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Regioselectivity

Chemo- and Regioselective Rhodium(I)-Catalyzed [2+2+2] Cycloaddition of Allenynes with Alkynes

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Abstract: A highly chemo- and regioselective partially intramolecular rhodium(I)-catalyzed [2+2+2] cycloaddition of allenynes with alkynes is described. A range of diverse polysubstituted benzene derivatives could be synthesized in good to excellent yields, in which the allenynes served as synthetic equivalent to the diynes. A high regioselectivity could be observed when allenynes were treated with unsymmetrical alkynes.

Introduction

The transition-metal-catalyzed [2+2+2] cycloaddition of alkynes[1] provides the most straightforward as well as a powerful methodology for the synthesis of polysubstituted benzene derivatives. It is well known that the cycloaddition of two or three different alkynes[2] generally suffers from a poor chemo- and/or regioselectivity. As one of the promising methods to solve such problems, intramolecular approaches employing tethered alkynes, diynes, or triynes, have been developed.[1] Although the partially intramolecular cycloaddition of diynes with the appropriate monoalkynes often led to a high chemoselectivity, the control of the regioselectivity still remains an unsolved issue upon utilizing unsymmetrical alkynes as an external π component.[1] Indeed, diynes **A** possessing a fairly bulky R such as trimethylsilyl group at an alkyne terminus underwent the [2+2+2] cycloaddition with unsymmetrical monoalkynes **B** to produce the cycloadducts **C** with high regioselectivity in many cases. The preferential formation of **C** over **C′** would be attributed to avoidance of the steric hindrance between a substituent of diyne **A** and that of **B** (Scheme 1).[3] This was, however, not the case in the reactions of **A** having a less bulky R with monoalkynes **B** resulting in nonregioselective production of **C** and **C′**.[4]

On the other hand, Cheng et al.[5a] reported a new and reliable procedure using the allene functionality instead of an alkyne as the external π component, in which the nickel catalysis worked well for the [2+2+2] cycloaddition between the diyne and allene groups, resulting in the formation of polysubstituted benzene derivatives in a highly chemo- and regioselective manner (Scheme 2). Our continuous interests in the field of rhodium(I)-catalyzed cycloadditions and cycloisomerizations of allene species with additional π components[6,7] prompted us to investigate the cycloaddition reaction between allenynes (allene–alkyne derivatives)[8] and alkynes. We now describe some promising results of the rhodium(I)-catalyzed partially intramolecular [2+2+2] cycloaddition of allenynes with alkynes[9–15] in which a variety of polysubstituted benzene derivatives could be synthesized in satisfactory yields and with high regioselectivity (Scheme 2).

Results and Discussion

Our initial attempt used the phenylsulfonylallene-alkyne **1a** for screening the reaction conditions. Treatment of **1a** and the symmetrical diester **2a** with 10 mol% of the $[Rh(cod)_2]BF_4$/BINAP complex,[16] in 1,2-dichloroethane at 60 °C for 1 h produced the tetrahydronaphthalene derivative **3aa** in 58% yield (Table 1, entry 1). Compound **3aa** must be formed through **4**, followed by aromatization. In the absence of BINAP, the reaction was less efficient and the yield decreased (Table 1, entry 2). $RhCl(PPh_3)_3$ with or without a silver salt afforded similar results (Table 1, entries 3 and 4). A neutral Rh^I complex, adjusted from $[RhCl(cod)]_2$ and BINAP, was found to be effective for our purpose providing **3aa** in a quantitative yield (Table 1, entry 5). The reaction without BINAP was very sluggish and the yield was rather low (Table 1, entry 6). Other biaryl biphosphine ligands, such as tol-BINAP, xyl-BINAP, Segphos, DTBM-Segphos, and BIPHEP, were screened and confirmed to be effective except for BIPHEP (Table 1, entries 7–11).

The best conditions (5 mol% $[RhCl(cod)]_2$ and 10 mol% BINAP in 1,2-dichloroethane at 60 °C)[17] were then used for the reaction of several allenynes and symmetrical alkynes (Table 2). The simple carbon tether analogue **1b** without the *gem*-disubstituent effect[18] was treated with **2a** to afford **3ba** in 84% yield (Table 2, entry 1). The nitrogen congener **1c** produced the aza-compound **3ca** in 98% yield (Table 2, entry 2).

A phenylsulfonyl substituent on the allenyl moiety was found not to be essential for this transformation. Indeed, both allenynes **1d** and **1e** produced **3da** (64%) and **3ea** (60%), respectively (Table 2, entries 3 and 4). These results indicate that the electron-withdrawing groups such as phenylsulfonyl, ethyl

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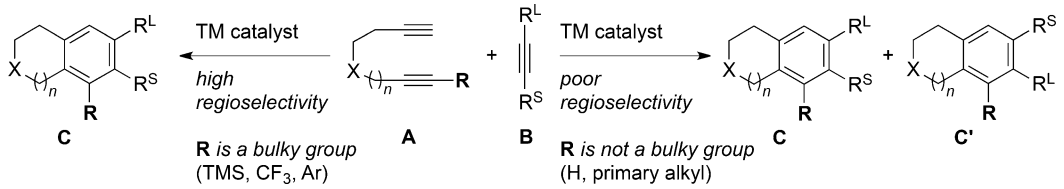
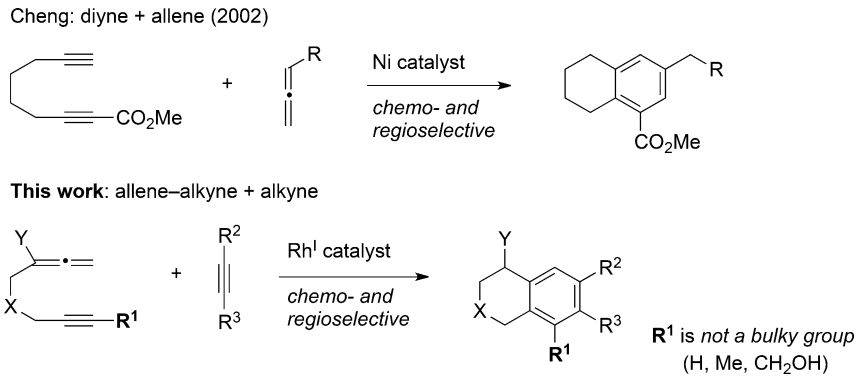
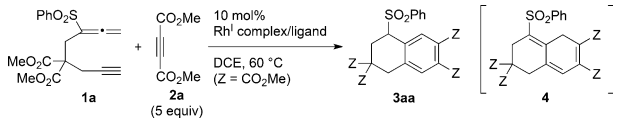


Scheme 1. Regioselectivity in transition-metal-catalyzed partially intramolecular [2+2+2] cycloaddition between unsymmetrical diyne and alkyne.



Scheme 2. Regioselective partially intramolecular [2+2+2] cycloaddition producing polysubstituted benzene derivative.

Table 1. Optimization of reaction conditions for rhodium(I)-catalyzed [2+2+2] cycloaddition of allenyne **1a** with alkyne **2a**.



Entry	Rh^{I} complex	Ligand	*t* [h]	Yield [%][a]
1	$[Rh(cod)_2]BF_4$	BINAP	1	58
2	$[Rh(cod)_2]BF_4$	–	1	44[b]
3	$RhCl(PPh_3)_3$	–	5	51
4[c]	$RhCl(PPh_3)_3$	–	5	62
5	$[RhCl(cod)]_2$	BINAP	0.5	99
6[d]	$[RhCl(cod)]_2$	–	6	45
7	$[RhCl(cod)]_2$	tol-BINAP	1	98
8	$[RhCl(cod)]_2$	xyl-BINAP	1	97
9	$[RhCl(cod)]_2$	Segphos	1	98
10	$[RhCl(cod)]_2$	DTBM-Segphos	1.5	83
11	$[RhCl(cod)]_2$	BIPHEP	24	45

[a] Yield of the isolated product. [b] Yield was determined by ^{1}H NMR analysis with $CHBr_3$ as the internal standard. [c] Reaction was carried out with 20 mol% $AgBF_4$ in benzene. [d] Heated at reflux in DCE. DCE = 1,2-dichloroethane; cod = 1,5-cyclooctadiene.

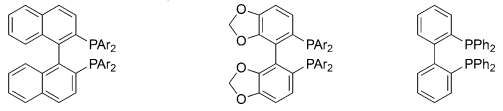
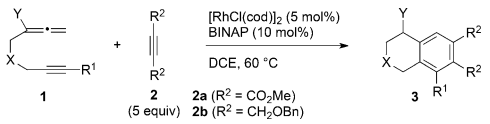


Table 2. Rhodium(I)-catalyzed [2+2+2] cycloaddition of allenyne **1** with alkyne **2**.



Entry	**1**	R^1	X	Y	**2**	*t* [h]	Yield [%][a]
1	**1b**	H	CH_2	SO_2Ph	**2a**	1.5	**3ba**: 84
2	**1c**	H	NTs	SO_2Ph	**2a**	0.5	**3ca**: 98
3	**1d**	H	$C(CO_2Me)_2$	CO_2Me	**2a**	1.5	**3da**: 64
4	**1e**	H	$C(CO_2Me)_2$	$P(O)(OEt)_2$	**2a**	2	**3ea**: 60
5	**1f**	H	$C(CO_2Me)_2$	Me	**2a**	0.2	–[b]
6[c]	**1g**	H	$C(CO_2Me)_2$	H	**2a**	7	–[b]
7[c]	**1h**	Me	$C(CO_2Me)_2$	SO_2Ph	**2a**	2.5	**3ha**: 72
8[c]	**1i**	CH_2OBn	$C(CO_2Me)_2$	SO_2Ph	**2a**	5.5	**3ia**: 64
9	**1a**	H	$C(CO_2Me)_2$	SO_2Ph	**2b**	7	**3ab**: 54

[a] Yield of the isolated product. [b] An intractable mixture was obtained. [c] Heated at reflux in 1,2-dichloroethane (DCE).

phosphonate, and methoxycarbonyl groups on the allenyl moiety served as a suitable substituent. We further examined the cycloaddition of two additional substrates **1f** (Y = Me) and **1g** (Y = H) to see the effect of the substituent on the allenyl moiety. Thus, the reaction of the methyl derivative **1f** and **2a** was carried out under the standard conditions to furnish an intractable mixture (Table 2, entry 5). The unsubstituted substrate **1g** (Y = H) also gave the similar result upon treating with **2a** (Table 2, entry 6). As a result, it might be concluded that the electron-withdrawing group is essential for this [2+2+2] cycloaddition. Although higher reaction temperatures were needed, the allene-internal alkynes **1h** and **1i** afforded the corresponding ring-closed products **3ha** (72%) and **3ia** (64%; Table 2, entries 7 and 8). Bis(benzyloxymethyl)acetylene (**2b**) was treated with **1a** to afford **3ab** in 54% yield (Table 2, entry 9). In sharp contrast to the result of the 1,1-disubstituted allenes **1a**–**1i**,

the allenyne **5** having a methyl group at the allenic terminus (1,1,3-trisubstituted allene) did not yield the desired product at all, but the benzene derivative **7** in 78% yield, which should have arisen from the cycloaddition between the alkyne moiety of **5** and two molecules of the external alkyne **2a** [Eq. (1)].

The rhodium(I)-catalyzed [2+2+2] cycloaddition of allenynes with unsymmetrical alkynes was the next subject (Table 3). Treatment of **1a** with ethyl phenylpropiolate (**8a**) under the standard conditions provided a mixture of two tetrahydronaphthalene derivatives **9aa**/**10aa** in 53% yield in the ratio of 62 to 38 (Table 3, entry 1).[19] The alkyl analogue **8b** showed a better reactivity and regioselectivity furnishing **9ab**/**10ab** (82:18 mixture) in 85% yield (Table 3, entry 2). The terminal alkynes **8c** and **8d** having ester functionality and simple alkyl group both reacted with **1a** to afford the cycloadducts **9ac**/**10ac** (84%, 87:13 mixture) and **9ad**/**10ad** (72%, 89:11 mixture), respectively (Table 3, entries 3 and 4). On the other hand, the reaction of the allene-internal alkyne substrate **1h** with **8b** produced a mixture of **9hb**/**10hb** in 88% NMR yield in a ratio of 88 to 12 (Table 3, entry 5 vs. entry 2),[20] a slightly better regioselectivity compared to that of **9ab**/**10ab** (82:18; Table 3, entry 2). Furthermore, the reaction of **1h** with **8c** smoothly proceeded to exclusively furnish **9hc** in 90% yield (Table 3, entry 6). Similarly, a high regioselectivity was observed in the reactions of **1h** (93:7), **1j** (91:9) with **8d** (Table 3, entries 7 and 8). Thus, the preferential production of **9** over **10** was consistently recorded. In particular, the results of entries 3, 4 and 6–8 (Table 3) obviously indicated that higher regioselectivity was attained with terminal alkynes.

It should be emphasized that the reverse regioselectivity was observed when the propargyl alcohol derivative **11a** was treated with **1a** to provide a mixture of **12aa**/**13aa** in 85% yield in the ratio of 91:9 (Scheme 3). The major product **12aa** has a benzyloxymethyl group at the *p*-position to the phenylsulfonylmethine residue. This is obviously different from the results in Table 3, in which cycloadducts having the substituent at the *m*-position to the phenylsulfonylmethine residue were consistently obtained as the major product. Furthermore, propargyl alcohol (**11b**) itself exhibited a similar behavior, exclusively forming **12ab** in 94% yield.

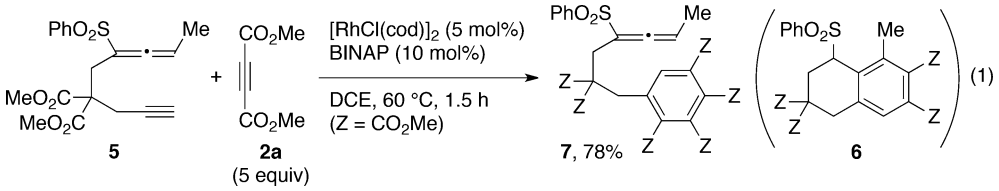
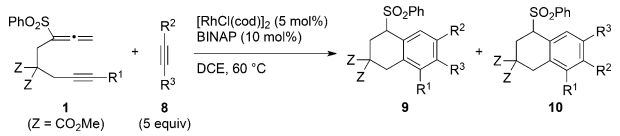
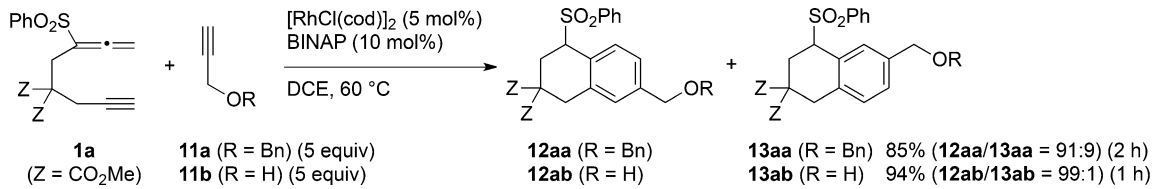


Table 3. Rhodium(I)-catalyzed [2+2+2] cycloaddition of allenyne **1** with unsymmetrical alkyne **8**.



Entry	**1**	R^1	**8**	R^2	R^3	*t* [h]	Yield [%] (**9**+**10**)[a]	Rs (**9**/**10**)[b]
1[c]	**1a**	H	**8a**	CO_2Et	Ph	11	53 (**9aa**+**10aa**)	62:38
2[c]	**1a**	H	**8b**	CO_2Et	Me	4	85 (**9ab**+**10ab**)	82:18
3	**1a**	H	**8c**	CO_2Me	H	1	84 (**9ac**+**10ac**)	87:13
4	**1a**	H	**8d**	*n*Bu	H	1.5	72 (**9ad**+**10ad**)	89:11
5[c]	**1h**	Me	**8b**	CO_2Et	Me	6	88 (**9hb**+**10hb**)[d]	88:12
6	**1h**	Me	**8c**	CO_2Me	H	0.5	90 (**9hc**)	**9hc** only
7	**1h**	Me	**8d**	*n*Bu	H	11	72 (**9hd**+**10hd**)	93:7
8[c]	**1j**	CH_2OH	**8d**	*n*Bu	H	7	70 (**9jd**+**10jd**)	91:9

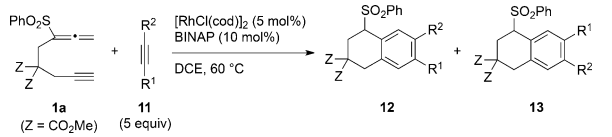
[a] Yield of the mixture of **9**+**10**. [b] Regioselectivity (Rs) determined by ^{1}H NMR analysis of the mixture of **9**+**10**. [c] Heated at reflux in DCE. [d] Yield was determined by ^{1}H NMR analysis with $CHBr_3$ as the internal standard.



Scheme 3. Rhodium(I)-catalyzed [2+2+2] cycloaddition of allenyne **1a** with propargyl alcohol (**11b**) and its derivative **11a**.

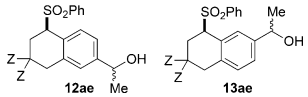
Several propargyl alcohol analogues were examined to determine the scope and limitations (Table 4). Treatment of **1a** with homopropargyl alcohol (**11c**) produced **12ac** in a highly regioselective manner (**12ac**/**13ac** = 94:6) and 90% yield (Table 4, entry 1). The two-carbon homologated substrate **11d** again regioselectively furnished **12ad** (**12ad**/**13ad** = 93:7; Table 4, entry 2). The secondary and tertiary propargyl alcohols **11e** and **11f** did not disturb the reaction and selectively produced the cyclized products **12ae**/**13ae** (96:4)[21] and **12af**/**13af** (83:17; Table 4, entries 3 and 4). Similarly, the exclusive production of the nitrogen analogue **12ag** was achieved in a quantitative yield (Table 4, entry 5). The reaction of 2-butyn-1-ol (**11h**) proceeded in line with the preferential formation of **12ah** over **13ah** (75:25), but a prolonged reaction time (4 h) was required and the selectivity decreased (Table 4, entry 6).

Table 4. Rhodium(I)-catalyzed [2+2+2] cycloaddition of allenyne **1a** with alkyne **11**.



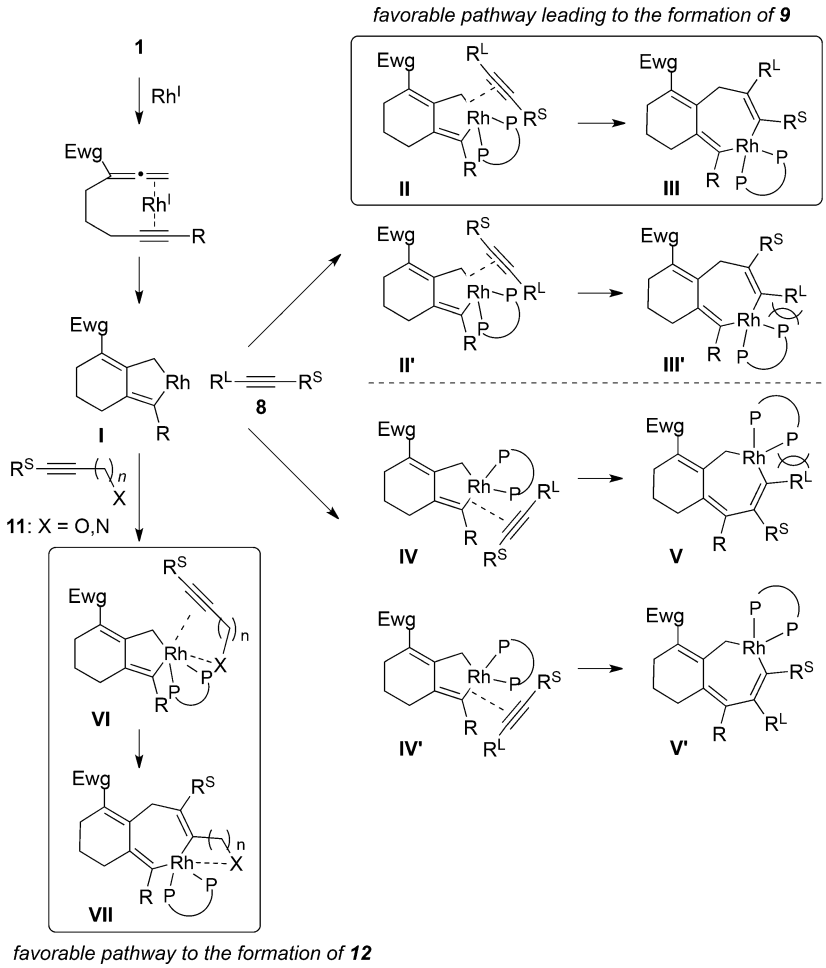
Entry	11	R^1	R^2	t [h]	Yield [%] (12 + 13)[a]	Rs (9/10)[b]
1	**11c**	$(CH_2)_2OH$	H	1	90 (**12ac** + **13ac**)	94:6
2	**11d**	$(CH_2)_3OH$	H	1	88 (**12ad** + **13ad**)	93:7
3	**11e**		H	1	95 (**12ae** + **13ae**)[c]	96:4
4	**11f**		H	1.5	86 (**12af** + **13af**)	83:17
5	**11g**	CH_2NHTs	H	1	quant. (**12ag**)	**12ag** only
6	**11h**	CH_2OH	Me	4	71 (**12ah** + **13ah**)	75:25

[a] Yield of the mixture of **12** + **13**. [b] Determined by ^{1}H NMR analysis of the mixture of **12** + **13**. [c] Compounds **12ae** and **13ae** were obtained as a 1:1 mixture of diastereomers.



The regioselectivity in the [2+2+2] cycloaddition of allenynes with unsymmetrical alkynes could be highly controlled by proper choice of alkynes (with or without a hydroxyl group). Treatment of **1** with unsymmetrical alkynes **8** without a hydroxyl functionality predominantly produced **9** (Table 3), whereas the reaction with unsymmetrical alkynes **11** having a hydroxyl group (e.g., propargyl alcohol) furnished **12** in a highly reverse regioselective manner (Scheme 3 and Table 4). We tentatively interpreted these experimental results based on the following plausible mechanism (Scheme 4). The reaction would initiate the formation of the rhodabicyclic intermediate **I**,[7e,f,j] which was postulated as a key intermediate in the most cases of our previous works.[7e,f,j] There might be two possible pathways for the following insertion process of the external alkyne **8**. One is the insertion into the C_{sp2}—Rh bond leading to the two intermediates **V** and **V′** and the other is the insertion into the C_{sp3}—Rh bond resulting in the formation of the two other intermediates **III** and **III′**. These four intermediates could subsequently collapse to the final tetrahydronaphthalenes through reductive elimination, followed by aromatization. If the reaction proceeded through the insertion of alkyne into the C_{sp3}—Rh bond, the observed complementary regioselectivity can be reasonably explained as follows. Alkyne derivatives **8** would approach to the C_{sp3}—Rh bond of the intermediate **I** in which sterically less hindered substituent (R^S) on the triple bond should be taken a place close to Rh atom (coordinating with biphosphine ligand) as described in **II** to avoid a nonbonding interaction resulting in the formation of the seven-membered rhodacycle **III**. Consecutive reductive elimination of **III** and aromatization would then lead to the formation of **9**. The opposite approach of **8** to the C_{sp3}—Rh bond of **I** (i.e., **II′**), however, would suffer from unfavorable steric repulsion between R^L and biphosphine ligand on Rh. As a result, the reaction pathway through the intermediates **II′** and **III′** must be the unfavorable and minor one, thereby the alternative reaction route through **II** and **III** would become more favored route. The situation must be drastically changed when alkyne derivatives **11** possessing hydroxyl functionality were used. Prior to direct insertion of the triple bond of **11** into the C_{sp3}—Rh bond of **I**, it is reasonable to consider coordination of Rh atom of **I** with hydroxyl functionality of **11** to form **VI**. Thus, the insertion of the triple bond of **11** would subsequently occur from the intermediate **VI** to afford the seven-membered rhodacycle **VII**. Finally, reductive elimination of **VII** was followed by aromatization to afford **12** in a highly regioselective manner. Although the possibility of the route that involves the intermediacy of **V** and **V′** through **IV** and **IV′**, respectively, cannot be completely ruled out, we now do not have good and clear explanation of the observed complementary regioselectivity. In the reaction of the trisubstituted allene species **5**, the formation of the desired tetrahydronaphthalene derivative **6** could not be observed. The benzene derivative **7** was obtained instead (see above). This result might be rationalized by considering that the key rhodabicyclic intermediate such as **I** could not be so easily formed because of the sterically congested trisubstituted allene functionality and the conventional [2+2+2] cycloaddition of three alkyne components preferentially occurred. The similar interpretation for the by-production of the benzene derivative **17′** can be made (see below). The formation of seven-membered ring is known to be more difficult than the six-membered one. Thus, the formation of seven-membered rhodabicyclic intermediate (one-carbon homologated **I**) was retarded in part and the desired allene-two alkynes [2+2+2] cycloaddition reaction became the minor pathway.

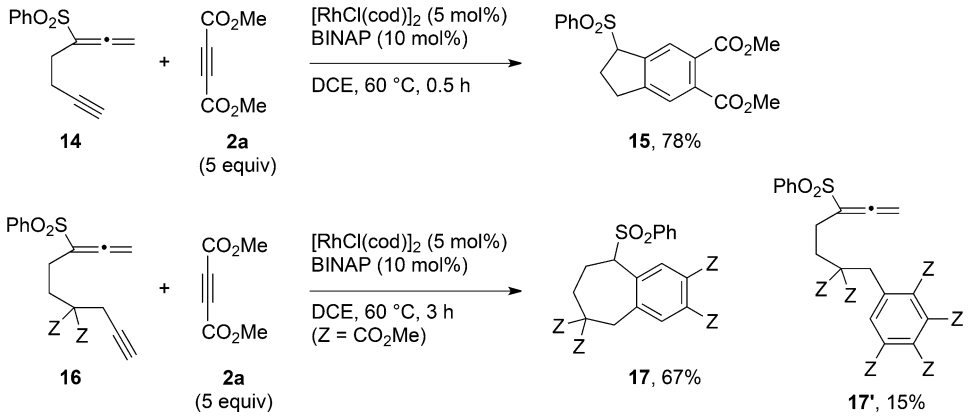
Some additional experiments were carried out to reveal the scope of this method (Scheme 5). Exposure of the one-carbon shortened substrate **14** and **2a** to the standard conditions provided the indane derivative **15** in 78% yield. Construction of the larger-sized **17** (67%) could also be attained along with the formation of the benzene derivative **17′** (15%), the latter of which should have been derived from the cycloaddition between **16** and two molecules of **2a**, similar to the formation of **7** from **5**.



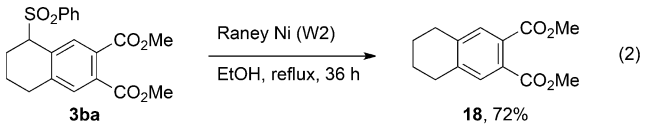
Scheme 4. Explanation for the observed regioselectivity on the basis of the plausible mechanism.

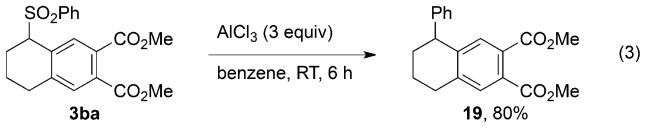
A phenylsulfonyl group can be easily removed by the conventional procedure[22] to afford **18** in 72% yield when compound **3ba** was exposed to Raney nickel in ethanol[22c] heated at reflux [Eq. (2)]. Exposure of **3ba** to Friedel–Crafts alkylation conditions in benzene effected substitution of a phenyl group for a phenylsulfonyl moiety to afford **19** in 80% yield [Eq. (3)].[23]

The allenynes could be regarded as the synthetic equivalent of the corresponding diynes (proton tautomer of propargyl moiety). As indicated in Table 4, the ring-closing reactions of allenynes with propargyl alcohol derivatives proceeded in a highly regioselective manner to produce the tetrahydronaphthalene derivatives **12**. It would be of particular interest from a synthetic point of view to see how the reaction proceeds



Scheme 5. Synthesis of indane derivative **15** and benzocycloheptane derivative **17**.





with diynes instead of allenynes. Thus, the reaction of the allenyne **20** with propargyl alcohol (**11b**) under the standard conditions furnished **21** in a highly regioselective manner (**21**/**22** = 93:7) and 92% yield, which was then transformed into the desulfonylated one **25** in 69% yield (59% overall yield from **20**; Scheme 6). Similar treatment of the corresponding diyne **27** with **11b** in the presence of H_8-BINAP[16] nonregioselectively produced a mixture of **25** and its regioisomer **28** (**25**/**28** = 50:50) in 93% yield. Another control experiment using ester-substituted alkyne **8c** instead of **11b** was conducted. Treatment of **20** with **8c** resulted in the preferential formation of **24** over **23** (87%, **23**/**24** = 24:76), which was subsequently desulfonylated to afford **26** in 72% yield (48% overall yield from **20**). On the other hand, treatment of **27** with **8c** provided a 1:1 mixture of **29** and **26** in 66% yield. These experiments would strongly indicate the superiority of the allenyne instead of the diyne in terms of regioselectivity.

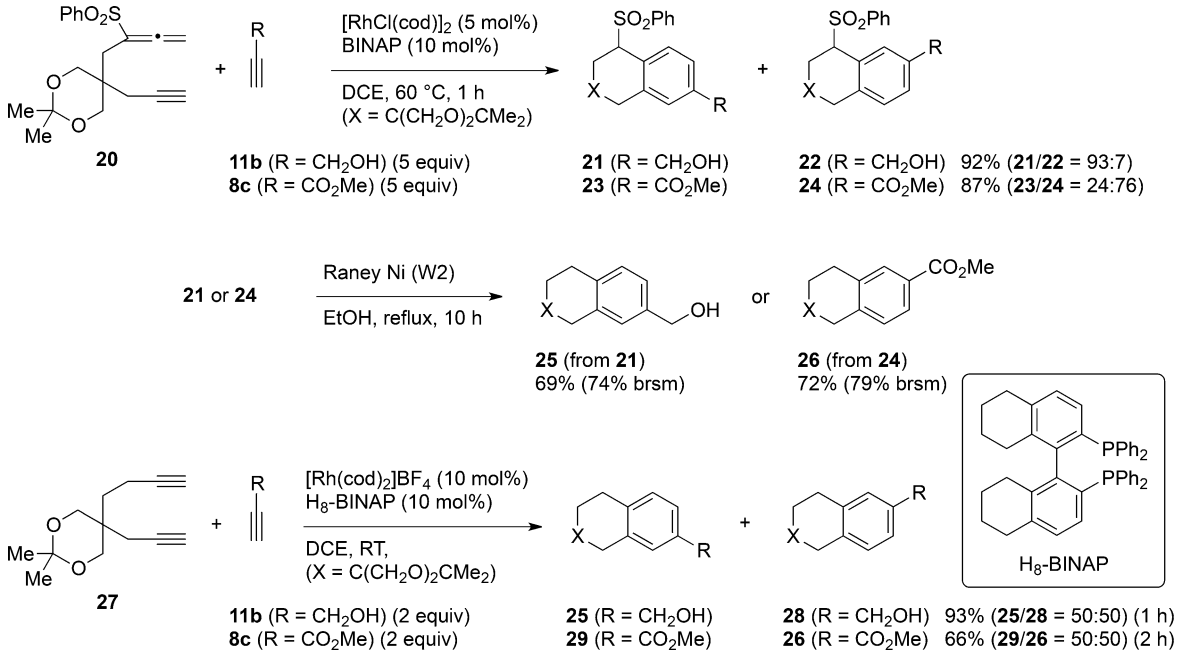
Conclusions

We have developed a highly chemo- and regioselective new type of [2+2+2] cycloaddition of allenynes with alkynes leading to the efficient formation of polysubstituted benzene-fused bicyclic derivatives. The combination of allenynes with alkynes, especially with propargylic alcohols, was found to produce the desired products with an excellent regioselectivity as well as high chemical yields. This is not the case of the corresponding diyne, a synthetic equivalent of the allenyne, affording the tetrahydronaphthalenes in a high yield but in a nonregioselective way. Thus, we could demonstrate the superiority of the allenyne in place of the diyne as the π component in the [2+2+2] cycloaddition. We are currently investigating the scope and limitations of this method as well as the development of other [2+2+2] cycloadditions utilizing allene species.

Experimental Section

General methods

Melting points were measured with YANAGIMOTO micro melting point apparatus, and are uncorrected. Infrared spectra were measured with a SHIMADZU FTIR-8700 spectrometer for samples in $CHCl_3$. ^1H NMR spectra were measured with JNM-ECS400 or JNM-ECA600 spectrometers for samples in [D]-chloroform ($CDCl_3$), using either tetramethylsilane (for compound with a phenyl group, δ = 0.00 ppm), $CHCl_3$ (δ = 7.26 ppm) as an internal reference. ^{13}C NMR spectra were measured with JNM-ECS400 or JNM-ECA600 spectrometers for samples in $CDCl_3$ (δ = 77.0 ppm) as an internal reference. High-resolution mass spectra were measured with JMS-T100TD (DART) mass spectrometers, and mass spectra were measured with JMS-T100TD (DART) mass spectrometers. Commercially available $[RhCl(cod)]_2$ (Kanto Chemical) and $[Rh(cod)_2]BF_4$ (Wako Pure Chemical Industry) were employed for reactions. Silica gel (Silica gel 60 N, 40–50 μm, Kanto Chemical) was used for chromatography. All reactions were carried out under N_2 atmosphere. Organic extracts were dried over Na_2SO_4. Synthetic procedure and characterization data of allenynes (**1**, **5**, **14**, **16**, **20**) and diyne **27** are summarized in Supporting Information. Characterization data



Scheme 6. Control experiments using allenyne **20** and the corresponding diyne **27**.

of the products of the [2+2+2] cycloaddition other than **3aa**, **9ab**, **9ac**, **9fc**, and **12ab** are summarized in the Supporting Information.

Representative procedure for rhodium(I)-catalyzed [2+2+2] cycloaddition of allenynes with alkynes

$[RhCl(cod)]_2$ (1.2 mg, 2.5 μmol) and *rac*-BINAP (3.1 mg, 5.0 μmol) were dissolved in DCE (0.20 mL), and the mixture was heated at 60 °C for 0.5 h under an atmosphere of Ar. A solution of the allenyne **1a** (18 mg, 0.05 mmol) and the alkyne **2a** (36 mg, 0.25 mmol) in DCE (0.80 mL) was added to the reaction mixture, which was stirred at 60 °C for 0.5 h. The residue was chromatographed with hexane/AcOEt to afford **3aa** (25 mg, 99%).

3,3,6,7-Tetrakis(methoxycarbonyl)-1-(phenylsulfonyl)-1,2,3,4-tetrahydronaphthalene (3aa): Colorless plate. M.p. 178–181 °C (hexane/AcOEt); ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.67–7.64 (m, 2H), 7.59–7.57 (m, 2H), 7.50–7.48 (m, 2H), 7.40 (s, 1H), 4.77 (dd, 1H, J = 9.6, 7.0 Hz), 3.90 (s, 3H), 3.87 (s, 3H), 3.79 (s, 3H), 3.47 (s, 3H), 3.21 (dd, 1H, J = 15.6, 2.9 Hz), 3.04 (ddd, 1H, J = 14.8, 9.6, 2.9 Hz), 2.81 (d, 1H, J = 15.6 Hz), 2.49 ppm (dd, 1H, J = 14.8, 7.0 Hz); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 170.4, 169.7, 167.5, 166.9, 139.6, 135.6, 134.2, 132.3, 131.6, 130.1, 129.9, 129.5, 129.2, 63.3, 54.2, 53.4, 53.1, 52.8, 52.7, 35.0, 29.2 ppm; IR: $\tilde{\nu}$ = 1736, 1310, 1148 cm^{-1}; DART MS *m/z* 505 (M^+ + 1, 100); DART HRMS: *m/z* calcd for $C_{24}H_{25}O_{10}S$: 505.1168; found: 505.1158.

7-(Ethoxycarbonyl)-3,3-bis(methoxycarbonyl)-6-methyl-1-(Phenylsulfonyl)-1,2,3,4-tetrahydronaphthalene (9ab): Colorless amorphous solid. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.70 (s, 1H), 7.64–7.61 (m, 1H), 7.59–7.57 (m, 2H), 7.48–7.45 (m, 2H), 6.94 (s, 1H), 4.73 (dd, 1H, J = 10.0, 6.9 Hz), 4.33–4.24 (m, 2H), 3.78 (s, 3H), 3.46 (s, 3H), 3.14 (dd, 1H, J = 15.5, 3.1 Hz), 3.04 (ddd, 1H, J = 15.1, 10.0, 3.1 Hz), 2.81 (d, 1H, J = 15.5 Hz), 2.55 (s, 3H), 2.52 (dd, 1H, J = 15.1, 6.9 Hz), 1.35 ppm (t, 3H, J = 7.2 Hz); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 170.7, 170.0, 166.7, 140.9, 139.9, 135.9, 134.0, 133.2, 132.3, 129.6, 128.9, 128.5, 124.0, 63.1, 60.7, 54.4, 53.2, 52.9, 35.0, 29.1, 21.4, 14.3 ppm; IR: $\tilde{\nu}$ = 1735, 1306, 1143 cm^{-1}; DART MS *m/z* 475 (M^+ + 1, 81.9); DART HRMS: *m/z* calcd for $C_{24}H_{27}O_8S$: 475.1427; found: 475.1414.

3,3,7-Tris(methoxycarbonyl)-1-(phenylsulfonyl)-1,2,3,4-tetrahydronaphthalene (9ac): Colorless needle. M.p. 171–173 °C (hexane/AcOEt); ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.91 (dd, 1H, J = 7.9, 1.7 Hz), 7.88 (s, 1H), 7.65–7.62 (m, 1H), 7.56–7.54 (m, 2H), 7.47–7.44 (m, 2H), 7.14 (d, 1H, J = 7.9 Hz), 4.76 (dd, 1H, J = 10.0, 6.5 Hz), 3.88 (s, 3H), 3.78 (s, 3H), 3.43 (s, 3H), 3.20 (dd, 1H, J = 15.5, 3.1 Hz), 3.05 (ddd, 1H, J = 14.8, 10.0, 3.1 Hz), 2.80 (d, 1H, J = 15.5 Hz), 2.53 ppm (dd, 1H, J = 14.8, 6.5 Hz); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 170.6, 169.9, 166.3, 141.3, 135.8, 134.1, 132.3, 129.9, 129.5, 129.3, 129.0, 127.0, 63.6, 54.5, 53.3, 52.8, 52.1, 35.4, 29.3 ppm; IR: $\tilde{\nu}$ = 1721, 1294, 1143 cm^{-1}; DART MS *m/z* 447 (M^+ + 1, 100); DART HRMS: *m/z* calcd for $C_{22}H_{23}O_8S$: 447.1114; found: 447.1115.

3,3,7-Tris(methoxycarbonyl)-5-methyl-1-(phenylsulfonyl)-1,2,3,4-tetrahydronaphthalene (9fc): Colorless powder. M.p. 161 °C (hexane/AcOEt); ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.79 (s, 1H), 7.65–7.62 (m, 2H), 7.54–7.53 (m, 2H), 7.47–7.44 (m, 2H), 4.74 (dd, 1H, J = 10.0, 6.2 Hz), 3.86 (s, 3H), 3.79 (s, 3H), 3.42 (s, 3H), 3.37 (dd, 1H, J = 15.8, 2.7 Hz), 3.05 (ddd, 1H, J = 14.8, 10.0, 2.7 Hz), 2.58 (dd, 1H, J = 14.8, 6.2 Hz), 2.55 (d, 1H, J = 15.8 Hz), 2.28 ppm (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 170.8, 170.0, 166.5, 140.3, 136.7, 135.8, 134.0, 131.1, 130.2, 129.5, 128.9, 128.0, 126.8, 64.0, 54.5, 53.3, 52.8, 52.1, 31.4, 28.9, 19.5 ppm; IR: $\tilde{\nu}$ = 1734, 1308, 1148 cm^{-1}; DART MS: *m/z* 461 (M^+ + 1, 4.15); DART HRMS: *m/z* calcd for $C_{23}H_{25}O_8S$: 461.1270; found: 461.1287.

6-(Hydroxymethyl)-3,3-bis(methoxycarbonyl)-1-(phenylsulfonyl)-1,2,3,4-tetrahydronaphthalene (12ab): Colorless powder. M.p. 147–149 °C (hexane/AcOEt); ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.63–7.60 (m, 1H), 7.56–7.55 (m, 2H), 7.46–7.40 (m, 3H), 7.18–7.17 (m, 1H), 7.05 (s, 1H), 4.77 (dd, 1H, J = 9.6, 7.2 Hz), 4.67 (s, 2H), 3.77 (s, 3H), 3.45 (s, 3H), 3.12 (dd, 1H, J = 15.3, 2.9 Hz), 3.00 (ddd, 1H, J = 14.8, 9.6, 2.9 Hz), 2.68 (d, 1H, J = 15.3 Hz), 2.41 (dd, 1H, J = 14.8, 7.2 Hz), 1.75 ppm (br s, 1H); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 170.9, 170.1, 141.7, 136.1, 136.0, 133.9, 131.3, 129.5, 128.9, 127.2, 125.5, 125.3, 64.6, 63.5, 54.5, 53.2, 52.8, 35.2, 29.7 ppm; IR: $\tilde{\nu}$ = 3603, 1734, 1308, 1146 cm^{-1}; DART MS: *m/z* 419 (M^+ + 1, 14.5); DART HRMS: *m/z* calcd for $C_{21}H_{23}O_7S$: 419.1165; found: 419.1161.

Representative procedure for desulfonylation of 1,2,3,4-tetrahydronaphthalenes

An excess amount of Raney Ni was added to a solution of **3ba** (19 mg, 0.05 mmol) in EtOH (1.0 mL). The reaction was conducted at reflux condition with vigorous stirring for 36 h. Then, the reaction mixture was cooled to room temperature and filtered through a pad of Celite. The filtrate was quenched with brine, and then extracted with CH_2Cl_2. The extract was washed with water and brine, dried and concentrated to dryness. The residue was chromatographed on silica gel with hexane/AcOEt to afford **18** (8.9 mg, 72%).

6,7-Bis(methyloxycarbonyl)-1,2,3,4-tetrahydronaphthalene (18): Colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.42 (s, 2H), 3.88 (s, 6H), 2.81–2.79 (m, 4H), 1.82–1.80 ppm (m, 4H); ^{13}C NMR (151 MHz, $CDCl_3$): δ = 168.3, 140.8, 129.7, 128.9, 52.5, 29.2, 22.6 ppm; IR: $\tilde{\nu}$ = 1720 cm^{-1}; DART MS *m/z* 249 (M^+ + 1, 100); DART HRMS: *m/z* calcd for $C_{14}H_{17}O_4$: 249.1127; found: 249.1116.

Transformation of 3ba by Friedel–Crafts alkylation [Eq. (3)] 7,8-Bis(methoxycarbonyl)-1-phenyl-1,2,3,4-tetrahydronaphthalene (19)

$AlCl_3$ (20 mg, 0.15 mmol) was added to a solution of **3ba** (19 mg, 0.050 mmol) in benzene (1.0 mL) at room temperature. After being stirred for 6 h at the same temperature, the reaction was quenched by addition of 1 M aqueous NaOH and the mixture was extracted with AcOEt. The extract was washed with water and brine, dried and concentrated to dryness. The residue was chromatographed with hexane/AcOEt (7:1) to afford **19** (13 mg, 80%) as a colorless amorphous solid: ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.50 (s, 1H), 7.30–7.27 (m, 2H), 7.25 (s, 1H), 7.23–7.20 (m, 1H), 7.04–7.03 (m, 2H), 4.14 (t, 1H, J = 6.2 Hz), 3.89 (s, 3H), 3.79 (s, 3H), 2.95 (dt, 1H, J = 17.5, 6.5 Hz), 2.87 (dt, 1H, J = 17.5, 5.8 Hz), 2.18–2.14 (m, 1H), 1.92–1.86 (m, 2H), 1.79–1.72 ppm (m, 1H); ^{13}C NMR: δ = 168.4, 168.0, 146.0, 142.8, 141.4, 130.9, 129.6, 129.5, 129.0, 128.7, 128.5, 126.3, 52.5, 52.4, 45.3, 32.7, 29.6, 20.1 ppm; IR: $\tilde{\nu}$ = 1721 cm^{-1}; DART MS *m/z* 325 (M^+ + 1, 100); DART HRMS *m/z* calcd for $C_{20}H_{21}O_4$: 325.1440; found: 325.1433.

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Keywords: alkynes · allenes · cycloaddition · regioselectivity · rhodium

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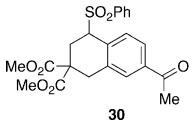
[20] Yield of **9hb**/**10hb** was determined by ^{1}H NMR analysis because **9hb**/**10hb** could not be purified effectively. Compound **9hb**/**10hb** was therefore obtained as a mixture with a slight amount of some impurities.

[21] Ratio of **12ae** to **13ae** was determined by ^{1}H NMR analysis of the mixture of their oxidized derivatives **30** and **31**, which were obtained by a standard oxidation condition using 2-iodoxybenzoic acid (IBX) as an oxidant (see the Supporting Information for details).



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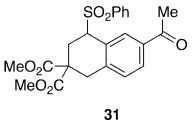

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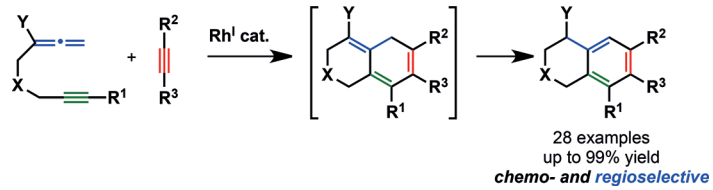

Under control: A highly chemo- and regioselective partially intramolecular rhodium(I)-catalyzed [2+2+2] cycloaddition of allenynes with alkynes is described (see scheme). A range of diverse polysubstituted benzene derivatives could be synthesized in good to excellent yields, in which the allenynes served as synthetic equivalent to the diynes. A high regioselectivity could be observed when allenynes were treated with unsymmetrical alkynes.

Regioselectivity

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Chemo- and Regioselective Rhodium(I)-Catalyzed [2+2+2] Cycloaddition of Allenynes with Alkynes