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Convenient synthesis of aryl substituted 3-hexene-1,5-diynes

Kakuzo Isagawa,[a] Kazuhiko Mizuno[b] and Tetsuro Majima[a,*]
[a]*The Institute of Scientific and Industrial Research, Osaka University, Mihogaoka 8-1, Ibaraki, Osaka 567-0047, Japan*
[b]*Department of Applied Chemistry, College of Engineering, Osaka Prefecture University, 1-1 Gakuencho, Sakai, Osaka 599-8531, Japan*

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Abstract

Dimerization of alkynyl carbenes generated from the reaction of 1,1-dibromo-2,3-diarylcyclopropanes (aryl=phenyl, 4-methylphenyl, 4-chlorophenyl) with a strong base under phase-transfer conditions occurs to give *E*- and *Z*-1,3,4,6-tetraaryl-3-hexene-1,5-diynes with 1:1 ratio in high yields at ambient temperature. On the other hand, the similar reaction of 1,1-dibromo-2,3-di-(4-methoxy)phenylcyclopropane gave 4,4′-dimethoxychalcone.

Keywords: enediynes; carbenes; dibromocyclopropanes; phase transfer catalysts.

Enediyne derivatives are known as the noteworthy compounds to give 1,4-biradical intermediates in the Bergman cyclizations.[1] Attempts to synthesize some natural antitumor antibiotics containing enediyne functional groups have been recently reported.[2] A variety of enediyne derivatives has been synthesized by the Pd catalyzed reactions of haloalkenes with alkynes or intermolecular coupling–elimination of propargyl halides.[3]

It is well known that carbenes dimerize to give olefins.[4,5] This reaction can be applicable to synthesis of enediyne derivatives from ethynylcarbenes[5,6] with various substituents. We have reported that reactions of 2-substituted and 2,2-disubstituted 1,1-dibromocyclopropanes with a strong base occurs to generate carbenes as the intermediates.[7] Judging from the reaction mechanism, carbenes with an acetylene group are supposed to be generated as the intermediate in the similar reactions of 2,3-disubstituted 1,1-dibromocyclopropanes with a strong base, of which dimerization occurs to form enediyne derivatives.

Reactions of 1,1-dibromo-2,3-diarylcyclopropanes **1** with a strong base under phase-transfer conditions have been performed to give *E*- and *Z*-1,3,4,6-tetraaryl-3-hexene-1,5-diynes **2** with 1:1 ratio in high yields. A mixture of Bu_4NHSO_4 and aqueous 50% NaOH were added to a toluene solution containing **1a** (Ar=phenyl). The mixture was vigorously stirred at ambient temperature. The purified products were obtained by a column chromatography and fractional crystallization. The reaction is presumed to proceed

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[*] Corresponding author. Fax: +81 6 6879 8499; e-mail: majima@sanken.osaka-u.ac.jp

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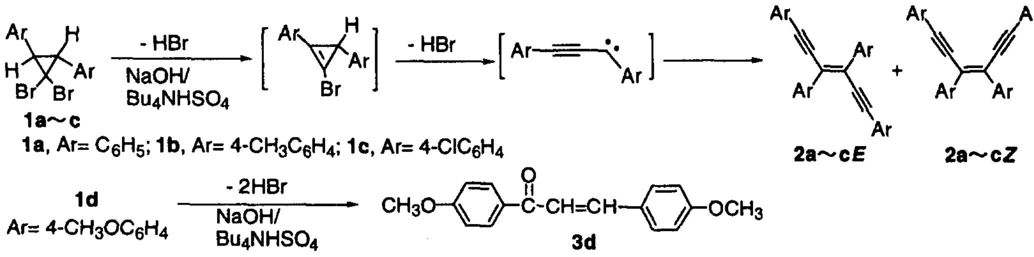
via the dimerization of two phenyl(ethynylphenyl)methylene carbenes generated from two sequential dehydrobrominations and ring opening at the C2–C3 bond of **1a** (Scheme 1).



Scheme 1.

The syntheses of several enediyne derivatives of **2*E*** and **2*Z*** with substituents such as 4-methyl, 4-chloro, and 4-methoxyl were attempted by the similar reactions of the corresponding 1,1-dibromo-2,3-diarylcyclopropanes (**1b**, **1c** and **1d**, respectively). The 4-methyl and 4-chloro derivatives **2b** and **2c** were obtained in good yields. However, the 4-methoxyl derivative **2d** was not obtained but 4,4′-dimethoxychalcone **3d** formed (Scheme 1). The structures of **2*E*** and **2*Z*** were confirmed by their elemental analyses and spectral properties. The reaction conditions, isolated yields, ratio of **2*E***:**2*Z***, and ^{13}C NMR data were summarized in Table 1.

Table 1
Reaction conditions and results in preparation of **2** from **1**

1	Ar	Reaction condn.		Total yield/%	Ratio of **2*E***:**2*Z***	^{13}C NMR of C≡C/δ in $CDCl_3$	
		Temp./°C	Time/h			**2*E***	**2*Z***
1a	C_6H_5	25	2	83	51:49	90.86, 98.47	91.74, 96.80
1b	$4\text{-}CH_3C_6H_4$	25	2	83	54:46	90.73, 98.34	91.57, 96.53
1c	$4\text{-}ClC_6H_4$	25	0.2	68	44:56	90.72, 98.05	94.28, 96.31
1d	$4\text{-}CH_3OC_6H_4$	30	2.5	0[a]	—	—	—

[a] 4,4'-Dimethoxychalcone **3d** was obtained in 24% yield as the main product in the reaction of **1d**.

The present reaction has been found to be a convenient method for synthesis of **2*E*** and **2*Z*** from **1** by the mild conditions, and can be applicable to the synthesis of enediyne derivatives with aryl groups. This is the first study to synthesize new enediyne derivatives **2*E*** and **2*Z*** from the two sequential dehydrobrominations and ring opening of **1**.

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