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REGIOSPECIFIC AND SEQUENTIAL SUBSTITUTION OF TRIMETHYLSILYL-1,6-METHANO[10]ANNULENES VIA THE ELECTROPHILIC ipso-REACTION

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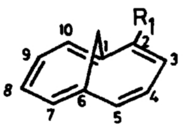
2-Substituted 7-trimethylsilyl-1,6-methano[10]annulenes have been prepared and their electrophilic ipso-desilyl-substitution has been studied, providing a new route for the regiospecific polyfunctionalization of 1,6-methano[10]annulenes.

In the electrophilic substitution of 1,6-methano[10]annulene, the first substitution occurs exclusively at C2 position giving 1,[1)] and the second substitution occurs at the position(s) specified by the orientation effect of the first substituent R_1 of 1,[2)] namely an electron-donating group directs the second substitution to the C5 (or C7) and an electron-attracting group does to the C10 (or C7) position predominantly. Unfortunately, the synthetic utility of this substitution, especially of the second substitution, suffers disadvantages because it is sometimes imperative to be functionalized at unfavorable position(s) of 1,6-methano-[10]annulene. The bromo substituent of 2-bromo-1,6-methano[10]annulene can be replaced by another function by means of (i) halogen metal interconversion followed by substitution with electrophiles or (ii) direct nucleophilic substitutions.[3)] However, the two bromo substituents of 2,7-dibromo derivative 2,[1b)] obtainable easily from 1 (R=H, or Br), have reactivities fairly close to each other in these reactions, so that only derivatives carrying two identical functions at 2,7-positions have been obtained, those carrying two different functions not being easily obtained, from 2. In order to find a method of regiospecific substitution in a 1,6-methano[10]annulene series, we have now prepared various types of trimethylsilyl derivatives of this series and studied their electrophilic substitution. Consequently, it has proved that electrophilic ipso-desilyl-substitution affords an efficient and promising route for the clean and regiospecific polyfunctionalization of 1,6-methano[10]annulene, which are reported herein.

2,7-Bistrimethylsilyl-1,6-methano[10]annulene 3[4)] was obtained in quantitative yield by lithiation of 2 with butyllithium (4 equiv.) in ether and subsequent quenching with trimethylsilyl chloride. Selective ipso-monobromodesilylation of 3 to 4 was performed in 93% yield when 3 was allowed to react with an equimolar amount of NBS in dichloromethane at 0 °C. It was also possible to replace the bromo substituent of 4 with another functional group without affecting the carbon-silicon bond, i.e., monosilyl derivatives 5 (70% yield) and 6 (80% yield) were prepared by lithiation of 4 followed by reaction with MeI and CO_2-CH_2N_2, respectively. The compounds 7 (77% yield) and 8 (65% yield) were also obtained by



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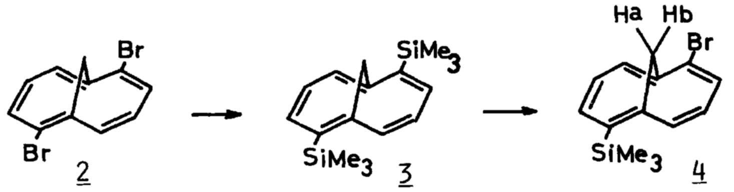
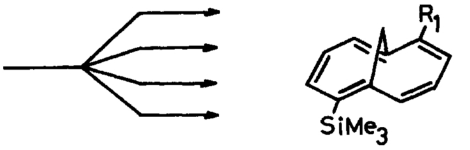


2 3 4

4



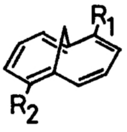
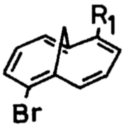
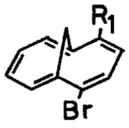
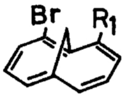
5 : R_1 = Me
6 : R_1 = CO_2Me
7 : R_1 = CHO
8 : R_1 = OBu^t

the Grignard reaction of the magnesium derivative of 4 with DMF and t-butyl perbenzoate, respectively.

In order to get an insight into a problem concerning which of the directing ability of the C2 substituent or the ipso-directing ability of C7 trimethylsilyl group plays more important role in specifying the position of the electrophilic substitution, we allowed these silyl derivatives to react with NBS, a typical electrophile, in dichloromethane. The results were summarized in Table 1, and the structural proof of products were made on the bases of their ^1H NMR data summarized in Table 2.

As seen in Table 1, an interesting contrast is found in the regiospecificity between entries A and B series. Firstly, all compounds of A series underwent selective ipso-bromodesilylation excluding normal bromination, giving no regioisomeric mixture of the products unlike some compounds of B series (see entries 3B and 6B). Ipso-desilylation resulted successfully even in the annulene carrying a strong electron-donating t-butoxy group, revealing that the ipso-directing ability of the trimethylsilyl group is more significant than the C5-directing ability of t-butoxy group. This result appears to be a good experimental support for the reported σ^+ value of -0.8 for the trimethylsilyl group of 1 (R_1=$SiMe_3$),(6) since the σ^+ value should be less than that (around -0.78)(7) of t-butoxy group. Secondly, bromodesilylation of entry A series proceeded at lower temperature and/or in shorter reaction time than the corresponding normal bromination of B series, whereas the reactivity difference between entries A and B is smaller than the difference between Ar-H and Ar-$SiMe_3$ bond in benzenoid system. The trimethylsilylannulene derivatives listed in Table 1 underwent ipso-desilylation much faster than the corresponding trimethylsilylbenzene derivatives. These observations are quite reasonable by reference to the protodesilylation of 2-trimethylsilylannulene (1: R_1=$SiMe_3$) which is 20 times more reactive than trimethylsilylbenzene.(6) It is also clear from the Table 1 that the order of the reactivity of 2-substituted 7-trimethylsilylannulenes (A series) correlates well with the order of σ^+ values of the C2 substituents, OBu^t (-0.78) > Me (-0.31) > Br (0.15) > CO_2Me (0.49) > CHO (0.55). This implies that the formation of a σ-complex is a rate-determining step in the ipso-desilyl-substitution reaction. In addition, the reactions of series A compounds proceed in good yield, thus this electrophilic ipso-desilyl-substitution is applicable to the preparation of a wide variety of poly-functionalized annulene

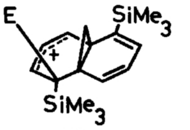
Table 1. Bromination of Substituted 1,6-methano[10]annulenes with NBS[a)]

Entry	Substrate		Reaction conditions		Yield of products[b)]/%		
							
	R_1	R_2	Temp/°C	Time			
1A	OBu^t	$SiMe_3$	-20	1.5 h	60 (9)	——	——
1B[c)]	OMe	H	0	30 min	——	52	——
2A	$SiMe_3$	$SiMe_3$	0	20 min	93	——	——
2B	H	H	40	1 h	2-bromo derivative		
3A	Me	$SiMe_3$	0	25 min	70 (10)	——	——
3B	Me	H	40	30 min	19	43	——
4A	Br	$SiMe_3$	r.t.	30 min	93	——	——
4B	Br	H	40	4 h	85	——	——
5A	CO_2Me	$SiMe_3$	r.t.	10 h	85 (11)	——	——
5B	CO_2Me	H	40	24 h	——	——	78
6A	CHO	$SiMe_3$	r.t.	15 h	75 (12)[5)]	——	——
6B	CHO	H	40	24 h	89	——	6

a) Treated with 1 molar equivalent of NBS in dichloromethane.
b) Yield of isolated products after silica gel column chromatography.
c) Reactions of entries 1B, 3B, and 5B are cited from Ref. 2.

derivatives which can not be so readily available in the previous way.

According to the above-mentioned observation that 2,7-disilyl derivative 3 was mono-bromodesilylated stepwise giving 4, the structure of the σ-complex is regarded as charge distributed cation 14 rather than norcaradienyl allyl cation 13, because the difference in the reactivity between the first and second steps of the bromodesilylation of 3 is hard to be explained on the σ-complexes 14' and 15' respectively, and is best explained on 14 and 15 in which the C1-C6 transannular overlap is so weak that the substituent at C2 could affect the stability of the carbonium ion. Noticeably, this argument is in good agreement with the view that the C1-C6 transannular overlap is much less in protonated 1,6-methano[10]annulene 16 than in unprotonated one.[8)] Although the exact geometrical configuration of the incomed electrophile (E) in the σ-complex is not known, exo-configuration of E,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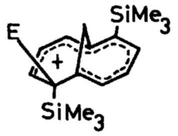
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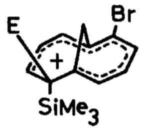
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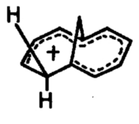
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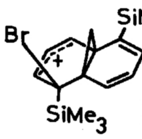
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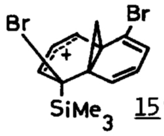
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such as shown in 14, would be quite plausible because a high exo-stereoselectivity has recently been demonstrated in electrophilic attack on this kind of bridged annulenes[9)] and the endo-axial C-Si bond in such a configuration appears to be nearly parallel to the neighboring p orbitals at C6 and C8 judging from the molecular model of 16.

Table 2. ^{1}H NMR Data of Substituted 1,6-Methano[10]annulenes in $CDCl_3$, δ (ppm), *J* (Hz)

Compd.	H-11a	H-11b	H-3	H-4	H-5	H-8	H-9	H-10	Others
3	-0.45		7.31	6.90	7.34	7.31	6.90	7.34	0.42
					J3,4=J8,9=9.0, J4,5=J9,10=9.0				
4	-0.43	-0.30	7.37	6.98	7.34	7.23	6.95	7.63	0.41
	J11a,b=9.6, J11a,5=1.0, J11b,10=0.8,				*J3,4=9.0, J4,5=9.0, J8,9=9.5, J9,10=9.0*				
5	-0.35	-0.62	6.92	6.93	7.28	7.33	6.90	7.43	0.41, 2.58
	J11a,b=10, J11a,5=1.0, J11b,10=0.9,				*J3,4=9.0, J4,5=8.7, J8,9=9.2, J9,10=9.0*				
6	-0.50	-0.33	8.08	7.17	7.59	7.43	7.12	8.26	0.40, 3.91
	J11a,b=9.5, J11a,5=1.0, J11b,10=1.0,				*J3,4=10, J4,5=9.0, J8,9=10, J9,10=9.0*				
7	-0.35	-0.21	7.69	7.16	7.66	7.36	7.12	8.19	0.42
	J11a,b=9.5, J11a,5=1.0, J11b,10=1.0,				*J3,4=9.2, J4,5=8.5, J8,9=9.2, J9,10=8.5*				
8	-0.67	-0.27	6.97	7.01	7.27	7.40	6.97	7.67	0.38, 1.47
	J11a,b=9.3, J11a,5=1.0, J11b,10=1.0,				*J3,4=9.7, J4,5=9.0, J8,9=9.2, J9,10=9.0*				
9	-0.53	-0.22	6.87	7.12	7.53	7.36	7.04	7.66	1.42
	J11a,b=10.2, J11a,5=1.1, J11b,10=1.0,				*J3,4=10, J4,5=9.2, J8,9=10, J9,10=8.7*				
10	-0.31	-0.49	7.12	7.11	7.55	7.48	7.08	7.62	2.58
	J11a,b=10.0, J11a,5=1.0, J11b,10=1.2,				*J3,4=9.0, J4,5=9.0, J8,9=10, J9,10=9.0*				
11	-0.51	-0.32	8.06	7.14	7.79	7.28	7.04	8.16	3.91
	J11a,b=10.0, J11a,5=1.0, J11b,10=0.9,				*J3,4=9.8, J4,5=9.2, J8,9=10, J9,10=8.9*				
12[a)]	-0.16	-0.28	7.81	7.33	8.04	7.43	7.24	8.25	10.14
	J11a,b=10.0, J11a,5=1.0, J11b,10=1.1,				*J3,4=9.2, J4,5=9.0, J8,9=10, J9,10=8.7*				

a) NOE enhancements at H-3 (7%), H-10 (3%), and H-5 (0%) were detected on saturation of CHO.

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4) All new compounds gave satisfactory elemental analyses.
5) Further structural confirmation of 12 was made by its transformation to 2,7-diformyl-1,6-methano[10]annulene upon successive reactions with 1) ethylene glycol/TsOH, 2) BuLi, 3) DMF, and then 4) 2 M HCl.
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