Tetrahedron Letters,Vol.28,No.6,pp 629-632,1987
Printed in Great Britain

0040-4039/87 $3.00 + .00
Pergamon Journals Ltd.

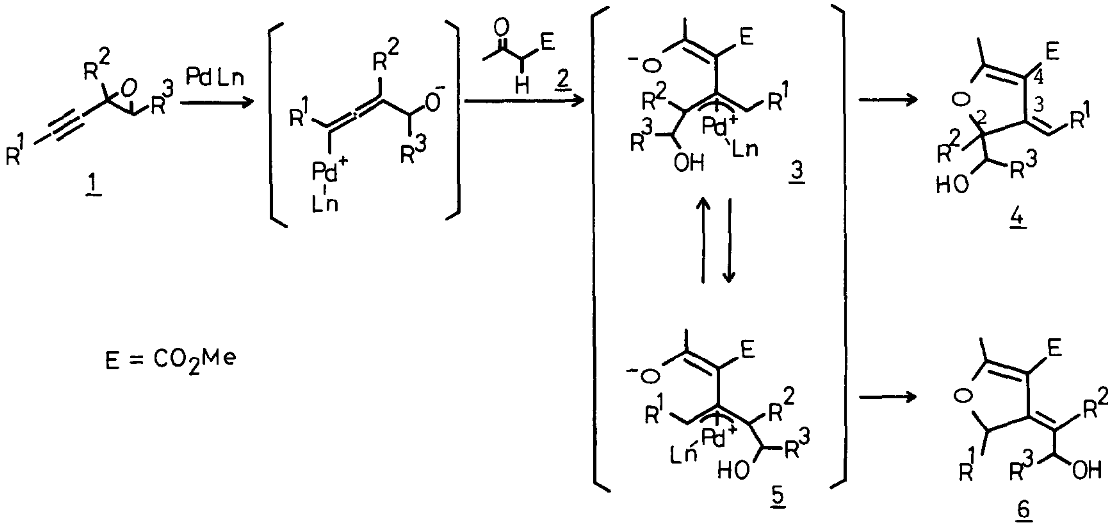
PREPARATION OF UNSTABLE 3-ALKYLIDENE FURANS BY THE PALLADIUM-CATALYZED REACTION OF α-ALKYNYL EPOXIDES WITH β-KETO ESTERS

Ichiro MINAMI, Masami YUHARA, and Jiro TSUJI*
Tokyo Institute of Technology, Meguro, Tokyo 152, Japan

Summary; Palladium-catalyzed reaction of α-alkynyl epoxides with β-keto esters gives unstable 3-alkylidene-2,3-dihydrofuran-4-carboxylates. It can be carried out under mild neutral conditions, and offers a good preparative method for 3-alkylidene furans.

Substituted furan structures abound in naturally occurring terpenoides.[1)] Also, alkylidene dihydrofurans are unstable compounds and their facile preparative methods are still unknown.[2)] We now wish to report a new synthetic method for 3-alkylidene-2,3-dihydrofuran-4-carboxylates from α-alkynyl epoxides 1 and β-keto esters by the catalysis of palladium-phosphine complex as expressed by Scheme 1. So far, palladium-catalyzed reaction of 3-butyn-1,2-epoxides 1 with alkyl zinc reagents[3)] or formic acid[4)] to give 1-hydroxy-2,3-dienes has been reported. The present reaction is the first example for the palladium-catalyzed reaction of α-alkynyl epoxides with soft carbonucleophiles.

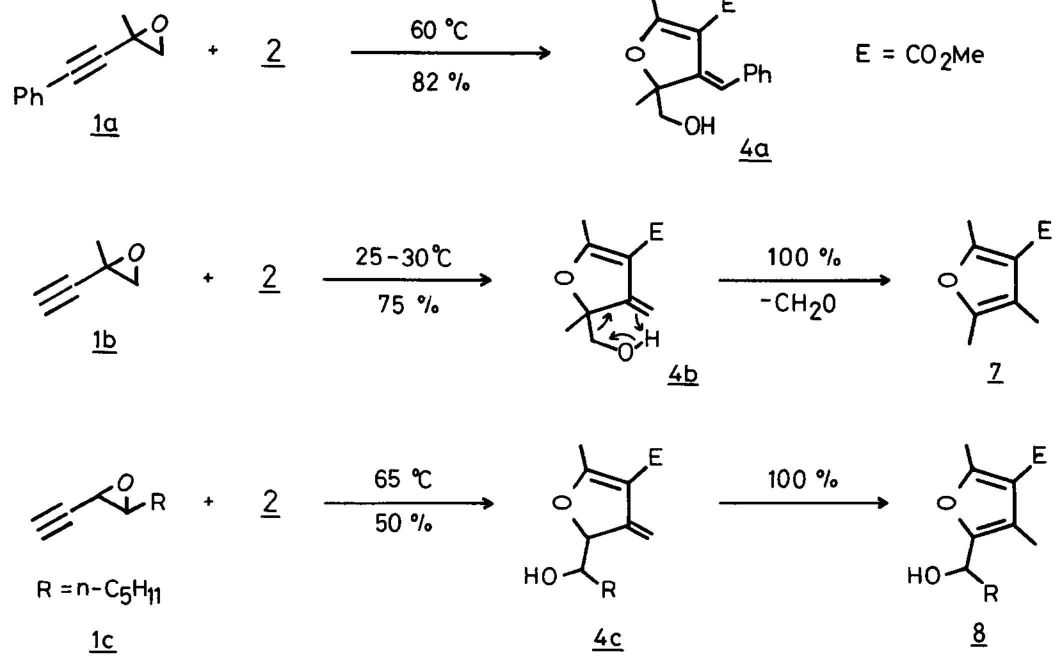
<Scheme 1>



A solution of 2-methyl-4-phenyl-3-butyn-1,2-epoxide (1a, 1 mmol), methyl acetoacetate (2, 1 mmol), $Pd_2(dba)_3 \cdot CHCl_3$ (0.025 mmol), and diphenylphosphinoethane (dppe, 0.05 mmol) in dry THF (5 mL) was stirred for 1 h at 60 °C under argon. Then methyl 3-benzylidene-2,5-dimethyl-2-hydroxymethyl-2,3-dihydrofuran-4-carboxylate (**4a**) was isolated by column chromatography on alumina in

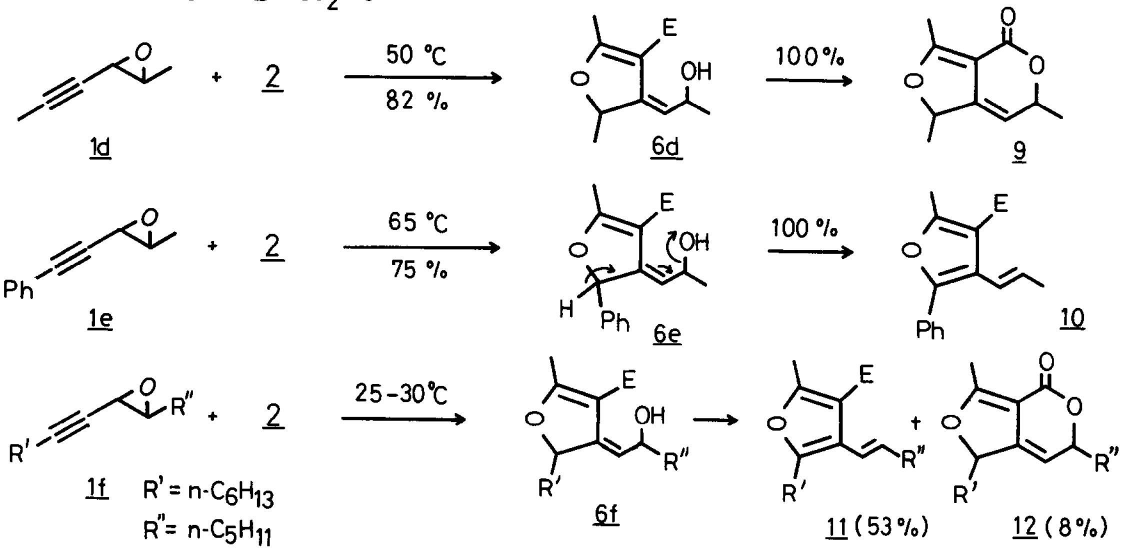
82% yield. [^{1}H NMR ($CDCl_3$) δ 1.51 (s, 3H, $-C-C\underline{H}_3$), 1.60 (bs, 1H, $-C-O\underline{H}$), 2.25 (s, 3H $-O-C(C\underline{H}_3)=C-$), 3.09 (s, 3H, $-CO_2C\underline{H}_3$), 3.52-3.68 (bs, 2H, $-C-C\underline{H}_2-OH$), 5.91 (s, 1H, $-C=C\underline{H}-Ph$), 7.00-7.30 (m, 5H, aromatic). ^{13}C NMR ($CDCl_3$) δ 14.4 (q, $-C-\underline{C}H_3$), 22.7 (q, $-O-C(\underline{C}H_3)=C-$), 50.4 (q, $-CO_2\underline{C}H_3$), 68.7 (t, $-C-\underline{C}H_2-OH$), 92.7 (s, $-O-\underline{C}-C=C-$), 107.3 (s, $-C=\underline{C}-CO_2Me$), 113.7 (d, $-C=\underline{C}H-Ph$), 125.9 (d, aromatic), 127.6 (d, aromatic), 127.7 (d, aromatic), 138.5 (s, aromatic), 141.2 (s, $-\underline{C}=CH-Ph$), 165.4 (s, $-\underline{C}O_2Me$), 172.5 (s, $-\underline{C}=C-CO_2Me$). IR (neat) 3450 (-OH), 2970 (-CH), 1700 ($-CO_2Me$), 1620 (-Ph), 790 (-C=C-Ph) 700 cm^{-1} High-mass m/z = 274.122 (M^+)] Careful studies of ^{13}C NMR spectrum of the furan **4a** revealed that only one stereo isomer due to benzylidene double bond was obtained by the reaction. We concluded that the geometry of the double bond is E form, since the reaction proceeds via (π-allyl)palladium intermediates, in which syn forms **3** or **5** are more preferential by steric hindrance.$^{5)}$ In addition, facile lactonization of **6d** to form **9** supports the Z stereochemistry of the exo-double bonds. The exo-methylene furan **4b**, prepared by the reaction of **1b** with **2**, is a highly acid-sensitive compound and underwent dehydroxymethylation to give methyl 2,4,5-trimethylfuran-3-carboxylate (**7**) during NMR analysis in $CDCl_3$ or CCl_4. The isomerization took place in a quantitative yield by acid treatment (short silica-gel column), while the phenyl substituted furan **4a** hardly underwent the dehydroxymethylation under the same conditions. With **4c**, bearing a tertiary carbon at C2, isomerization of the exo-methylene double bond took place to give the furan **8**.

<Scheme 2>



As shown in Scheme 1, the furan annelation reaction proceeds via (π-allyl)palladium complex **3** or **5**,6) and regioselectivity of the cyclization depends on the substituents, R^1-R^3. When 1,4-disubstitued-3-butyn-1,2-epoxides ($R^1 \neq H$, and $R^3 \neq H$), were employed to react, 3-alkylidene-2,3-dihydrofurans **6** were formed rather than **4**. For example, reaction of **1d** with **2** afforded **6d**, which underwent acid-promoted lactonization to give furolactone **9**. On the other hand, the phenyl substitued furan **6e**, was converted into the furan **10** by dehydration without giving furolactone. Also, **6f** underwent the dehydration to give **11**.

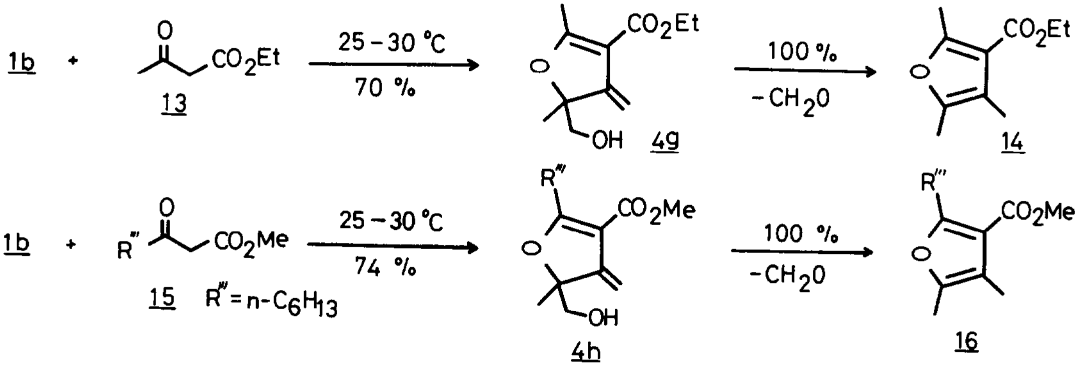
<Scheme 3> E = CO_2Me



Then the reaction of α-alkynyl epoxides with other β-keto esters was examined. As expressed by Scheme 4, reaction of **1b** with β-keto esters **13** and **15** gave the corresponding furans **14** and **16** respectively in good yields.

In conclusion, the present reaction offers a facile synthetic method for unstable 3-alkylidene-2,3-dihydrofurans **4** or **6**.

<Scheme 4>



ACKNOWLEDGMENT:

This research was financially supported by the Grant-in-Aids for Developmental Scientific Research, No. 60850153 and Encouragement of Young Scientist, No. 60790051 from the Ministry of Education, Science and Culture.

REFERENCES:

1) J. S. Glasby, "Encyclopedia of the Terpenoids" John Wiley & Sons, 1982.

2) W. S. Trahanovsky, T. J. Cassady, and T. L. Woods, **J. Am. Chem. Soc., 103,** 6691 (1981).

3) H. Kleijin, J. Meijer, G. C. Overbeek, and P. Vermeer, **Recl. J. R. Neth. Chem. Soc., 101,** 97 (1982).

4) J. Tsuji, T. Sugiura, M. Yuhara, and I. Minami, **Chem. Commun, 1986,** 922.

5) For recent reviews on reactions via (π-allyl)palladium intermediates;
J. Tsuji "Organic Synthesis with Palladium Compounds", Springer-Verlag, Berlin, **1980,** pp37.
B. M. Trost and T. R. Verhoeven, "Comprehensive Organometallic Chemistry" Pergamon Press, **1982,** 8, pp799.
B. M. Trost **J. Organometal. Chem., 300,** 263 (1986).
J. Tsuji **J. Organometal. Chem., 300,** 281 (1986).

6) J. Tsuji, H. Watanabe, I. Minami, and I. Shimizu, **J. Am. Chem. Soc., 107,** 2196 (1985).

7) Physical data of the products:
6e; ^{1}H NMR(CDCl$_3$) δ 1.12 (d, J=6.2 Hz, 3H), 2.31 (s, 3H), 3.10-3.40 (br, 1H), 3.83 (s, 3H), 4.50-4.88 (m, 2H), 5.91 (d, J=2.2 Hz, 1H), 7.16-7.50 (m, 5H). IR(neat) 3300, 2940, 1700, 1595, 1440, 1120, 980, 760, 700 cm^{-1} **7**; ^{1}H NMR(CDCl$_3$) δ 2.03 (s, 3H), 2.13 (s, 3H), 2.47 (s, 3H), 3.79 (s, 3H). IR(neat) 2940, 1710, 1580, 1080 cm^{-1} **8**; ^{1}H NMR(CDCl$_3$) δ 0.78-1.04 (m, 3H), 1.04-1.50 (m, 6H), 1.70-2.04 (m, 3H), 2.14 (s, 3H), 2.52 (s, 3H), 3.81 (s, 3H), 4.65 (t, J=7.0 Hz, 1H). IR(neat) 2950, 1700, 1630, 860 cm^{-1} **9**; ^{1}H NMR(CDCl$_3$) δ 1.44 (d, J=6.4 Hz, 3H), 1.47 (d, J=6.4 Hz, 3H), 2.33 (s, 3H), 4.95-5.04 (m, 1H), 5.08-5.40 (m, 2H). IR(neat) 2940, 1705, 1640, 895, 850 cm^{-1} **10**; ^{1}H NMR(CDCl$_3$) δ 1.82 (dd, J=6.6, 1.7 Hz, 3H), 2.58 (s, 3H), 3.84 (s, 3H), 5.92 (dq, J=16.0, 6.4 Hz, 1H), 6.48 (dq, J=16.0, 1.54 Hz, 1H), 7.29-7.50 (m, 3H), 7.60-7.76 (m, 2H). IR(neat) 2950, 1720, 1610, 790 cm^{-1} **11**; ^{1}H NMR(CDCl$_3$) δ 0.70-1.08 (m, 6H), 1.08-1.50 (m, 14H), 2.00-2.30 (m, 2H), 2.49 (s, 3H) 2.40-2.70 (m, 2H), 3.80 (s, 3H), 5.69 (dt, J=15.8, 6.6 Hz, 1H), 6.41 (d, J=15.8 Hz, 1H). IR(neat) 2950, 1620, 1580, cm^{-1} **12**; ^{1}H NMR(CDCl$_3$) δ 0.70-1.08 (m, 6H), 1.08-1.75 (m, 14H), 1.75-1.85 (m, 4H), 2.33 (s, 3H), 4.85-5.00 (br, 1H), 5.00-5.24 (br, 2H). IR(neat) 2950, 1720, 1640 cm^{-1} **14**; ^{1}H NMR(CDCl$_3$) δ 1.34 (t, J=7.0 Hz, 3H), 2.05 (s, 3H), 2.16 (s, 3H), 2.49 (s, 3H), 2.27 (q, J=7.0 Hz, 2H). IR(neat) 2970, 1710, 1640, 1210, 1080, 780, 740 cm^{-1} **16**; ^{1}H NMR(CDCl$_3$) δ 0.88 (t, J=5.5 Hz, 3H), 1.10-1.80 (m, 8H), 2.05 (d, J=0.9 Hz, 3H), 2.16 (s, 3H), 2.89 (t, J=7.0 Hz, 2H), 3.80 (s, 3H). IR(neat) 2900, 1720, 1640, 1210, 1080, 780 cm^{-1}

(Received in Japan 6 September 1986)