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Synthesis of naphtho[*b*]cyclobutenes from 1,2-bis(3-propynol)benzenes

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Abstract—We have demonstrated that the reaction of benzene-bridged bis(propargyl alcohol)s with chlorodialkylphosphines exclusively afforded 3,8-bis(dialkylphosphinyl)naphtho[*b*]cyclobutenes via the [2+2] cycloaddition of 1,2-bis(α-phosphinylallenyl)-benzenes. Dephosphinylation of the product has also been achieved.

Recent efforts from this laboratory disclosed the novel one-pot synthesis of the polycyclic aromatic compounds based on the sequential pericyclic reaction of the ene-bis(sulfinylallene) intermediates **3**,[1] derived from the ene-bis(propargyl alcohol) **1** and benzenesulfenyl chloride (PhSCl) via the ene-bis(propargyl sulfenate) **2**. Thus, the consecutive sequences, which entirely involves the sulfenic ester formation (first step), dual [2,3]-sigmatropic rearrangement of **2** (second step), 6π-electrocyclic reaction of ene-diallenes **3** (third step), and intramolecular [4+2] cycloaddition of *o*-quinodimethanes **4** (fourth step), enabled the one-pot construction of the polycyclic compounds **5** from **1** (Scheme 1). The intermolecular version of this methodology was also realized as exemplified by the conversion of **6** into the tetrahydroanthracene derivative **8**.

In the course of our studies on further development of the above procedure, we investigated the pericyclic reaction of the ene-bis(phosphinylallene) instead of the ene-bis(sulfinylallene). This letter describes the unexpected reactivity of the ene-bis(phosphinylallene), which led to the exclusive construction of the naphtho[*b*]cyclobutenes, useful molecules for Diels–Alder reaction or other transformations.[2]

According to the procedure for the reaction with PhSCl,[1,3] chlorodiphenylphosphine (Ph_2PCl), to the solution of benzene-bridged bis(propargyl alcohol) **6**, triethylamine, and dimethyl fumarate (as a dienophile) was added in THF at −78 °C, and the resulting mixture was warmed to room temperature. Despite the similarity in electronic nature between phosphinyl and sulfinyl groups,[4] the isolated product from the reaction mixture was not the expected cycloadduct **10a**, but the naphtho[*b*]cyclobutene **9a**[5] in a high yield (Scheme 2). This result obviously indicated that a dienophile did not take part in the formation of **9a**. Thus, the ring-closing reaction using PhSCl and other chlorophosphines *in the absence of* the dienophile became the next subject (Table 1).

The reactions with PhSCl and diethyl chlorophosphite [$(EtO)_2PCl$] under the standard conditions resulted in the complex mixtures of products (entries 5 and 6). In contrast to these results, the reactions with chlorodialkylphosphines exclusively afforded the corresponding 3,8-bis(dialkylphosphinyl)naphtho[*b*]cyclobutenes **9a–d** in high yields, regardless of the bulkiness of the alkyl groups on phosphorus atom (entries 1–4).[6] A full mechanistic discussion is premature at this point, but it might be rationalized that the bis(phosphinylallene) **11**, derived from the bis(propargyl phosphinite) by dual [2,3]-sigmatropic rearrangement,[3,7] would be converted into the biradical (*o*-quinodimethane) species **12**, which subsequently undergo intramolecular [2+2] cycloaddition to produce **9** (Scheme 3). Although there are several precedents that the *o*-quinodimethanes, possessing the

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Keywords: Bisallenes; [2+2] Cycloaddition; Naphtho[*b*]cyclobutenes; Dephosphinylation.

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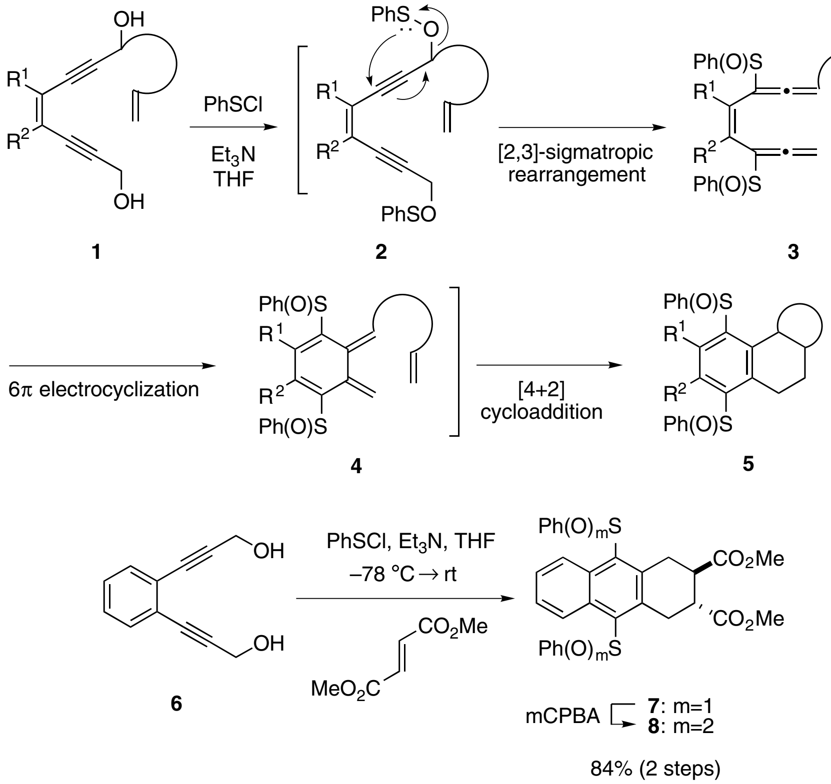
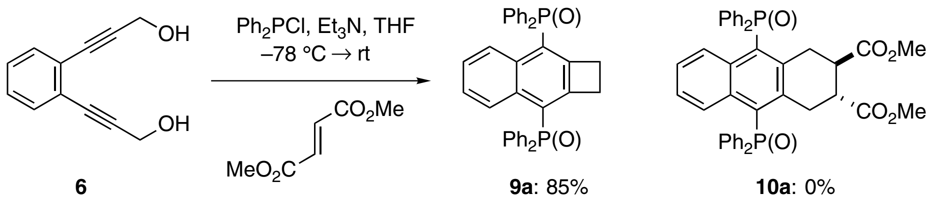


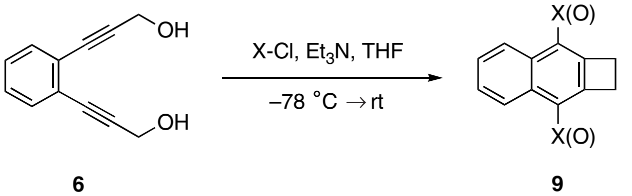
Scheme 1. Construction of polycyclic skeleton based on ene-diallene formation.



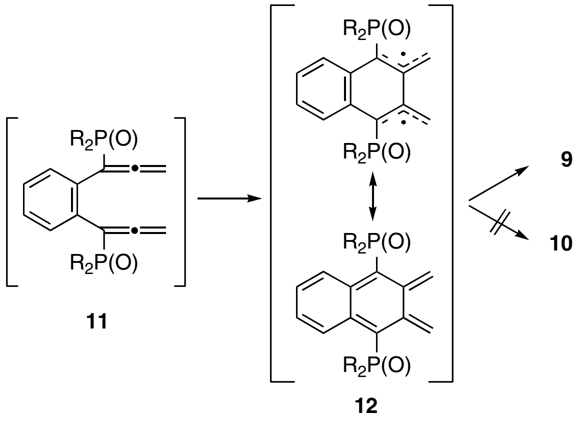
Scheme 2.

highly substituted exo-methylene unit, are subjected to [2+2] cycloaddition (or [1,5] hydrogen shift) rather than [4+2] cycloaddition with dienophiles,[8,9] the exclusive [2+2] cycloaddition of unsubstituted ones is rare to the best of our knowledge. Of particular interest is that the reaction mode of the intermediacy of the quinodimethanes is completely controlled by the nature of the substituents on the benzene ring (phosphinyl vs sulfinyl). The fact that $(EtO)_2PCl$ could not provide the cyclobutene derivative might be due to the comparatively low reactivity of the propargylic ester (e.g., first step in Scheme 1) for [2,3]-sigmatropic rearrangement.[3]

Table 1. Synthesis of naphtho[*b*]cyclobutene **9**



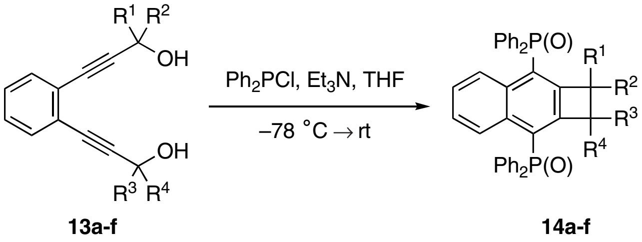
Entry	X	Product	Yield (%)
1	Ph_2P	**9a**	85
2	Cy_2P	**9b**	98
3	$(i\text{-}Pr_2)P$	**9c**	81
4	Et_2P	**9d**	99
5	$(EtO)_2P$	**9e**	0
6	PhS	**9f**	0



Scheme 3.

Having identified the effectiveness of the phosphinyl group on the [2+2] cycloaddition, we then investigated the synthesis of naphtho[*b*]cyclobutenes possessing some substituents on the cyclobutene ring.[10] The results are summarized in Table 2. Mono-, 1,2-di-, and 1,1-disubstituted naphtho[*b*]cyclobutenes **14a–e** were obtained from substituted bis(propargyl alcohol)s **13a–e** in high yields. However, fully methyl-substituted bis(propargyl alcohol) **13f** afforded hydrogen-shifted product **15** as the sole isolable product.

Table 2. Synthesis of naphtho[*b*]cyclobutene **14**

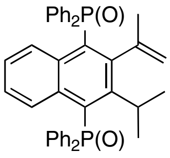


Entry	Substrate	R^1	R^2	R^3	R^4	Yield (%)
1	**13a**	Me	H	H	H	84
2	**13b**	CH_2OBn	H	H	H	90
3	**13c**	Me	H	Me	H	84[a]
4	**13d**	Ph	H	Ph	H	87[b]
5	**13e**	Me	Me	H	H	86
6	**13f**	Me	Me	Me	Me	0[c]

[a] Diastereomer ratio = 3:2. The relative configuration at two isomers was not determined.

[b] Diastereomer ratio = 2:1. The relative configuration at two isomers was not determined.

[c] Compound **15** was obtained in 61% yield.



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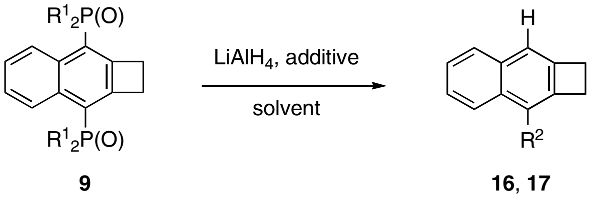
The next phase of this program was to search the conditions for the removal of the phosphinyl moiety on the naphthalene ring. The reaction of the naphtho[*b*]cyclobutene derivative **9a** with $LiAlH_4$[11] under refluxing conditions was screened (Table 3). As a result, 1,4-dioxane[12] was found to effectively provide the bisdephosphinylated naphtho[*b*]cyclobutene **16**[13] (entries 1 and 2).[14] A similar result was obtained when refluxed in THF (entry 3). Although the $LiAlH_4$ reduction in a mixed solvent of butyl ether and benzene (1:1) was reported to be effective for the conversion of triphenylphosphine oxide to triphenylphosphine,[15] the transformation of **9a** into **16** could not be realized (entry 4). The isopropyl derivative **9c** underwent the similar bisdephosphinylation to furnish **16** in a lower yield (entry 8). Alternatively, a selective monodephosphinylation of **9a** was achieved by treatment with $LiAlH_4$–metal halide systems as shown in entries 5–7. The best result was obtained when **9a** was exposed to $LiAlH_4$–$TiCl_4$[16] in THF at room temperature to give 3-(diphenylphosphinyl)naphtho[*b*]cyclobutene (**17a**) in 88% yield (entry 5). The application of these conditions to **9c** afforded **17c** in 79% yield (entry 9). $LiAlH_4$–$CuCl_2$[17] and $LiAlH_4$–$NiCl_2$[18] in refluxing THF were also effective in this conversion (entries 6 and 7). In addition, reaction of the dimethyl congener, 1,2-dimethylnaphtho[*b*]cyclobutene **14c**, with $LiAlH_4$ in refluxing dioxane gave **18** in 52% yield (Scheme 4).[19] The treatment of 1-methylnaphtho[*b*]cyclobutene **14a** with $LiAlH_4$–$TiCl_4$ furnished **19** and **20** in the yields of 40% and 40%, respectively.

In summary, we have developed a novel and general procedure for the construction of naphtho[*b*]cyclobutene derivatives from benzene-bridged bis(propargyl

Table 3. C–P bond cleavage of **9** with $LiAlH_4$

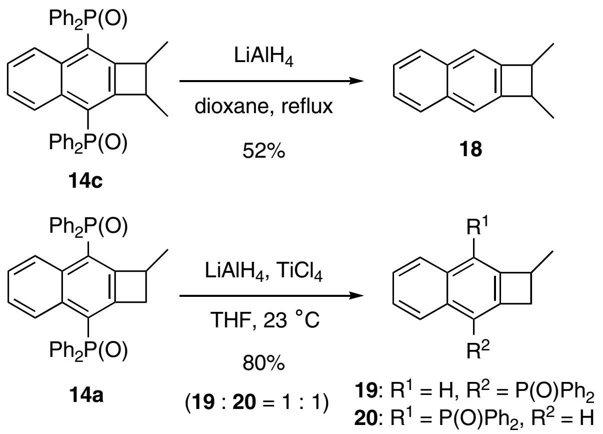


Entry	Substrate		Solvent	Additive	Temp (°C)	Time (h)	Product		
		R^1						R^2	Yield (%)
1	**9a**	Ph	Diglyme	None	162	5	**16**	H	50
2	**9a**	Ph	Dioxane	None	101	5	**16**	H	70
3	**9a**	Ph	THF	None	65	5	**16**	H	49
4	**9a**	Ph	Bu_2O/benzene[a]	None	100	5	**16**	H	0
5	**9a**	Ph	THF	$TiCl_4$[b]	23	1	**17a**	$P(O)Ph_2$	88
6	**9a**	Ph	THF	$CuCl_2$[b]	65	7	**17a**	$P(O)Ph_2$	68
7	**9a**	Ph	THF	$NiCl_2$[c]	65	2	**17a**	$P(O)Ph_2$	41
8	**9c**	*i*-Pr	Dioxane	None	101	7	**16**	H	41
9	**9c**	*i*-Pr	THF	$TiCl_4$	23	0.5	**17c**	$P(O)(i\text{-}Pr)_2$	79

[a] Volume ratio = 1:1.

[b] Molar ratio of $LiAlH_4$–metal halide = 2:1.

[c] Molar ratio of $LiAlH_4$–metal halide = 1:1.



Scheme 4.

alcohol)s via the consecutive pericyclic reactions, in which the 1,2-bis(α-phosphinylallenyl)benzenes effectively underwent the intramolecular [2+2] cycloaddition to give 3,8-diphosphinylnaphtho[*b*]cyclobutenes in sharp contrast to the case of the 1,2-bis(α-sulfinylallenyl)benzenes. The resulting phosphoryl groups on the naphthalene ring could be arbitrarily removed by proper choice of reducing conditions resulting in the selective preparation of monophosphinylated or dephosphinylated naphtho[*b*]cyclobutenes, the former of which may be useful as the precursors of new ligands or reagents. Studies on the reaction process of ene-bis(phosphinylallene) and related compounds are currently underway.

Acknowledgments

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14. Typical procedure: To a suspension of $LiAlH_4$ (45.5 mg, 1.20 mmol) in dioxane (3 mL), **9a** (165 mg, 0.300 mmol) was added at 0 °C, and the mixture was refluxed for 5 h. The mixture was cooled to room temperature and quenched by the addition of water. 10% aqueous HCl was added, and the mixture was extracted with AcOEt. The extract was washed with water and brine, dried over Na_2SO_4, and concentrated. Chromatography of the residue with hexane afforded **16** (32.3 mg, 70%) as a colorless solid.
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