Supporting Information for

Radical Arene Addition vs. Radical Reduction: Why Organometal-hydride Chain Reactions Stop and How to Make Them Go?

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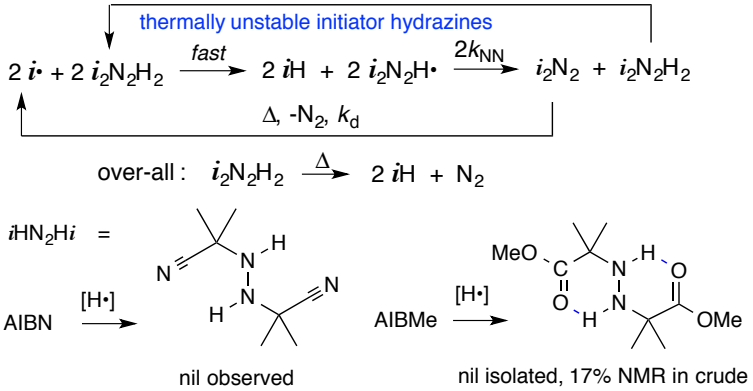
S1. Why Reduced Thermal Initiators are Thermally Unstable

A hitherto unresolved issue from earlier studies has been the absence of the reduced form of the putative oxidant – the azo initiator – in product and reaction mixtures. However, the weak, highly reactive N-H bonds seen in the gas phase studies (ref. 37) indicate the hydrazines of thermal initiators would spontaneously thermolyze in the sequence of upper Scheme S1:

Scheme S1. Radical-Induced then Spontaneous Decay of Azo-Initiator Hydrazines



Consequently, in the only report of a hydrazine being *detected* (not isolated) in a stannane HAS reaction (shown) the reduced azo diester of AIBMe was likely stabilized and deactivated to H-abstraction by internal H-bonding (shown). This is reflected the lack of aromatized products with AIBMe (vs. high yields with AIBN etc.) in all but one of the attempted HAS reactions in ref. 5.

S2. Hydrazine / Hydrazyl catalyzed aromatization.

Further to eqs 27 to 36, Curran (originally) and Larraufie et al (more explicitly) have proposed that the azo initiator acts as the oxidant. With AIBN (i_2N_2) as "oxidant" **Z** in Scheme 10, the implied *radical hydrogen transfer* (RHT) from RArH• to the azo i_2N_2 would afford a hydrazyl radical (i.e., **Z**H• = iNHN$^{(\bullet)}i$ in Scheme 6). The latter might, in principal, H-abstract from the stannane to complete a chain (per Scheme 6), but is unlikely to do so because (inter alia) H-transfer to the 3-electron-resonance-stabilized hydrazyl ***i***HN:N$^{\bullet}$***i*** would be slow. Rather, it is proposed (Scheme S2) some initial RArH• radicals are H-abstracted by the initiator and others by the hydrazyl. This terminates two potential chains but leads to the clean aromatization of the adduct and production of the hydrazine iHNNHi.

Scheme S2. Hydrazyl-Mediated Arylation of RX (blue path)

$$\frac{1}{\varepsilon}\ \boldsymbol{i}_2N_2 \xrightarrow{k_d} 2\boldsymbol{i}\bullet + N_2 \qquad (S1)$$

$$\boldsymbol{i}\bullet + Sn\text{H} \xrightarrow{k'_H} \boldsymbol{i}\text{-H} + Sn\bullet \qquad (S2)$$

$$\boldsymbol{i}\bullet + \boldsymbol{i}_2N_2H_2 \xrightarrow{k'_{NH}} \boldsymbol{i}\text{-H} + \boldsymbol{i}_2N_2H\bullet \qquad (S3)$$

$$Sn\bullet + \text{RX} \xrightarrow{k_X} \text{SnX} + 2\text{R}\bullet \qquad (S4)$$

$$\text{R}\bullet + \text{ArH} \xrightarrow{k_{ArH}} \text{RArH}\bullet \qquad (S5)$$

$$\text{RArH}\bullet + \boldsymbol{i}_2N_2H\bullet \xrightarrow{2k_{CN}} \text{RAr} + \boldsymbol{i}_2N_2H_2 \qquad (S6)$$

$$2\ \text{x}\ \boldsymbol{i}_2N_2H\bullet \xrightarrow{2k_{NN}} \boldsymbol{i}_2N_2 + \boldsymbol{i}_2N_2H_2 \qquad (S7)$$

$$2\ \text{x}\ \text{RArH}\bullet \xrightarrow{2k_{CC}} (\text{RArH})_2 \qquad (S8)$$

$$\Sigma:\ \frac{1}{\varepsilon}\ \boldsymbol{i}_2N_2 + Sn\text{H} + \text{RX} + \text{ArH} \xrightarrow{\Delta} 2\ \boldsymbol{i}\text{H} + \frac{1}{\varepsilon}\ N_2 + Sn\text{X} + \text{RAr}$$

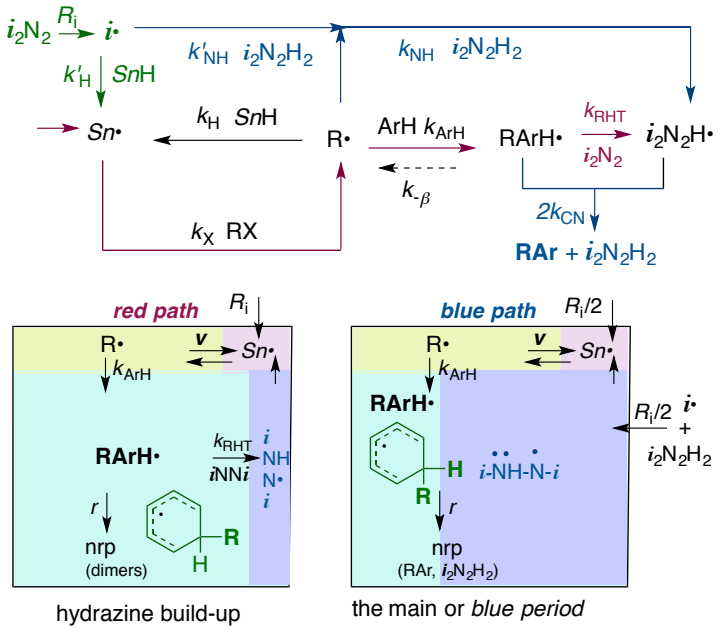


Figure S1. The build-up of hydrazine (red path) and hydrazyl radicals that oxidize RArH• to RAr (blue path). Areas represent radical concentrations and arrows the sources and sinks.

Once formed, the hydrazine would start generating hydrazyls from the initiating radicals (eq S3). Gas-phase kinetic data for MeHN-NHMe (cf. eq 31) indicate reduced initiators like $i_2N_2H_2$ are likely to be 50-fold, or more, more reactive than is the stannane towards initiator radicals. The hydrazine would therefore only reach a very low concentration roughly one 50^{th} that of the stannane. From this point forward the reaction can follow the catalytic-disproportionation or *blue* path in Scheme 8. In effect, one ***i***• radical from the $\boldsymbol{i}_2N_2$ produces the RArH• radical while the second initiator radical oxidizes RArH• to RAr; not directly, but indirectly, with the catalytic hydrazine as a hydrogen-atom transfer agent.

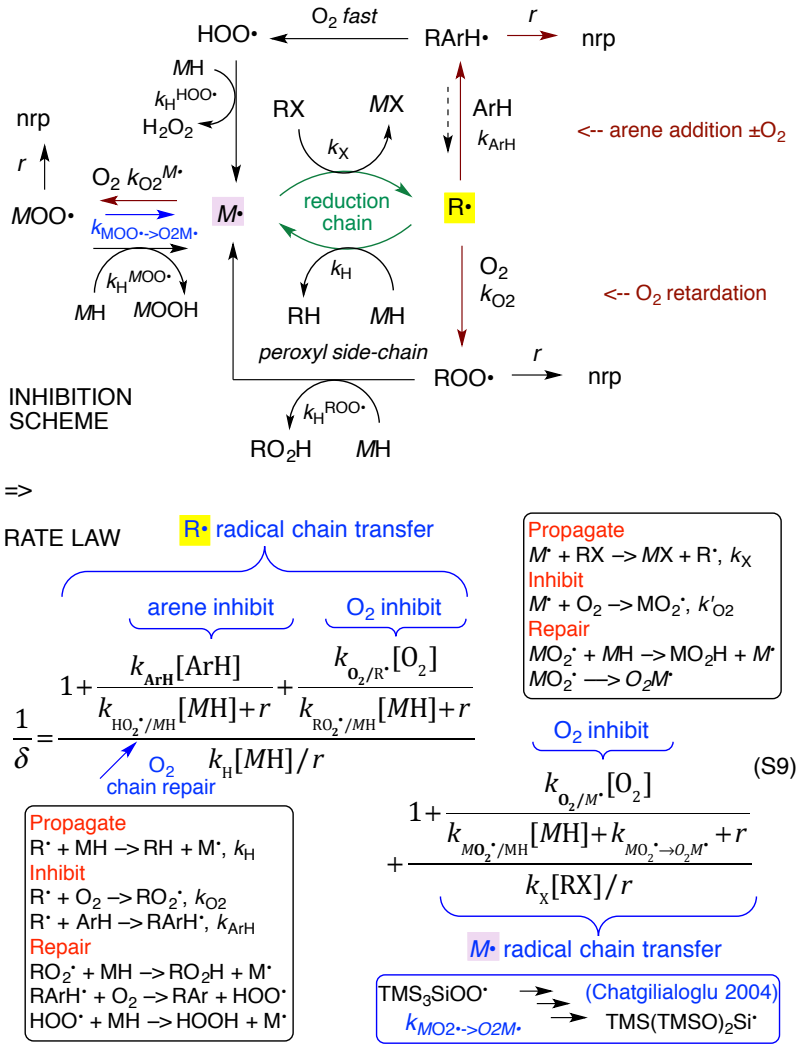
Notably, the *blue path* is compatible with observed time lags and AIBN thresholds (ref. 3); it would be catalytic in $\boldsymbol{i}_2N_2H_2$, and would be consistent with the optimized stoichiometry. The efficacy of this scheme for aromatization depends on the [$\boldsymbol{i}_2N_2H$•]/[RArH•] ratio (Fig. S1). Assuming uniform radical termination ($k_{NC} = k_{CC} = k_{NN}$), the radical ratio RArH•/i_2N_2H• ≈ 1 could yield ~65% RAr (thanks to combination statistics). While $\boldsymbol{i}_2N_2H$• is not a persistent radical, since homo-termination is likely quite rapid (e.g., $2k_{NN} = 9 \times 10^7$ M^{-1} s^{-1} for ***i*** = iPr), this is still ~50 times slower than diffusion controlled $2k_{CC}$. Provided cross-termination is rapid, then, the difference in termination rates may afford a cross-termination selectivity factor ($k_{NC}/\sqrt{(k_{CC}k_{NN})}$ of 5 or more; i.e., not "persistent" but sufficiently selective to account for observed arylation yields.

S3. Inhibition vs. Promotion by Air

Expanding on the text. Dioxygen (˙Ö-Ö˙) retards organometal-hydride reductions by trapping propagating radicals ($M^{\bullet}$ and $R^{\bullet}$) to form less reactive peroxyl species ($RO_2^{\bullet}$ and $MO_2^{\bullet}$) yielding peroxide by-products. Early studies of organotin hydride reductions were run without initiator but unprotected from air, which autoxidized some reagent, generating radicals, as well as peroxides that generated further radicals upon heating. With simple alkyl bromides or (especially) iodides this results in rapid spontaneous reduction.

Rate laws for initiated metal-hydride reduction under air were found by treating O_2 as a chain-transfer agent for both the $R^{\bullet}$ and $M^{\bullet}$ radicals (**B** = O_2, $\mathbf{A}_1$ = O_2 and $\mathbf{A}_2$ = ArH in eq 10), and by including O_2 as a chain-repair agent (Scheme S3).

Scheme S3. O_2 effect on arene inhibited reduction.



$$\frac{1}{\delta}=\frac{1+\dfrac{k_{\mathrm{ArH}}[\mathrm{ArH}]}{k_{\mathrm{HO_2^{\bullet}/MH}}[MH]+r}+\dfrac{k_{\mathrm{O_2/R^{\bullet}}}[O_2]}{k_{\mathrm{RO_2^{\bullet}/MH}}[MH]+r}}{k_{\mathrm{H}}[MH]/r}\qquad\qquad \frac{1}{\delta}=\frac{1+\dfrac{k_{\mathrm{ArH}}[\mathrm{ArH}]}{k_{\mathrm{HO_2^{\bullet}/MH}}[MH]+r}+\dfrac{k_{\mathrm{O_2/M^{\bullet}}}[O_2]}{k_{\mathrm{MO_2^{\bullet}/MH}}[MH]+k_{\mathrm{MO_2^{\bullet}\rightarrow O_2M^{\bullet}}}+r}}{k_{\mathrm{X}}[\mathrm{RX}]/r}\qquad\text{(S9)}$$

While O_2-trapping retards propagation, it also repairs inhibition by 'dead-end' radicals like $RArH^{\bullet}$. This results in oxygen *accelerating the rate of reduction* (!) if 'arene inhibition' (e.g.) is stronger than 'O_2 inhibition' (per eq 66, cf. eq 41 et seq.).

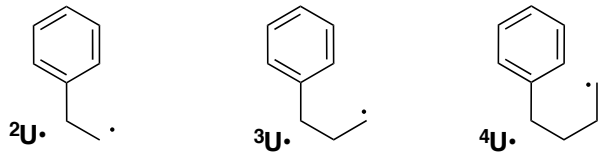
However, O_2-trapping of organometal radicals is *very* fast (e.g., $k_{Sn\bullet/O2} \approx 10^{10}$ $M^{-1}s^{-1}$) and produces electron-rich, low-activity peroxyls. Consequently, another type of chain-repair may

occur with the silyl reagent TMS_3SiH, in which peroxyl $TMS_3SiO_2^{\bullet}$ rearranges back to a propagating radical (see Scheme 10d). This chain-repair mechanism of the silane ($k_{MOO\bullet->OOM\bullet}$ in eq 66) may indeed be the reason TMS_3SiH is much more effective than Bu_3SnH in Curran's innovative O_2/HAS chain method (e.g., eq 67). Interestingly, inadvertent $SnO_2^{\bullet}$ has been proposed to aromatize the adduct in the $(Bu_3Sn)_2/h\nu$ system (cf. Scheme 8) (see ref 3).

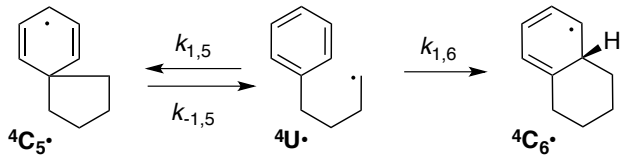
S4. Slow Reduction Kinetics

Expanding on the text. In a preliminary study for ref. 4 (and ultimately ref. 8), the kinetics of ring-closures onto the benzene ring were semi-quantitatively examined by measuring the stannane-reduction rates of ω-phenylalkyl bromides (Chart S1).

Chart S1



Only acyclic products (**2**UH, **3**UH, **4**UH) were formed under standard test conditions (those used in ref. 8). No cyclized products were detected (GC) even with dilute stannane solution (RX:SnH:BONNOB = 5/5/2.2 mM in Ar-sparged cyclohexane at 42 °C for 0.5 hr). Reaction rates were calculated from the product ratio $\alpha = (SnBr/SnCl)_{gc}$ (the chloride being formed from reaction of the remaining SnH with the CCl_4). This afforded the observed first-order reaction rate constant ($k_{obs} = [\ln(1 + \alpha)]/t$) and initial reaction velocity, $v_0 = -(d[SnH]/dt)_0 = [SnH]_0[\ln(1 + \alpha)]/t$. While **2**UBr and **3**UBr at RX were reduced at the same rate (±20%) as the benchmark, n-heptyl bromide, the rate for 4-phenylbutyl bromide (**4**UBr) was ~10-fold slower ($v_0 = 1 \times 10^{-6}$ M/s from $t = 200$ s). If this results from 1st-order chain termination, the observed chain length, $\delta = v_0 / R_i = 1 \times 10^{-6}$ M/s / 4×10^{-8} M/s = 25, indicates a ring-closure rate (eq 9), $k_{1,6}^{315K} \approx k_H[SnH]/\delta = 5 \times 10^6$ $M^{-1}s^{-1} \times 0.005$ M / 25 ≈ 1×10^3 s^{-1}.



(S10)

In preliminary kinetic tests on "refractory" **2**Br with excess stannane and the efficient initiator di-*t*-butyl hyponitrite (BONNOB = *t*-BuON=NOBu-*t*), it was found that this 'stannane-resistant halide' had, in fact, a normal halide-abstraction reactivity, and that the initial reaction yielded *Sn*Br (G.C.) at a rate equal to the normal initiation rate for this initiator, (i.e., chain length ≈ 1 *Sn*Br per ***i*•** with no sign of induced decay). No aromatized product was produced with catalytic initiator (up to 0.25 equiv or ~0.4 equiv of radicals), but addition of further initiator (to a total 2.0 equiv *t*-BuO• radicals) produced cyclo-aromatized product **2**$C_6^{(-H)}$ in fair yield (70% g.c.). In quantitative kinetic tests (see ref. 8) it was shown that tiny amounts of **2**Br or (especially) **3**I, strongly suppressed the co-reduction of simple halides; i.e., that **2**Br and **3**I were chain-terminating inhibitors for the stannane reduction.