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INTRAMOLECULAR CARBOMETALLATION OF GRIGNARD REAGENTS HAVING THE TERMINAL TRIMETHYLSILYLACETYLENE GROUP

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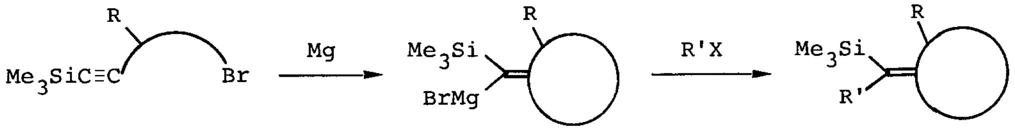
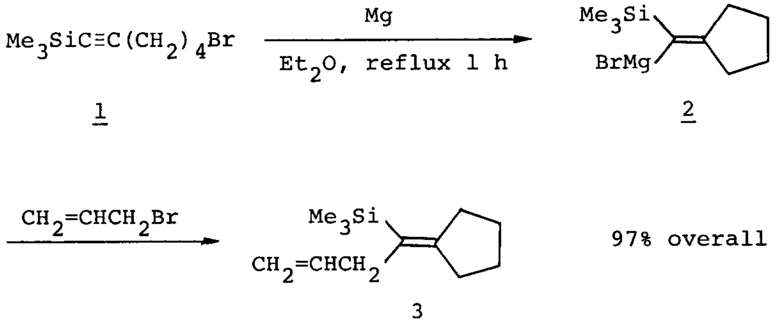
Abstract: Reaction of 6-bromo-1-trimethylsilyl-1-hexyne with magnesium affords the corresponding Grignard reagent whose C-Mg bond intramolecularly adds to the trimethylsilylacetylene moiety in 5-Exo-Dig manner and suprafacially. The reaction can be applied to the synthesis of some cycloalkanes having stereodefined alkylidene substituents.

Intramolecular carbometallation of an acetylene group is a promising route to stereodefined alkylidenecycloalkanes.[1] Synthetically useful reaction of this type utilizing Li,[2] Mg,[3,4,5] Al,[6] or Cu[7] as a key element has not been reported because of the lack of stereoselectivity. This paper discloses a stereoselective intramolecular carbomagnesation of alkynylsilanes forming stereodefined exocyclic alkenes.



Treatment of 6-bromo-1-trimethylsilyl-1-hexyne (1) with magnesium in ether afforded the Grignard reagent 2 which gave 4-trimethylsilyl-4-cyclopentylidene-1-butene (3) in 97% overall yield upon coupling with allyl bromide.[8] The 6,6-dideuterated compound 4 gave the expected deuterated product 5 in 77% yield stereoselectively.[9] Accordingly, the overall reaction proceeds regio and stereoselectively.[10]

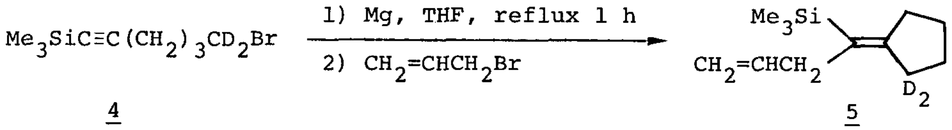


1

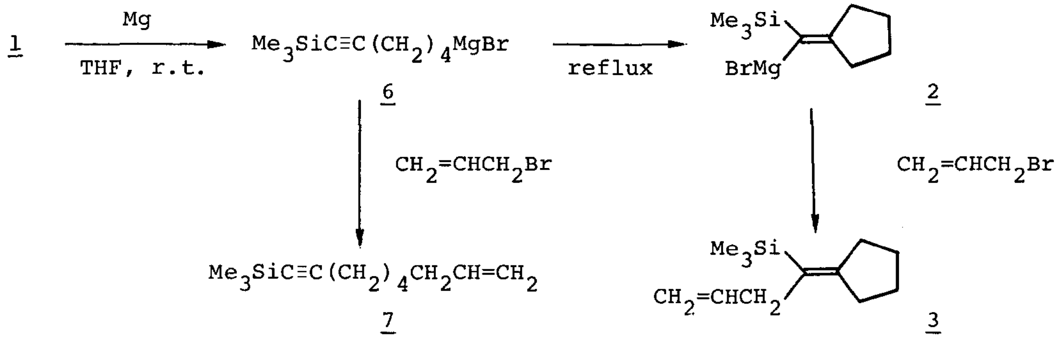
2

3

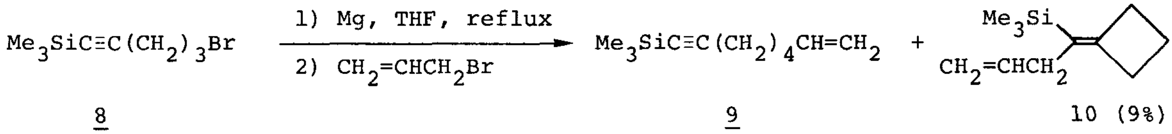
97% overall yield

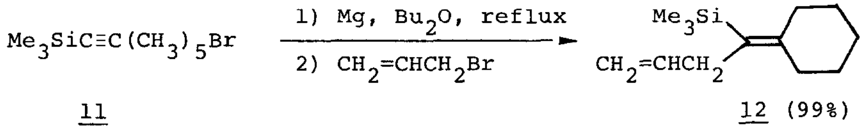


When 1 was treated with magnesium in THF at room temperature for 1 h, an acyclic Grignard reagent 6 was produced mainly. Treatment of the reaction mixture with allyl bromide gave 9-trimethylsilyl-1-nonen-8-yne (7) in 81% yield besides 9% of the cyclized product 3. Heating the reaction mixture containing 6 under reflux for 1 h gave the cyclized Grignard reagent 2 exclusively by intramolecular carbometallation.

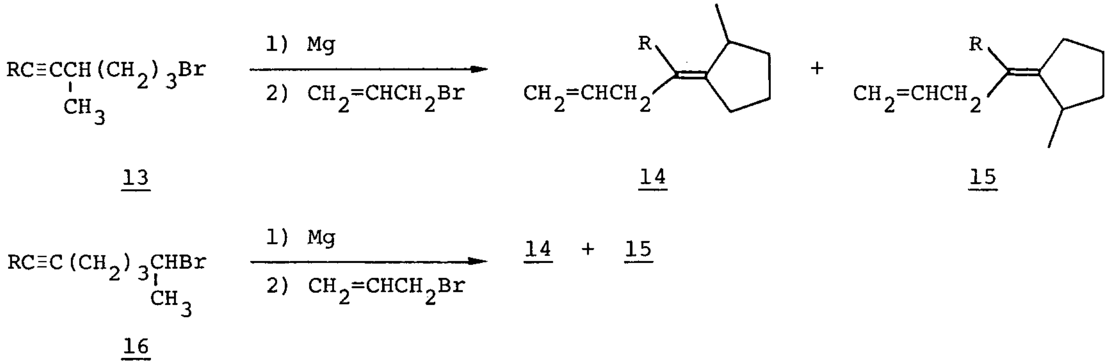


The reaction of the lower homolog, 5-bromo-1-trimethylsilyl-1-pentyne (8), gave only 9% yield of the cyclized product 10 in addition to the non-cyclized, major one 9 (72%). The higher homolog, 7-bromo-1-trimethylsilyl-1-heptyne (11), afforded the cyclized product 12 in 99% yield when the reaction was carried out in refluxing dibutyl ether.[11]





Stereoselective synthesis of methyl-substituted cyclopentylidene compounds utilizing the above reaction is shown in the following scheme. Reactions in ether gave better results compared with those in THF.

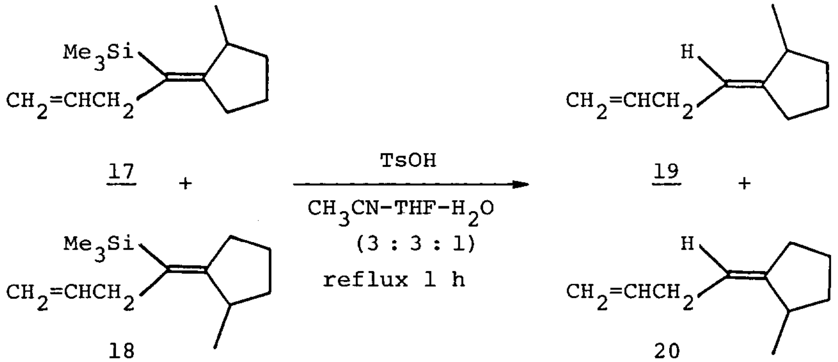


$RC\equiv C\underset{CH_3}{C}H(CH_2)_3Br$ $\xrightarrow[2)\ CH_2=CHCH_2Br]{1)\ Mg}$ 14 + 15

$RC\equiv C(CH_2)_3\underset{CH_3}{C}HBr$ $\xrightarrow[2)\ CH_2=CHCH_2Br]{1)\ Mg}$ 14 + 15

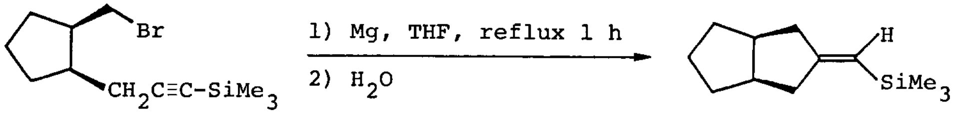
	R	Et_2O, reflux			THF, reflux		
		Yield (%)	14	15	Yield (%)	14	15
13	Me_3Si	87	91	9	92	92	8
	Me_2PhSi	86	96	4	87	88	12
	Et_3Si	99	98	2	99	86	14
16	Me_3Si	86	5	95	94	9	91
	Me_2PhSi	93	3	97	79	12	88
	Et_3Si	95	3	97	92	8	92

Stereospecific protodesilylation proceeded successfully upon treatment with p-TsOH in CH_3CN-THF-H_2O. Combination of the above described intramolecular carbomagnesation and stereospecific protodesilylation provided a novel route to stereoselective synthesis of alkylidenecyclopentanes.[12]



Starting Material 17	Starting Material 18	Yield (%)	Product 19	Product 20
92	8	73	9	1
9	91	75	1	9

Analogous reaction leading to 3-alkylidenebicyclo[3.3.0]octane is given below.



21

22 (78%)

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REFERENCES AND NOTES

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6. Professor E. Negishi of Purdue University has informed us of their unpublished results on an intramolecular carboalumination of alkynylsilanes.
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8. Typical Procedure: An ethereal solution of 1 (272 mg, 1,17 mmol in 2 ml of anhydrous ether) was added to a mixture of slight excess of magnesium and 1 ml of ether. The whole was stirred at room temperature for 20 min. and then heated under reflux for 1 h. Allyl bromide (0.26 ml, 3 mmol) was added and the reaction mixture was stirred for 12 h at room temperature. The product 3 (221 mg, 97% yield) was obtained: PMR ($CDCl_3$) δ ppm, 0.25 (s, 9H), 1.61 (m, 4H), 2.33 (br-t, 2H), 2.37 (br-t, 2H), 2.90 (d, J = 6 Hz, 2H), 4.95 (m, 2H), 5.79 (m, 1H).
9. PMR and CMR showed the product was homogeneous. Configuration of the product 5 was estimated by the analogy to the result shown in Note 12.
10. Hitherto known carbomagnesation without assistance of silicon moity needed high reaction temperature and long time and afforfed a mixture of stereoisomers.
11. Reaction in refluxing THF gave uncyclized product.
12. Stereochemistry of the product was determined as followes: Carbomagnesation of 13 (R = Me_3Si) followed by the treatment with MeI gave (E)-2-methyl-(2-trimethylsilylpropylidene)cyclopentane. Stereospecific protodesilylation afforded (Z)-2-methyl-1-propylidenecyclopentane (ref. 13).
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