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Contrasteric Regiochemical Incorporation of Stannylacetylenes in the Benzannulation Reaction

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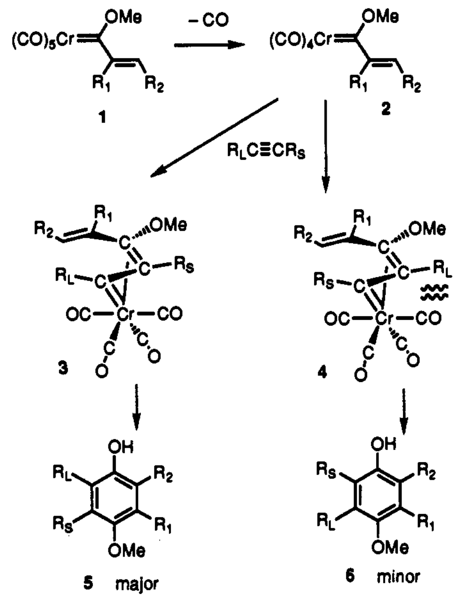
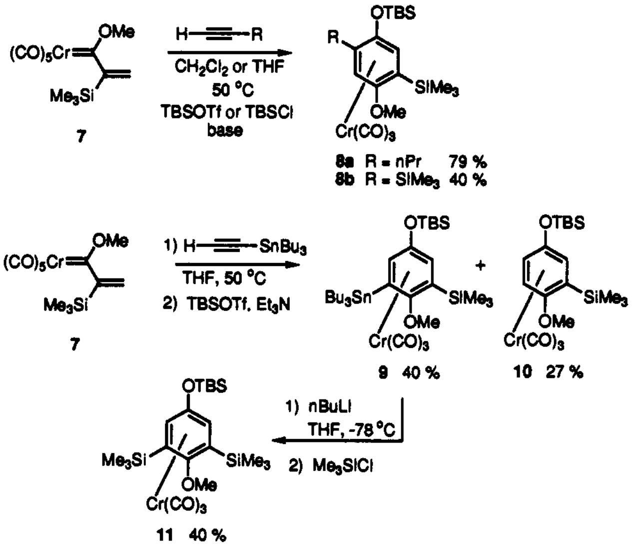
The high degree of regioselectivity in the benzannulation reaction of α,β-unsaturated Fischer carbene complexes with terminal alkynes is one of the more attractive aspects of this synthetically important reaction.[2] It has long been established that the major contributor to the regioselectivity of this reaction is the steric differential between the two substituents on the alkyne which leads to the preferential formation of the phenol **5** where the larger substituent (R_L) is incorporated adjacent to the hydroxyl group[3] (Scheme 1). Terminal alkynes typically give a single regioisomer; however, unsymmetrically substituted internal alkynes give mixtures of the two possible regioisomers where the ratio of the two phenols **5** and **6** approaches unity as the difference in steric demand of the two alkyne substituents decreases.[3] Examples where the regioselectivity is controlled by electronic factors are rare and include ketone and aldehyde groups on the alkyne[4] (but not esters[3d]). We report here that stannyl substituents on the alkyne can reverse the normal regioselectivity of the benzannulation reaction and can function as a highly regioselective synthon for internal acetylenes since the stannyl substituent in the phenol product can be used in carbon–carbon coupling reactions.[5]

We first observed the unusual effect of stannylacetylenes in the benzannulations of the α-silylated vinyl carbene complex **7**[6] (Scheme 2). Whereas the reactions of **7** with 1-pentyne and (trimethylsilyl)acetylene in the presence of a silylating agent produced a single isomer of the silylated phenol chromium tricarbonyl complexes **8**,[2a] the reaction with (tributylstannyl)acetylene produced the opposite regioisomeric complex **9** as a single isomer.[14] This was very surprising since never before has there been a case of a benzannulation reaction of a terminal acetylene where the major product has the acetylene incorporated in a reverse fashion. The regiochemistry of **9** was confirmed when **9** was subjected to a tin/lithium exchange with *n*-butyllithium followed by treatment with trimethylsilyl chloride. This process produced the bis-silylated phenol complex **11**, which was nonidentical with the complex **8b** from the reaction of **7** with (trimethylsilyl)acetylene. The assignment of **11** as the 3,5-silylated complex was straightforward from its spectral data given the symmetry differences between **8b** and **11**. It was found

Scheme 1



Scheme 2



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(1) American Chemical Society Organic Division American Cyanamid Fellow, 1991-1992.

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(12) The reaction also produces a 13% yield of the destannylated phenol **19c** (R′ = H).

(13) The reaction of complex **15** with 1.5 equiv of 1-bromo-1-pentyne in benzene (45 °C, 11 h) produced a complex mixture of eight minor products that were not separated and characterized.

(14) The two aryl protons in **9** were judged to be meta on the basis of a 1.8-Hz coupling constant and because the two methyl groups on the TBS group were identical in both ^1H and ^{13}C NMR, which is not the case for complexes with at least one substituent ortho to the (*tert*-butyldimethylsilyl)oxy group.

(15) The ratios of the products **13** and **14** as well as **16** and **17** were determined by capillary GC, and the ratios of **19** and **20** were determined by ^1H NMR.

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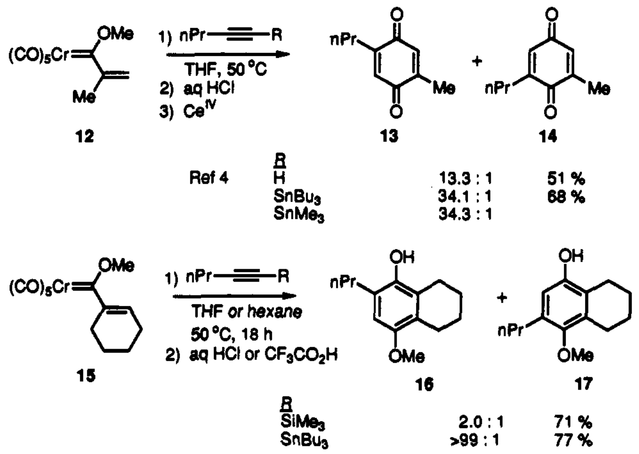
Scheme 3

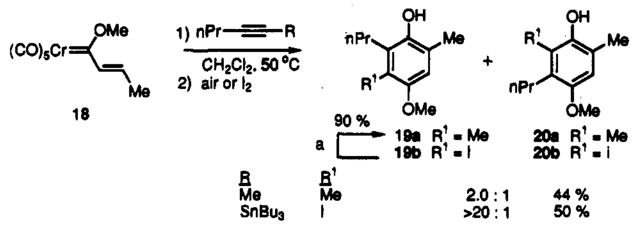


difficult to prevent the formation of the destannylated phenol complex **10** since the stannylated aryl chromium tricarbonyl complexes are quite sensitive to protodestannylation. The regioselectivity with 2-deuterio-1-(tributylstannyl)acetylene was found[16] to be 2.0:1.0 in favor of the phenol **6** (R_S = D, R_L = $SnBu_3$), and thus it is likely that phenol complex **10** is largely derived from protodestannylation of the regioisomer of **9**.

The effect of tin groups on the regioselectivity of acetylene incorporation is more clearly defined in the reactions shown in Scheme 3, where the regiochemical origin of each of the products can be determined. The reactions of the α-methylvinyl carbene complex **12** with 1-pentyne has been reported to give a 13.3:1 mixture of the quinones **13** and **14**.[3c] The reaction of **12** with 1-(tributylstannyl)-1-pentyne, after protodestannylation of the phenols with aqueous HCl prior to oxidation, occurs with incorporation of the propyl group in the same position with an even higher fidelity (34:1) than obtained with 1-pentyne.[15] The comparison of the relative ability of a tributylstannyl versus a trimethylsilyl group to control the regiochemical incorporation of 1-pentyne was examined in the reaction with the cyclohexenyl carbene complex **15**. Whereas the silylalkyne produced a 2:1 mixture of phenols **16** and **17** after protodesilylation (CF_3CO_2H), the stannylalkyne gave greater than a 99:1 selectivity for the phenol **16** after protodestannylation (HCl).

The most recent and perhaps most intriguing explanation of the source of sterics in the control of the regiochemistry of the benzannulation reaction involves the η^3-vinyl carbene complex intermediate **3**.[7b] Hofmann has suggested that the preference for the formation of **3** over **4** (Scheme 1) is that the substituent R_S is much closer to the apical CO ligand than R_L is to the equatorial CO ligand. This model very nicely explains the normal benzannulation reaction such as the reaction of complex **12** with 1-pentyne where there would be a 13:1 preference for **3** over **4** (R_S = H, R_L = nPr). Steric considerations obviously cannot explain the result from the reaction of **12** with 1-(tributylstannyl)-1-pentyne where there would be a 34:1 preference for **4** over **3** (R_L = Bu_3Sn, R_S = Pr) since this would require that a tributylstannyl group be smaller than a proton.[18] A reasonable explanation also does not come from any electronic differences in the starting acetylenes since the chemical shifts of alkyne carbons are known to be virtually the same for silyl- and stannyl-substituted alkynes.[8] Two possible explanations can be put forward regarding the control of tin in the regiochemistry of alkyne incorporation but at this point must be considered as suggestions. The chromium–carbon bond to the carbon bearing substituent R_S in **4** is a non-heteroatom-stabilized carbene linkage, and the resonance structure bearing a positive charge on this carbon could be stabilized by a tin substituent at R_L.[9] Alternatively, the complex **4** could be stabilized by a tin substituent at position R_L by a tin interaction with the adjacent carbon monoxide ligand.[10,11,17]

Scheme 4



[a] i NaH, THF. 0 °C; ii nBuLi. -78 °C; iii MeI. -78 °C

While the determination of the origin of the effect of stannyl substituents must await future experiments, this effect should be exploitable for a solution to one of the main limitations of the benzannulation reaction: the lack of regioselectivity for internal alkynes. This is demonstrated in Scheme 4 for one particular tactic that involves taking advantage of the high reactivity of aryl–tin bonds with halogens. The reaction of complex **18** with 2-hexyne gives a 2:1 mixture of phenols **19a** and **20a**, which are difficult to separate by normal methods. The reaction of complex **18** with 1-(tributylstannyl)-1-pentyne followed by a quench of the reaction with iodine gives a single regioisomer of iodophenol **19b**, which can be converted easily to a pure sample of phenol **19a** which is uncontaminated by its regioisomer **20a** as judged by ^1H NMR.[12] An equivalent solution would have been a benzannulation with a haloacetylene, but our attempts at these reactions have not met with success.[13]

The unique aspects of the benzannulation of stannylacetylenes that have been uncovered to this point will be of value in the synthetic implementation of the benzannulation reaction and also provide new mechanistic issues to be understood.

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Supplementary Material Available: Experimental procedures and spectral data for all new compounds (11 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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[16] (16) Details of this labeling experiment can be found in the supplementary material.

[17] (17) Construction of a model of **4** with bond lengths and angles taken from the calculations of Hofmann[7] with a stannyl substituent at R_L reveals that both the carbon (3.1 Å) and oxygen (3.2 Å) of the adjacent carbon monoxide ligand are within the sum of their van der Waals radii (Sn–O, 3.7 Å) with the tin atom. This is near the range of bonding distance found in tin–oxygen bonds in pentacoordinate tin coordination compounds.[11] Construction of a model of **3** with a stannyl group at position R_L reveals that the tin atom is now approximately 1.0 Å further away from the nearest carbon monoxide ligand than the tin atom at the R_L position in **4**.

[18] (18) The following *A* values have been reported: CH_3, 1.7;[19] Me_3Si, 2.5;[20] and Me_3Sn, 1.0.[21]

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