Electron-Transfer and Hydride-Transfer Pathways in the Stoltz–Grubbs Reducing System (KOTBu/Et₃SiH)

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Abstract: Recent studies by Stoltz, Grubbs et al. have shown that triethylsilane and potassium tert-butoxide react to form a highly attractive and versatile system that shows (reversible) silylation of arenes and heteroarenes as well as reductive cleavage of C–O bonds in aryl ethers and C–S bonds in aryl thioethers. Their extensive mechanistic studies indicate a complex network of reactions with a number of possible intermediates and mechanisms, but their reactions likely feature silyl radicals undergoing addition reactions and Si–H reactions. This paper focuses on the same system, but through computational and experimental studies, reports complementary facets of its chemistry based on a) single-electron transfer (SET), and b) hydride delivery reactions to arenes.

Recently, Stoltz, Grubbs et al. have discovered a simple and elegant system comprising Et₃SiH (2) and KOTBu which achieves a number of remarkable reactions: 1) converting arenes and heteroarenes, and their alkylated counterparts, into silyl-substituted products, often with excellent regiocontrol (e.g. 1→3; Scheme 1); 2) achieving reductive C–S bond cleavage in aryl thioethers (e.g. 4→5) in a reaction which has potential importance in removing sulfur traces from hydrocarbon fuels; 3) triggering reductive C–O bond cleavage in aryl ethers (e.g. 6→7) in a reaction with potential applications to controlled lignin degradation. A number of intermediates likely arise from reaction of these two reagents, and spectroscopic evidence has resulted in informed proposals being made for their structures. These reactions have proved puzzling, but a recent coordinated study by synthetic, mechanistic, and computational chemists has allowed significant advances to be made. The conclusions are: 1) the combination of Et₃SiH and KOTBu leads to triethylsilyl radicals which have a major role to play in the reductive cleavage of the C–O and C–S bonds; 2) triethylsilyl radicals are also likely to be involved in the silylation reactions, although nonradical routes to the silylation have also been considered in depth and may also play a central role. The mechanistic details are not fully in place, for example, on how formation of the silyl radicals occurs, but rational working hypotheses have been advanced. We had wondered if single-electron transfer mechanisms were playing a significant role in some of these reactions, notably for the cleavage of C–O and C–S bonds. An early suggestion mentioned pentavalent silicates (e.g. 13b; see Scheme 2) as reagents that were likely involved in the C–O cleavage, but the more recent computational studies on the substrates 4 and 6 instead support an alternative mechanism. In this regard, Scheme 1 shows ipso addition to the carbon atom of the C–O bond by triethylsilyl radicals, followed by C–O bond cleavage in conversion of 6 into 7.

Our recent interest in reductive chemistry carried out by reactions involving KOTBu attracted us to this area. Studies mentioned above suggest that the reactive species produced could include the radical anion 12b (Scheme 2) and the silyl anion 13b. Because of their subsequent importance in this paper, we mention here that the radical anions may be formed in a number of ways, two of which are shown (inset) in Scheme 2 (see Figure 14 in Ref. [1e] for an addi-
To these, we add the triethylsilyl anion \( \text{Et}_3\text{Si}^- \) on to 3-methylindole (entry 18). The radical anion of this compound is almost barrierless and is exergonic (entry 1; the scheme also shows facile fragmentation of the radical anion 31), while the electron-transfer reactions from 13a and 14a (entries 2 and 3) show prohibitive energy profiles.

![Diagram](image)

**Scheme 2.** Indole-based substrates as probes of electron-transfer activity. [a] See the Supporting Information for a discussion of the mechanism of formation of this compound.

![Diagram](image)

**Figure 1.** Representations of the spin density of the SOMO of the radical anion of N-benzyl-3-methylindole 17 (a) and N-benzylcarbazole 22 (b). Geometry optimizations and frequency calculations were carried out in Gaussian 16 at M062X/6-31 + + G(d,p) level of theory, with solvation modelled implicitly using the C-PCM model. (For full computational details, see the Supporting Information).

| Entry | Substrate | Silane (3 or 0 equiv) | Base (3 equiv) | Yield [%] | Product | Recovered Substrate |
|-------|-----------|-----------------------|---------------|-----------|---------|---------------------|
| 1     | Et\_3SiH  | KO\_tBu              |              | 24 (29)   |         |                     |
| 2     | \(\text{-}\text{blank}\) | KO\_tBu              |              | (85)      |         |                     |
| 3     | Et\_3SiH  | KO\_tBu              |              | 25 (49)   |         |                     |
| 4     | \(\text{-}\text{blank}\) | KO\_tBu              |              | 29 (15)   |         |                     |
| 5     | Et\_3SiH  | KO\_tBu              |              | 26 (73)   |         |                     |
| 6     | Et\_3SiH  | Na\_O\_tBu\_tBu      |              | (98)      |         |                     |
| 7     | \(\text{-}\text{blank}\) | KO\_tBu              |              | (88)      |         |                     |
| 8     | Et\_3SiH  | KO\_tBu              |              | 26 (76)   |         |                     |
| 9     | \(\text{-}\text{blank}\) | KO\_tBu              |              | (98)      |         |                     |
| 10    | Et\_3SiH  | KO\_tBu              |              | 26 (63)   | Trace   |                     |
| 11    | \(\text{-}\text{blank}\) | KO\_tBu              |              | (86)      |         |                     |
| 12    | Et\_3SiH  | KO\_tBu              |              | 26 (47)   | trace   |                     |
| 13    | \(\text{-}\text{blank}\) | KO\_tBu              |              | (93)      |         |                     |
| 14    | Et\_3SiH  | KO\_tBu              |              | 27 (80)   |         |                     |
| 15    | \(\text{-}\text{blank}\) | KO\_tBu              |              | (100)     |         |                     |
| 16    | Et\_3SiH  | KO\_tBu              |              | 28 (57)   | (26)    |                     |
| 17    | \(\text{-}\text{blank}\) | KO\_tBu              |              | (99)      |         |                     |
| 18    | Et\_3SiH  | KO\_tBu              |              | 26 (55)   | (23)    |                     |
| 19    | \(\text{-}\text{blank}\) | KO\_tBu              |              | (88)      |         |                     |

Yields of products and recovered substrates are those for the isolated compounds. [a] As in Ref. [1], Na\_O\_tBu\_tBu is not a successful substitute for KO\_tBu.
We also tested energy profiles for the debenzylation reaction with two possible competing pathways (Table 2; lower panels). The first of these recognizes that 13a could be a very powerful hydroxide-transfer agent and might facilitate an S$_\text{N}$2 reaction, although an unusual one, at the benzylic carbon center. However, transfer of hydroxide from 13a to 15 shows a barrier of 36.9 kcal/mol for the benzylic cleavage, and so this type of reaction will not occur under our reaction conditions in the laboratory. The second competing reaction type would involve an S$_\text{N}$1 reaction by a R-Si radical at the benzylic carbon center. This path would also be an unexpected reaction, as radical displacements at tetrahedral carbon centers are almost unknown, and indeed the kinetic barrier (44.3 kcal/mol) is again insurmountable. From these results, SET from 12a is overwhelmingly the most likely of the mechanisms to be realized (97%) and so this SET mechanism was taken to be the reaction afforded the hydrocarbon 32.

In a more challenging probe for electron-transfer potency, we subjected the benzyl methyl ether 47 to reduction by this system (Scheme 3). A close analogue of this substrate had proven a very tough substrate in previous studies. It did not undergo fragmentation until two electrons had been transferred. In this case, the reduced product 48 was produced in 52% yield [a blank reaction afforded recovered starting material exclusively (62%)]. Additionally, subjecting the nitrile 49 to the reaction afforded the hydrocarbon 50 as the sole product, consistent with electron transfer followed by loss of cyano anion.

We calculated the oxidation potential of 12a to be $E = -3.74$ V vs. SCE (MeCN). This potential makes it much more powerful than alkali metals. Such a powerful electron donor should provide a good probe for the Marcus inverted region of SET reactions with substrates that show low reorganization energies, e.g. polycyclic arenes. Stoltz, Grubbs et al reported small amounts of partially reduced arenes from reduction of naphthalenes. In our hands, and in the presence of excess of KO$_3$/EtSiH, anthracene, phenanthrene, and naphthalene all afforded significant amounts of their dihydro counterparts (Scheme 4). These compounds would be expected products from Birch-type electron-transfer processes, but to probe the mechanism we undertook computational studies of electron transfer from 12a to the hydrocarbons 51–53 to yield the corresponding radical anions 60–62. (Table 3) Here, the expected normal order of reactivity is 51 > 52 > 53. This order is also reflected in the $\Delta G^\text{rel}$ values shown in Table 3. However, the reverse pattern is seen for the $\Delta G^\ast$ values. SET to 51 from the radical anion 12a shows an interesting difference of the allyl radical leaving group. Accordingly, the substrates 43 and 45 were prepared. The indole products were indeed formed from these substrates (35% and 33% respectively). The low yields may indicate the wealth of alternative reactions open to this reagent system. Indeed, a second product was isolated from the reaction of 43, namely $\alpha$-isopropylaniline (44: 18%), although we have not explored the mechanism of its formation as yet. It was clear that the KO$_3$/EtSiH system is a more than competent electron-donating system.
extraordinary barrier of 90 kcal mol\(^{-1}\),\(^{[11]}\) while reduction of 52 and 53 show progressively lower barriers; if this can be verified by detailed experimental studies, it will be a very rare intermolecular ground-state illustration of the Marcus inverted region, (stronger driving force leads to retarded electron transfer).

In comparison, hydride transfer from 13a to afford the corresponding anions 63–65 featured low barriers and favorable thermodynamics (Table 4). At least for the reduction of anthracene, hydride transfer from 13a is indeed likely to occur. With the other substrates, hydride-transfer reactions again show lower barriers than electron transfer from 12a and this will of course be modulated by the concentration of the reducing species present. Finally, the alkyne 54 and stilbene 55 were reacted and gave (PhCH\(_2\)SiH) as the sole product (21 and 93 % respectively; Scheme 4).\(^{[12]}\)

In summary, the KOtBu/Et\(_3\)SiH system provides access to a broad range of mechanisms for reductive chemistry, now including electron transfer and hydride delivery to arenes. The electron-donor 12b is identified as a uniquely powerful agent.

**Table 3: Energy profiles: SET from 12a.**

| Substrate | Energy profile [kcal mol\(^{-1}\)] | Radical anion product |
|-----------|-----------------------------------|-----------------------|
| S1        | \(\Delta G^\circ : 90.0\) | 60                    |
| S2        | \(\Delta G^\circ : 28.3\)  | 61                    |
| S3        | \(\Delta G^\circ : 25.7\)  | 62                    |

**Table 4: Energy profiles: Hydride transfer from 13a.**

| Substrate | Energy profile [kcal mol\(^{-1}\)] | Anionic product |
|-----------|-----------------------------------|-----------------|
| S1        | \(\Delta G^\circ : 16.7\)  | 63              |
| S2        | \(\Delta G^\circ : 20.0\)   | 64              |
| S3        | \(\Delta G^\circ : 21.7\)   | 65              |

**Scheme 4.** Reductions of polycyclic arenes by KOtBu/Et\(_3\)SiH. [a] Yield determined by NMR spectroscopy.

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**Conflict of interest**

The authors declare no conflict of interest.

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