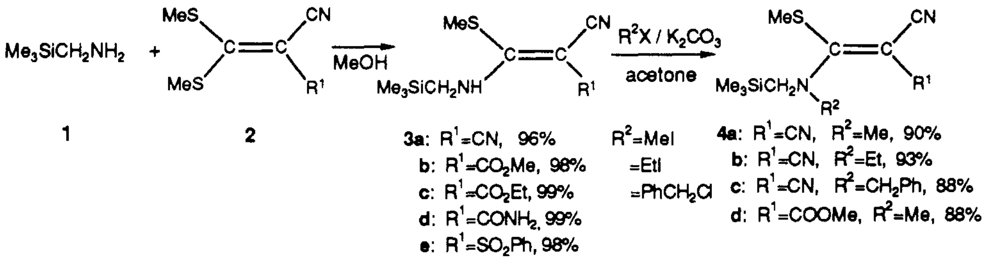
Scheme I



Scheme II



cycloaddition was slow and the trans cycloadduct **9a** was obtained selectively with inversion of the stereochemistry, in sharp contrast to the results with the parent azomethine ylid synthon promoted by acid.[3a] N-Unsubstituted *N*,*S*-acetals **3** did not give cycloadduct **9**[10] under similar reaction conditions. Although the mechanism of these cycloadditions has not been clarified, the results may be rationalized by assuming faster *Z*-*E* isomerization of the maleate to the fumarate than cycloaddition under the present conditions.[11] Acids such as trimethylsilyl triflate, trimethylsilyl iodide, or trichloroacetic acid did not promote the reaction.

The synthetic utility of the reaction was further demonstrated with representative heterodipolarophiles, affording the corresponding N-containing α-alkylideneheterocycles. The results are listed in Table II.

Not only N-unsubstituted ketene *N*,*S*-acetals **3** but also N-alkylated acetals **4** react effectively with various aldehydes and ketones **7**. Substituted aromatic and heteroaromatic aldehydes, including those bearing electron-donating and electron-withdrawing groups, α,β-unsaturated aldehydes, aromatic ketones, and ketomalonate react with **4** to give the corresponding alkylideneoxazolidines **10** in modest yields. Furthermore, thioketones **8**[12] are also good acceptors for this [3 + 2] cycloaddition, giving the corresponding alkylidenethiazolidines **11**.

This work demonstrates that *N*-(silylmethyl)-substituted ketene *N*,*S*-dithioacetals **3** and **4** are storable and easy to handle synthetic equivalents of alkylideneazomethine ylids **5**. The reaction displays complete regiospecificity in the cycloaddition with heterodipolarophiles.

Acknowledgment. Financial support for our work is provided by Grants-in-Aid for Scientific Research and Grants-in-Aid for Scientific Research on Priority Areas from the Ministry of Education, Science and Culture, the Naito Foundation, the CIBA-GEIGY Foundation for the promotion of Science, Japan. We thank Dow Corning Toray Silicone Co. Ltd. for a gift of organosilicon compounds.

Supplementary Material Available: Spectra and analytical data for 3, 4, 9, 10, and 11 (4 pages). Ordering information is given on any current masthead page.

---

(8) For the synthesis of α-alkylidenepyrrolidines, see: Meerwein, H.; Borner, P.; Fuchs, O.; Sasse, H. J.; Schrodt, H.; Spille, J. *Chem. Ber.* **1956**, *89*, 2060.

(9) The regiochemical outcome with methyl acrylate (unsymmetrical dipolarophile) is important for elucidating the reaction mechanism, but the structure **9b** is not yet known.

(10) A complex mixture, presumably including a 1:2 adduct of 3 to alkenes was obtained in these reactions.

(11) It was found that methylthiolate, generated in situ, catalyzed this *Z*-*E* isomerization and cycloaddition to the fumarate was faster than to the maleate.

(12) (a) Padwa, A.; Dent, W. *J. Org. Chem.* **1987**, *52*, 235. (b) Aono, M.; Terao, Y.; Achiwa, K. *Chem. Lett.* **1987**, 1851.

Regioselective Synthesis of Highly Substituted Furans via Tantalum-Alkyne Complexes

Kazuhiko Takai,* Makoto Tezuka, Yasutaka Kataoka, and Kiitiro Utimoto*

Department of Industrial Chemistry, Faculty of Engineering, Kyoto University, Yoshida, Kyoto 606, Japan

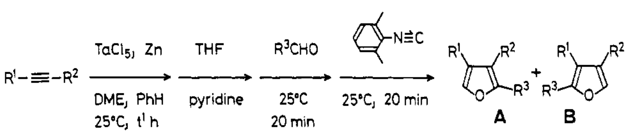
Received July 12, 1990

Summary: A variety of 2,3,4-trisubstituted furans are prepared by treatment of tantalum-alkyne complexes with aldehydes, followed by addition of an isocyanide in DME-PhH-THF (1:1:1).

Transition metals exhibit a variety of interesting reactivities, thereby suggesting new methods in organic synthesis. We disclose here a regioselective preparation of highly substituted furans[1] from three components, i.e.

0022-3263/90/1955-5310$02.50/0

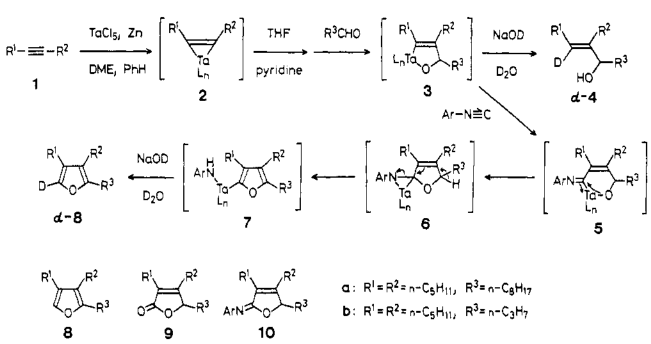
Table I. Synthesis of Furans from Alkynes, Aldehydes, and Isonitriles[a]



run	R^1	R^2	R^3	ArNC	time t^1, h	yield,[b] %	A/B[c]
1	n-$C_{10}H_{21}$	H	n-C_3H_7	2,6-$Me_2(C_6H_3)NC$	0.5	8[d]	>98/<2
2	n-C_5H_{11}	n-C_5H_{11}	n-C_8H_{17}		0.5	66	–
3				[$Me_3CCH_2CMe_2NC$]	0.5	28	–
4				[Me_3SiCN]	0.5	29[e]	–
5	c-C_6H_{11}	n-C_6H_{13}	n-C_5H_{11}	2,6-$Me_2(C_6H_3)NC$	2	55	69/31
6	t-Bu	n-C_7H_{15}	n-C_3H_7		5	40[f]	98/2
7	Me_3Si	n-$C_{10}H_{21}$			2	57	94/6[g]
8		Ph			3.5	42[f]	>98/<2[g]
9	t-$BuMe_2Si$	n-$C_{10}H_{21}$			3.5	54[f,h]	>98/<2[g]

[a] Reactions were carried out on a 1-mmol scale. Conditions: 2.0 equiv of $TaCl_5$, 3.0 equiv of zinc, 4.0 equiv of pyridine, 1.2 equiv of aldehyde, 1.0 equiv of isonitrile, DME–PhH–THF (1:1:1), 25 °C. [b] Isolated yields. [c] Reference 12. [d] Polymer of 1-dodecyne was produced in the reaction of 1-dodecyne with the low-valent tantalum, and remained until workup; 0.5 equiv of the isonitrile was used. [e] Reaction was conducted without pyridine. [f] Conditions: 4.0 equiv of $TaCl_5$, 6.0 equiv of zinc, 8.0 equiv of pyridine, 2.0 equiv of isonitrile. [g] Reference 13. [h] The reaction mixture was stirred at 25 °C for 40 min after addition of the isonitrile.

Scheme I



acetylenes, aldehydes, and an isonitrile by means of low-valent tantalum.

Insertion of carbon monoxide[2] or isonitrile[3] into metal-carbon bonds is a typical method for introducing one carbon units into organometallic compounds. Although the insertion of isonitrile into tantalum–carbon bonds was first recognized in 1974,[4] the process has not been utilized in organic synthesis. Recently, we found a general and simple method for the preparation of tantalum–alkyne complexes[5] derived from low-valent tantalum and acetylenes.[6] These complexes add to carbonyl compounds in a stereoselective manner to yield (E)-allylic alcohols.[6a] In this reaction, oxatantallacyclopentene **3** was postulated, because quenching the reaction mixture of **3a** ($R^1 = R^2 = n\text{-}C_5H_{11}$, $R^3 = n\text{-}C_8H_{17}$) with alkaline D_2O furnished 3-deuterated allylic alcohol *d*-**4a** in 86% yield (94% deuterated). Thus we tried to examine the insertion of isonitrile into the tantalum–carbon bond of the complex **3**.

Reactive tantallacyclopropene **2a** ($R^1 = R^2 = n\text{-}C_5H_{11}$) was generated by the reaction between 6-dodecyne (1.0 equiv) and the low-valent tantalum derived from $TaCl_5$ (2.0 equiv) and zinc (3.0 equiv) in a mixed solvent of 1,2-dimethoxyethane (DME) and benzene at 25 °C. Successive addition of THF, pyridine, and nonanal (1.2 equiv) to the reaction mixture gave oxatantallacyclopentene **3a** (not isolated).[6a] Treatment of **3a** with 2,6-dimethylphenyl isonitrile[7] (1.0 equiv) at 25 °C for 20 min did not give butenolide[8] **9a** (or imino lactone[9] **10a**), but afforded furan **8a** in 66% yield.[10]

Yields of furans were critically dependent on the amounts of the isonitrile, and excess isonitrile retarded the formation of furans.[11] For example, treatment of **3a** with 2.0 equiv of the isonitrile gave **8a** in 40% yield along with unreacted allylic alcohol **4a** in 15% yield. The reaction also took place with cyanotrimethylsilane and carbon monoxide (ca. 1.2 atom), but the desired furan **8a** was obtained in only 29% and 13% yields, respectively.

The reaction proceeds under mild conditions, and 2,3,4-trisubstituted furans were produced (Table I). The regioselectivities displayed in the products are determined at the addition step of the tantallacyclopropene **2** to aldehydes and are controlled by the bulkiness of the substituents of the acetylenes.[6a] (Trialkylsilyl)acetylenes gave one of the regioisomers with high stereocontrol (runs 7–9).[13]

Plausible mechanisms for the reaction are outlined in Scheme I. Insertion of an isonitrile into the carbon–tantalum bond of **3** would produce a tantallacycle **5**.[4,14]

---

(1) Sargent, M. V.; Cresp, T. M. In *Comprehensive Organic Chemistry*; Sir Barton, D., Ollis, W. P., Eds.; Pergamon Press: Oxford, 1979; Vol. 4, p 693.

(2) (a) Calderazzo, F. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 299. (b) Kuhlmann, E. J.; Alexander, J. J. *Coord. Chem. Rev.* **1980**, *33*, 195.

(3) (a) Yamamoto, Y.; Yamazaki, H. *Coord. Chem. Rev.* **1972**, *8*, 225. (b) Tamao, K.; Kobayashi, K.; Ito, Y. *J. Am. Chem. Soc.* **1988**, *110*, 1286.

(4) Wilkins, J. D. *J. Organomet. Chem.* **1974**, *67*, 269.

(5) (a) Cotton, F. A.; Hall, W. T. *J. Am. Chem. Soc.* **1979**, *101*, 5094. (b) Smith, G.; Schrock, R. R.; Churchill, M. R.; Youngs, W. J. *Inorg. Chem.* **1981**, *20*, 387. (c) Bruck, M. A.; Copenhaver, A. S.; Wigley, D. E. *J. Am. Chem. Soc.* **1987**, *109*, 6525. (d) Strickler, J. R.; Wexler, P. A.; Wigley, D. E. *Oganometallics* **1988**, *7*, 2067. (e) Kwon, D.; Curtis, M. D. *Ibid.* **1990**, *9*, 1.

(6) (a) Takai, K.; Kataoka, Y.; Utimoto, K. *J. Org. Chem.* **1990**, *55*, 1707. (b) Kataoka, Y.; Takai, K.; Oshima, K.; Utimoto, K. *Tetrahedron Lett.* **1990**, *31*, 365. (c) Kataoka, Y.; Miyai, J.; Tezuka, M.; Takai, K.; Oshima, K.; Utimoto, K. *Ibid.* **1990**, *31*, 369.

(7) 2,6-Dimethyl isonitrile was prepared from 2,6-dimethylaniline in 65% yield according to the following reference. Niznik, G. E.; Morrison, W. H., III; Walborsky, H. M. *Organic Syntheses*; Wiley: New York, 1988; Collect. Vol. VI, p 751.

(8) (a) Larock, R. C.; Riefling, B.; Fellows, C. A. *J. Org. Chem.* **1978**, *43*, 131. (b) Cowell, A.; Stille, J. K. *J. Am. Chem. Soc.* **1980**, *102*, 4193.

(9) Ito, Y.; Kato, H.; Saegusa, T. *J. Org. Chem.* **1982**, *47*, 741.

(10) Similar process, i.e. sequential insertion–deoxygenation, was observed by Buchwald in the reaction of azazirconacyclopentene with carbon monoxide (ca. 100 atom) which afforded pyrroles. Buchwald, S. L.; Wannamaker, M. W.; Watson, B. T. *J. Am. Chem. Soc.* **1989**, *111*, 776.

(11) Insertion of isonitrile into a nickel–carbon bond is also sensitive to the amount of isonitrile. See ref 3b.

(12) The regiochemistry was determined by comparison with authentic samples.[13] Isomeric purities were ascertained by examination of ^1H or ^{13}C NMR spectra and/or capillary GLPC.

(13) Removal of the trimethylsilyl groups on furans was accomplished with $(HF)_x$-pyridine according to the following paper. Danheiser, R. L.; Stoner, E. J.; Koyama, H.; Yamashita, D. S.; Klade, C. A. *J. Am. Chem. Soc.* **1989**, *111*, 4407.

(14) Curtis, M. D.; Real, J.; Hirpo, W.; Butler, W. M. *Organometallics* **1990**, *9*, 66.

Migration of oxygen from tantalum to the imino carbon would give an η^2-acylimidoyl complex **6**,[15] which would produce 2-tantalofuran **7** via oxygen-assisted elimination of NAr. The affinity of tantalum for heteroatoms (and hence the formation of the η^2-acylimidoyl complex **6**) is the driving force for this migration process. The presence of the 2-tantalofuran **7** was ascertained by the fact that quenching of the reaction mixture of **7b** with alkaline D_2O afforded 2-deuterated furan *d*-**8b** ($R^1 = R^2 = n\text{-}C_5H_{11}$, $R^3 = n\text{-}C_3H_7$, 47% yield, 91% deuterated).

Acknowledgment. Financial support from the Kawakami Memorial Foundation is acknowledged.

Supplementary Material Available: A typical experimental procedure for the synthesis of 2-octyl-3,4-dipentylfuran (**8a**) and spectral data for all new compounds (5 pages). Ordering information is given on any current masthead page.

---

(15) For η^2-acylimidoyl complexes of tantalum, see: (a) Takahashi, Y.; Onoyama, N.; Ishikawa, Y.; Motojima, S.; Sugiyama, K. *Chem. Lett.* **1978**, 525. For η^2-acyl complexes of tantalum, see: (b) Wood, C. D.; Schrock, R. R. *J. Am. Chem. Soc.* **1979**, *101*, 5421. (c) van Asselt, A.; Burger, B. J.; Gibson, V. C.; Bercaw, J. E. *J. Am. Chem. Soc.* **1986**, *108*, 5347.

Articles

New Functionalized Horner–Wadsworth–Emmons Reagents: Useful Building Blocks in the Synthesis of Polyunsaturated Aldehydes. A Short Synthesis of (±)-(*E*,*E*)-Coriolic Acid

Nina Kann,[1a] Tobias Rein,*,[1a] Björn Åkermark,*,[1a] and Paul Helquist[1b]

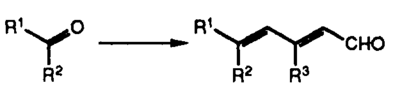
Department of Organic Chemistry, Royal Institute of Technology, S-100 44 Stockholm, Sweden, and Department of Chemistry and Biochemistry, University of Notre Dame, Notre Dame, Indiana 46556

Received November 20, 1989

The new Horner–Wadsworth–Emmons reagents **4** and **5** transform carbonyl compounds into 2,4-pentadienals and 3-methyl-2,4-pentadienals, respectively. Reagent **4** gives good yields of the desired products with a variety of aldehydes and ketones; reagent **5** generally gives good yields with aldehydes, but gives lower yields with ketones. The reactions proceed under mild conditions and give the products as predominantly 2*E*,4*E* isomers, with moderate to good stereoselectivity. In general, pure samples of the 2*E*,4*E*-dienals can be obtained after chromatography. Reagents **4** have been used in the key step in a short synthesis of (±)-13-hydroxy-9(*E*),11(*E*)-octadecadienoic acid ((*E*,*E*)-coriolic acid, **45**).

Introduction

The direct transformation of a carbonyl compound **1** into an elongated conjugated dienal (**2** or **3**, eq 1) is a very attractive reaction from a synthetic point of view.



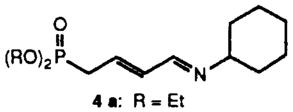
(1)

1

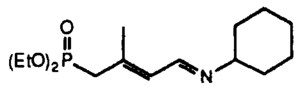
2: $R^3 = H$
3: $R^3 = CH_3$

From the dienals, substructures of many interesting target compounds can be obtained in a few steps: (1) a polyene derivative can be obtained by a further condensation reaction (e.g. Horner–Wadsworth–Emmons[2] (HWE) or Wittig[3]); (2) selective nucleophilic addition to the carbonyl group will give a polyunsaturated secondary allylic alcohol; (3) the dienal itself, or compounds derived from it, can participate in cycloaddition reactions[4] to give carbo- or heterocyclic rings. Synthetic applications include many classes of natural products with useful biological activity.

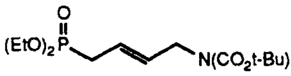
We recently introduced the functionalized HWE reagent **4a**, which converts carbonyl compounds directly into dienals **2** (eq 1; $R^3 = H$).[5] We now introduce the reagent **5**, which transforms carbonyl compounds directly into methyl-substituted dienals **3** (eq 1; $R^3 = CH_3$). In other work, we had previously developed the related reagent **6**.[6]



4 a: R = Et
b: R = i-Pr



5



6

---

(1) (a) Royal Institute of Technology. (b) University of Notre Dame.

(2) For reviews, see: (a) Wadsworth, W. S. *Org. React.* (*N.Y.*) **1977**, *25*, 73–253. (b) Boutagy, J.; Thomas, R. *Chem. Rev.* **1974**, *74*, 87–99.

(3) For reviews, see: (a) Pommer, H. *Angew. Chem.* **1977**, *89*, 437–443. (b) Maryanoff, B.; Reitz, A. B. *Chem. Rev.* **1989**, *89*, 863.

(4) For some relevant examples, see: (a) Takeda, K.; Yano, S.-G.; Yoshii, E. *Tetrahedron Lett.* **1988**, *29*, 6951–6954. (b) Roush, W. R.; Brown, B. B.; Drozda, S. E. *Ibid.* **1988**, *29*, 3541–3544. (c) Tapolczay, D. J.; Thomas, E. J.; Whitehead, J. W. F. *J. Chem. Soc., Chem. Commun.* **1985**, 143–145. (d) Roush, W. R.; Peseckis, S. M.; Walts, A. E. *J. Org. Chem.* **1984**, *49*, 3429–3432.

(5) Rein, T.; Åkermark, B.; Helquist, P. *Acta Chem. Scand., Ser. B* **1988**, *42*, 569–572.

0022-3263/90/1955-5312$02.50/0