A mechanistic rationale for the outcome of Sonogashira cross-coupling of 9-bromoanthracene and ethynyltrimethylsilane: An unexpected product 4-(9-anthracenyl)-1,3-bis(trimethylsilyl)-3-en-1-yne

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Dedicated to Professor Richard Puddephatt on the occasion of his 75th birthday, and in recognition of his many pioneering investigations into the chemistry of the platinum metals.

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ABSTRACT

The Sonogashira reaction of 9-bromoanthracene and ethynyltrimethylsilane furnishes not only the anticipated 9-(trimethylsilylethynyl)anthracene and 2-(trimethylsilyl)aceanthrylene but also (E)-4-(9-anthracenyl)-1,3-bis(trimethylsilyl)-but-3-en-1-yne, all in moderate yields. A mechanistic rationale is proposed that invokes the intermediacy of bromo(anthracenyl)bis(triphenylphosphine)palladium(II) that can undergo coupling either directly, or after coordination and migratory insertion of the free alkyne.

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1. Introduction

9-(Trimethylsilylethynyl)anthracene, 1, has been widely used as a precursor for a wide range of applications, including photo- and electro-luminescent molecules [1–3], anthracene-stacked oligomers [4], triptycene-based molecular rotors [5,6], species immobilized on nanoparticles [7], cross-linked polymers [8], syntheses of fullerene fragments [9,10], electrochemical behaviour of tetracenes and pentacenes [11], and in sensitive probes for mechanical stress in polymers [12]. The obvious synthetic route via a palladium-catalyzed cross-coupling of 9-bromoanthracene and ethynyltrimethylsilane turns out to be exquisitely sensitive to the experimental conditions (catalyst and base used, solvents, temperatures) and gives rise to a number of products.

2. Results and discussion

2.1. Syntheses and structures

In 1997, Tour reported the successful synthesis (84% yield) of 9-(trimethylsilylethynyl)anthracene, 1, as a red solid via Negishi cross-coupling of trimethylsilylethynyl lithium and 9-bromoanthracene with ZnCl2, Pd(dba)2 and PPh3 in THF at 75 °C [13]. However, since this procedure requires such scrupulously dry conditions, other routes have also been investigated. In 2001, Dang and Garcia-Garibay found, surprisingly, that the analogous Sonogashira reaction using PdCl2(PPh3)2, PPh3, CuSO4/Al2O3 and Et3Ni refluxing benzene gave 1 only as a minor product, and instead yielded 2-(trimethylsilyl)aceanthrylene, 2, in the ratio 16:84, respectively [14] (Scheme 1). Under the same conditions, but in a sealed tube, this ratio was amplified to 7:93. Since then, this peri-
cyclopentenelation process has been exploited to produce polycyclic systems that represent fragments of fullerences [9,10].

Dang’s and Garcia-Garibay’s latter observation parallels an initial attempt to prepare 9-(2-indenyl)anthracene [15], en route to 9-(2-indenyl)triptycene that was subsequently utilized in an organometallic molecular brake [16]. Once again, unexpected cyclization to form the indenyl-fused anthracene, rac-3, resulted (Scheme 2).

In retrospect, it is evident that the two possible modes of insertion of indene into the aryl-palladium linkage of 9-(anthracenyl)Pd(PPh3)2Br, generated from 9-bromoanthracene and the catalytic species Pd(PPh3)2, can lead to intermediates 4 and 5 (Scheme 3). In the former case, syn-elimination of HPdL2Br occurs readily to yield 9-(1-indenyl)anthracene (that subsequently isomerizes to its 3-indenyl counterpart). In contrast, intermediate 5 lacks a suitably positioned hydrogen syn to palladium, and instead undergoes intramolecular palladation of the adjacent anthracene ring to form the polycycle 3.

Analogously, the lack of a hydrogen syn to palladium in intermediate 6a (Scheme 4) also leads, via cyclization to 6b, to the aceanthrylene 2.

More recently, the route to 1 employing the Sonogashira reaction has been very markedly improved. Typically, reaction of 9-bromoanthracene and ethynyltrimethylsilane in the presence of PdCl2(PPh3)2, CuI, Et3N and piperidine at 110 °C/Et3N, benzene, reflux, has been very markedly improved. Typically, reaction of 9-bromoanthracene and ethynyltrimethylsilane in the presence of palladium catalyst, temperature and length of reaction are unspecified. The principal differences between the reactions leading to the desired product in 75% yield [17]; it has since been improved to 98% [18]. A synthesis using THF as solvent has also been reported [19]. A synthesis using THF as solvent has also been reported [19].

The principal differences between the reactions leading to the alkynylanthracene, 1, or the aceanthrylene, 2, are the changes in solvent, identity of the copper salt, and relative ratios of the anthracene and alkynyl. The former case (Et3N, piperidine, Cu, 4-fold excess of alkynyl) yields 1 almost quantitatively whereas the latter (benzene, CuSO4/Al2O3, and 2.7-fold excess of alkynyl) yields primarily 2, and is even better in the absence of copper [9,14]. The palladation catalyst, temperature and length of reaction are unchanged. We note, however, that in many cases where a Cu salt is not listed as a reagent it is still present in the solvent in trace quantities as a stabilizer.

As shown in Scheme 5, we here report the isolation and structural characterization of another product of the palladium-catalyzed cross-coupling of 9-bromoanthracene and ethynyltrimethylsilane using PdCl2[PPh3]2 (2 mol%), Et3N and THF at 70 °C for 24 h to give, in approximately equal yields, 9-(trimethylsilyl)anthracene, 1, 2-(trimethylsilyl)aceanthrylene, 2, and, remarkably, also (E)-4-(9-anthracenyl)-1,3-bis(trimethylsilyl)-but-3-en-1-yne, 7, that was characterized spectroscopically and whose structure was confirmed by X-ray crystallography (Fig. 1).

The enyne 7 crystallizes with four independent molecules in the unit cell. The average ene-yne bond distances were 1.331 and 1.210 Å, respectively, and this unit made an average torsion angle of 57.7° with the anthracene plane. The molecule contains three different carbon-silicon bond environments in which the mean sp3-C-Si, sp2-C-Si and sp-C-Si distances are noticeably dissimilar, 1.855, 1.892 and 1.832 Å, respectively.

The packing of the molecules in 7 (see ESI Figure S1) reveals that the enyne units are aligned face-to-face as enantionic pairs and the anthracenyls are arranged in an almost parallel fashion to form an outer wall which encloses them. This differs markedly from the very first report of enyne stacking in the Y-shaped molecule (C6F5CH=CC≡CPh2) in which the structure is dominated by face-to-face interactions of phenyl and pentafluorophenyl rings and the enyne units are sandwiched between phenyl groups [20].

In related earlier work it had been noted that the reaction of 1-bromo-2-(hydroxymethyl)naphthalene with ethynyltrimethylsilane catalyzed by Pd(PPh3)4 and Cu in piperidine gave the ethynyl-naphthalene, 8, together with a small amount of the double adduct, 9, (Scheme 6) that was characterized by NMR spectroscopy [21]. Much more recently, the Sonogashira reaction of a dialkylperimidine with ethynyltrimethylsilane to form 10 gave a low yield of the double adduct, 11, that was characterized by X-ray crystallography [22]. The structure of the but-3-en-1-yne moiety in 11 may be compared to that found here in 7; the double and triple C-C bond distances in 11 are 1.358 and 1.213 Å, respectively, and the enyne unit has rotated only 38.6° out of the naphthalene plane compared to 57.7° in 7, which of course has an additional proximate benzo ring.

The above-mentioned double and triple carbon-carbon bond distances in 7 may also be compared to those in a series of bis-(TMS-terminated enynes) connected by a spacer, such as a phenyl ring or a substituted thiophene, in which the analogous double and triple bonds have average values of 1.348 and 1.203 Å, respectively [23].

Although metal-catalyzed synthetic routes to enynes from terminal alkynes have been comprehensively reviewed [24], the only previously reported specifically designed syntheses of 1,3-bis(trimethylsilyl)-but-3-en-1-yne, of type 12, include the Cu-mediated cross-coupling reaction of (E)-alk-1-yl-diisobutyldienes, 13, with (trimethylsilyl)ethyl bromide [25] and the Sonogashira coupling of (E)-α-iodovinylsilanes, 14, with (trimethylsilyl)acetylene [26] (Scheme 7). It is also noteworthy that in 1988 Ishikawa reported that treatment of ethynyl(dimethylphenyl)silane with Pd[PPh3]4 at 100 °C produced the tail-to-tail dimer (E)-1,4-bis(dimethylphenylsilyl)but-3-en-1-yne in low yield [27].

### 2.2. Mechanistic rationale

The observation of the enyne 9 was initially attributed to subsequent carbopalladation of the alkynyl-hydroxymethylnaphthalene, 8 [21]. Likewise, suspecting that formation of 11 arose by Pd-catalyzed addition of the alkynyl to 10, a commonly invoked scenario [28], the authors carried out a control reaction whereby 10 was treated with excess alkynyl under the same reaction conditions, but only starting material was recovered [22]. Apparently, the alkyynes 8 and 10 and enynes 9 and 11 are formed competitively rather than sequentially.

It is particularly relevant to note reports by Canty and co-workers whereby multiple head-to-tail alkynyl insertions and concomitant cyclizations have been detected [29]. These observations were consistent with the view that such “daisy-chain” processes occur via a partial Sonogashira process involving incorporation of several PhC≡CH molecules into an arylpalladium intermediate. It is noteworthy that added Cu did not affect the reaction specificity.
We propose a plausible copper-free mechanism (Scheme 8) to account for the formation of all three products, 1, 2 and 7 in roughly equal quantities. Upon the generation of bis-phosphine active species (Ph₃P)₂Pd(0) oxidative addition of the 9-anthracenyl bromide gives the Pd(II) intermediate trans-15. At this point, palladium coordination to the alkyne enhances the base-promoted formation of the palladium acetylide, trans-16, which, after isomerization to cis-16 and subsequent reductive elimination, leads to the "normal" coupling product 9-(trimethylsilyl)anthracene, 1 (blue coupling pathway). However, trans-16 can undergo a competitive process whereby coordination of the terminal alkyne, always present in excess, also occurs to give intermediate trans-17. Now, migratory insertion affords the anthracene coordinated alkenyl palladium intermediate 18 as the cis-isomer. However, upon recoordination of phosphine, the square planar Pd geometry is restored in 19, and reductive elimination proceeds with retention of the olefin geometry to afford the enyne product 7 and regenerate the Pd(0) catalytic species (red insertion-coupling pathway). Of course, in the insertion-cyclization route, (green in Scheme 8) the intermediate, 15, can also bind to the alkyne in an η² fashion giving complex 20 which, after migratory insertion, affords intermediate 21. This species, having bromide, a good leaving group, attached to Pd, undergoes cyclopalladation to give 22 which is poised to yield aceanthrylene 2 and regenerate the Pd(0) species thus closing this catalytic cycle.

Clearly, these mechanisms have a common precursor intermediate, 15, and the overall outcome of the process strongly depends...
on the ability of the ethynyl group to coordinate directly to the Pd(II) forming intermediates 17 and 20 in sufficient quantities, a factor that may also be dependent on the concentration of the phosphine; in the absence of such coordination only the “normal” Sonogashira product, 1, can be expected. Our attempts to obtain insertion or/and cyclization products in a very closely related reaction using ethynylbenzene under various conditions were unsuccessful - entirely consistent with observations earlier reported by the Garcia-Garibay group [14].

One could perhaps rationalize this remarkable discrepancy in the behaviour of trimethylsilyl- and phenyl-alkynes in terms of the steric size of the substituents. In that case, lower yields of the insertion products 2 and 7 might be expected with the bulky TMS derivative. However, a perceptive reviewer raised the possibility that the difference in the building up of steric constraints between the TMS group and the neighbouring bromine (in 21) or with the ethynyl ligand (in 18) versus the lower strain engendered by the two-dimensional phenyl substituent may be a factor. The presence of the TMS group could destabilize the respective precursor intermediates, 20 and 17, resulting in their higher kinetic energy, thus providing competition with the direct formation of the normal cross-coupling product.

We also suggest that a major cause of this difference lies in the electronic properties of the ethynyl fragment in both compounds. Our preliminary DFT level electron structure calculations indicate that the accessibility of the electron density associated with the carbon-carbon triple bond of the TMS system is significantly better than in the phenyl analogue (Fig. 2). This electron density is critical to the ability of the ethynyl moiety to coordinate to the palladium in an \(\eta^2\) fashion — the crucial process governing the formation of

![Fig. 2. Representation of the charge distribution through an electrostatic potential map in: a) trimethylsilylacetylene; b) phenylacetylene (blue - positive, red - negative potential, mV). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)](image-url)
cyclization and insertion products 2 and 7. In that case, the relatively lower electron density in the triple bond may be sufficient to explain the dearth of such products in the reactions employing phenylacetylene.

3. Conclusion

Under a range of experimental conditions, including a copper-free protocol, the reaction of 9-bromoanthracene and ethynyl-trimethylsilane furnishes not only the anticipated Sonogashira product 9-(trimethylsilyl)anthracene, 1, or the earlier reported 2-(trimethylsilyl)acenaphthylene, 2, but also the unexpected (E)-4-(9-anthracenyl)-1,3-bis(trimethylsilyl)-but-3-en-1-yne, 7, whose structure was confirmed by X-ray crystallography.

A mechanistic rationale is proposed that invokes the formation of a common arylpalladium(I) bromide intermediate, 15, that can follow each of three pathways. Specifically, (a) Sonogashira coupling, (b) an insertion-coupling leading to en-1-yne 7, and (c) the insertion-cyclization route giving the acenaphthylene 2. The distribution of electron density in the alkyn component is suggested to be the key factor affecting the balance between these three reaction pathways.

4. Experimental section

4.1. General comments

All reactions were carried out under an atmosphere of dry nitrogen. Column chromatography was carried out on a Buchi Sepacor column with UV absorbance detector using silica gel particle size 40–63 mm. NMR spectra were acquired on a Varian VNMR 500 MHz spectrometer, and assignments were based on standard $^1$H–$^1$H and $^1$H–$^{13}$C two-dimensional techniques. DFT calculations were carried out as described in previous reports from this laboratory [30].

4.2. Syntheses

Compounds 1, 2, 7: To a stirred mixture of 9-bromoanthracene (193 mg, 0.75 mmol), triethylamine (0.8 mL) and bis(triphenylphosphine)palladium dichloride (0.22 ml, 1.5 mmol) was added, and the mixture was stirred at 70°C for 24 h, after which time the solvent and amine were removed under reduced pressure. The residue was separated by flash chromatography (silica, hexane-ethyl acetate) to give three main fractions containing: (a) 10 mg of unreacted 9-bromoanthracene (0.04 mmol); (b) a red oily material which was identified by NMR spectral comparison to literature data [14], as an equal mixture of 1 and 2 (135 mg, corresponding to ~32% yield of each); (c) a red solid, 7 (91 mg, 32%).

$^1$H NMR (500 MHz, CDCl$_3$) atom numbering as in the X-ray structure:

<table>
<thead>
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<th>Atom</th>
<th>Chemical Shift (ppm)</th>
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<td>H1</td>
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</tr>
<tr>
<td>H2</td>
<td>8.07 (2H, m, H2, H3)</td>
</tr>
<tr>
<td>H3</td>
<td>7.79 (2H, m, H2, H3)</td>
</tr>
<tr>
<td>H4</td>
<td>7.79 (1H, s, H11)</td>
</tr>
<tr>
<td>H5</td>
<td>7.46 (2H, m, H4, H5)</td>
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<td>H6</td>
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<td>H7</td>
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<tr>
<td>C8</td>
<td>126.8 (C8)</td>
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<tr>
<td>C10</td>
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**References**


