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A NEW SYNTHESIS OF trans-2-SUBSTITUTED-2-BUTENE-1,4-DIOLS FROM 2-BUTYNE-1,4-DIOL VIA NUCLEOPHILIC ADDITION OF GRIGNARD REAGENTS

Yoshio ISHINO,* Kohji WAKAMOTO, and Tsuneaki HIRASHIMA

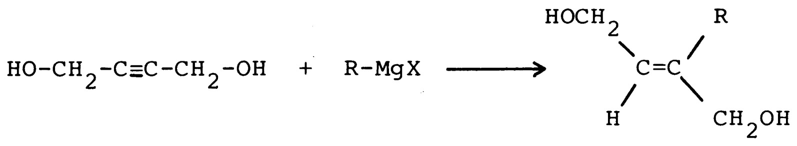
Osaka Municipal Techinical Research Institute, 1-6-50, Morinomiya,
Joto-ku, Osaka 536

trans-2-Substituted-2-butene-1,4-diols were readily obtained by reactions of 2-butyne-1,4-diol with Grignard reagents in good yields.

2-Butyne-1,4-diol (1), easily prepared by the reaction of acetylene with formaldehyde in a commercial scale, may be one of the most potential raw materials in organic synthesis and industrial utilization.$^{1)}$

We have already reported facile syntheses of 2,3-diaryl-1,3-butadienes,$^{2)}$ 2-acyloxy-2-butenes,$^{3)}$ and 3,4-di(methylene)hexanedioic esters$^{4)}$ starting from 1.

In the present communication, we describe a new and convenient synthesis of 2-substituted-2-butene-1,4-diol derivatives (3) via nucleophilic addition of Grignard reagents to 1.



$HO-CH_2-C\equiv C-CH_2-OH + R-MgX \longrightarrow (HOCH_2)(H)C=C(R)(CH_2OH)$

1 2 3

A few synthetic methods for 3 have been reported.$^{5)}$ The present reaction provides a new entry to synthesis of 2-butene-1,4-diols which are very important intermediates for organic synthesis and chemical industry because of their much availability and interesting reactivity.$^{1)}$ This is also the first and interesting example of alkylation of acetylenic diols by Grignard reagents.

A typical procedure is as follows; To a solution of 0.04 mol of p-chlorophenylmagnesium bromide in 150 ml of anhydrous ether was added 0.01 mol of 1 in 20 ml of anhydrous tetrahydrofuran dropwise at room temperature with vigorous stirring under a nitrogen atmosphere, and the resulting mixture was stirred for 30 min, and then refluxed for 2 h. After usual workup of the mixture, 2-(p-chlorophenyl)-2-butene-1,4-diol (3d) was isolated in an 85% yield by silica gel column chromatography.

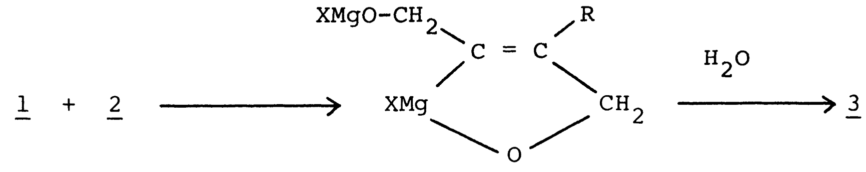
Under similar conditions, the addition of a variety of Grignard reagents to 1 easily took place to give the corresponding 3 in good yields (Table 1). Whereas cuprous halides are known as catalyst for the reaction of Grignard reagents with primary α-acetylenic alcohols,6) treatment of 1 with CuI/Grignard reagent gave only 3 in poor yields (ca. 20-30%). Also as is shown in Table 1, secondary and tertiary bromides(3k,l) could not give preferable yield of 3.

Table 1. The Reaction of 1 with 2

	R in 3	Yield/% a)	Mp θ_m/°C b)	^{1}H-NMR(δ , ppm) c)
a	p-$MeOC_6H_4$	72	93-95	1.88(s, 2H), 3.81(s, 3H), 4.13(d J=7.2 Hz , 2H), 4.32(s, 2H), 5.90(t J=6.5 Hz , 1H), 6.93(m, 4H)
b	p-MeC_6H_4	60	76-81	1.79(s, 2H), 2.36(s, 3H), 4.13(d J=8.0 Hz , 2H), 4.35(s, 2H), 5.91(m, 1H), 7.11(m, 4H)
c	C_6H_5	50	oil	1.92(s, 2H), 4.17(d J=7.2 Hz , 2H), 4.36(d J=1.7 Hz , 2H), 5.95(m, 1H), 7.31(m, 5H)
d	p-ClC_6H_4 d)	85	71-76	4.00(m, 2H), 4.25(m, 2H), 4.83(s, 2H), 5.92(m, 1H), 7.30(m, 4H)
e	p-FC_6H_4	59	oil	2.55(s, 2H), 4.07(d J=8.0 Hz , 2H), 4.11(s, 2H), 5.93(m, 1H), 7.10(m, 4H)
f	α-$C_{10}H_7$	98	oil	1.56(s, 2H), 3.90(d J=6.8 Hz , 2H), 4.40(s, 2H), 6.24(m, 1H), 7.50(m, 7H)
g	$C_6H_5C{=}C$ d)	48	83-92	4.25(m, 4H), 4.80(s, 2H), 6.13(m, 1H), 7.34(m,5H)
h	$C_6H_5CH_2$	33	oil	3.44(s, 4H), 3.93(s, 2H), 4.26(d J=9.0 Hz , 2H), 5.71(t J=3.0 Hz , 1H), 7,19(m, 5H)
i	C_2H_5	40	oil	0.99(t J=7.2 , 3H), 2.15(m, 4H), 4.15(m, 4H), 5.60(t J=6.5 Hz , 1H)
j	n-C_3H_7	97	oil	0.88(t J=8.0 Hz ,3H), 1.39(m, 2H), 2.06(t J=9.0 Hz, 2H), 3.02(s, 2H), 4.15(m, 4H), 5.65(t J=6.5 Hz, 1H)
k	sec-C_4H_9	37	oil	1.10(m, 8H), 2.47(m, 3H), 4.18(m, 4H), 5.71(t J=6.5 Hz , 1H)
l	tert-C_5H_{11}	0	---	---------------------
m	n-C_6H_{13}	59	49-52	0.80(t J=8.1Hz , 3H), 1.26(s, 8H), 2.07(t J=6.5 Hz, 2H), 2.98(s, 2H), 4.03(s, 2H), 4.17(d J=5.6 Hz, 2H), 5.61(t J=6.1 Hz , 1H)
n	n-C_8H_{17}	77	58-62	0.88(t J=6.5 Hz ,3H), 1.26(s, 12H), 1.94(m, 2H), 4.05(s, 2H), 4.20(d J=8.0 Hz , 2H), 5.65(t J= 7.0 Hz, 1H)
o	$CH_2{=}CHCH_2$	26	oil	2.16(s, 2H), 2.86(d J=7.0 Hz , 2H), 4.25(m, 4H), 5.13(m, 2H), 5.74(m, 2H)
p	cyclo-C_6H_{11}	33	oil	1.45(m, 11H), 2.40(s, 2H), 4.15(m, 4H), 5.58(t J=6.1 Hz , 1H)

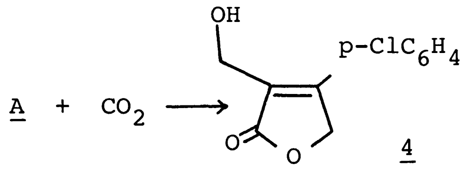
a) Isolated yield. b) Uncorrected melting points. c) $CDCl_3$ as solvent, unless otherwise stated. d) CD_3OD as solvent.

The trans geometry of 3 was confirmed by ^{1}H-NMR spectrum [7] and GLC,[9] and the reactivity of 3.[10] No cis isomers were formed. These results indicate that the addition of Grignard reagents to acetylene bond occurs in an anti-addition manner. In analogy with the mechanism proposed for the conventional addition of organomagnesium reagents to acetylenic alcohols,[11] we assume that the reaction proceeds via the initial formation of the organomagnesium intermediate A by anti-addition of Grignard reagents to 1 followed by hydrolysis to give 3.



A

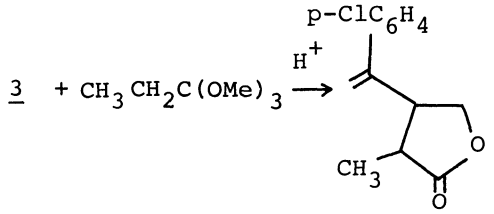
As further application of 3 to organic synthesis, we examined the reaction of A with the reagents such as carbon dioxide,[12] orthoesters,[4,13] and Fetizon's reagent[14] (or NaBrO$_2$[15]) to give the three types of interesting γ-butyrolactones as shown below.



4

Y ; 50%, $\nu_{C=O}$; 1720 cm^{-1}

^{1}H NMR(δ , ppm)
4.40(s, 2H), 4.73(s, 1H)
5.20(s, 1H), 7.59(m, 4H)

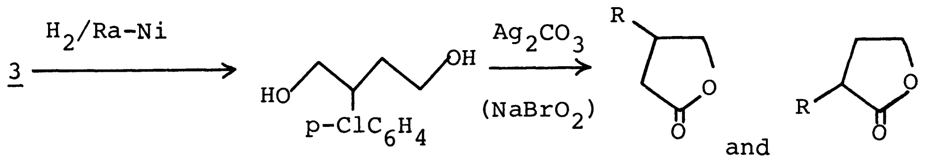


5

Y ; 67%

$\nu_{C=O}$; 1775 cm^{-1}

0.80(d J=7.5 Hz, 3H),
2.85(m, 1H), 3.95(m, 1H)
4.50(m, 2H), 5.09(d J=
1.1 Hz, 1H), 5.55(s, 1H)



6 (R = p-ClC$_6$H$_4$)

Y ; 95%

$\nu_{C=O}$; 1770 cm^{-1}

2.75(m,2H), 3.70(m, 1H)
3.70(m, 1H), 4.40(m, 2H)
7.20(m, 4H)

Therefore it is concluded that the present one-pot synthesis of 2-substituted-2-butene-1,4-diols may possess high potentiality in organic and industrial chemistry in terms of good yield, considerably wide generality, simple procedure and successful transformation of the industrial raw material to a variety of highly useful products.

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7) The trans olefinic protons of 3 to the aryl or alkyl function are estimated by additive rule to appear at approximately 5.83 and 5.86 ppm,[8)] (cis-form: 6.25 and 5.86 ppm). These values are in good agreement with the observed values.

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9) GLC conditions are as follows; column OV-1 1.5 m, column temp ca. 170 °C, carrier gas N_2.

10) Lactones(4) could be prepared by the reaction of A with carbon dioxide. Also, 2-butene-1,4-diols(3) did not react with alkyl aldehydes. In the case of cis-2-butene-1,4-diol, however, 1,3-dioxolane derivatives were given by the reaction with aldehydes in good yields.

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12) Carbon dioxide gas was bubbled into the mixture of A.

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