Perkin Transactions 1

COMMUNICATIONS

NORTH AMERICAN AUTHORS

'Giese-type' radical addition reactions to an acceptor that functions by a unimolecular chain transfer reaction of a silicon hydride

Dennis P. Curran * and Jinyou Xu

Department of Chemistry, University of Pittsburgh, Pittsburgh, Pennsylvania 15260, USA

The first examples of Giese reactions (reductive additions of radicals to electron-poor alkenes) conducted by unimolecular chain transfer reactions of silicon hydrides are reported.

We are currently espousing the idea that unimolecular chain transfer reactions (UMCT) of silicon hydride reagents have significant potential for conducting difficult radical reactions such as bimolecular additions or complex sequences.[1] In the accompanying Keynote Article,[1b] we demonstrated that radical chains based on UMCT reactions of silicon hydrides could propagate, and we conducted a few simple radical additions by this UMCT method. The Giese reaction[2]—that is, the reductive addition of radicals to electron-poor alkenes—is probably the most popular bimolecular radical reaction, so we set as an early goal the demonstration that a typical Giese reaction can be conducted by the UMCT method. This communication reports preliminary results suggesting that the UMCT method may provide an advantageous alternative to normal bimolecular chain transfer reagents [tributyltin hydride. tris(trimethylsilyl)silicon hydride[3]] for conducting Giese reactions.

Acceptor 1 was selected because of its ease of preparation in two steps from 1,2-dibromobenzene, as shown in eqn. (1).

82 %

1
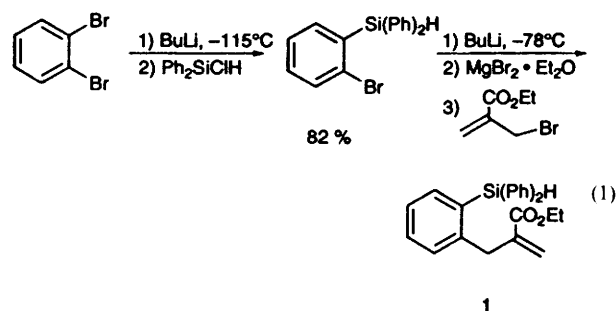
Monolithiation of dibromobenzene[4] in THF–diethyl ether–pentane (3:3:1) at −115 °C followed by trapping with diphenylchlorosilane provided the intermediate aryl bromide, which was again lithiated, this time in diethyl ether at −78 °C. Addition of magnesium bromide–diethyl ether to the presumed aryllithium intermediate followed by quenching with ethyl bromomethacrylate and standard workup provided 1 in about 50% overall yield.

Initial attempts to add adamantyl iodide to 1 on a stoichiometric basis are summarized in eqn. (2). Standard photolytic initiation with 10% hexabutylditin in benzene followed by exposure of the reaction mixture to triethylamine and methanol provided the adduct 3a in isolated yields ranging from 21–49%, depending on the reaction concentration. Though these yields were disappointing, they are not so bad considering than an excess of the alkene 1 was not used. It is well known that silicon iodides are reactive functional groups,[5] and

1 1 equiv   1 equiv

2
(presumed intermediate)

3a

Concentration	isolated yield
0.01 M	49%
0.03 M	31%
0.10 M	21%
0.10 M*	65%*
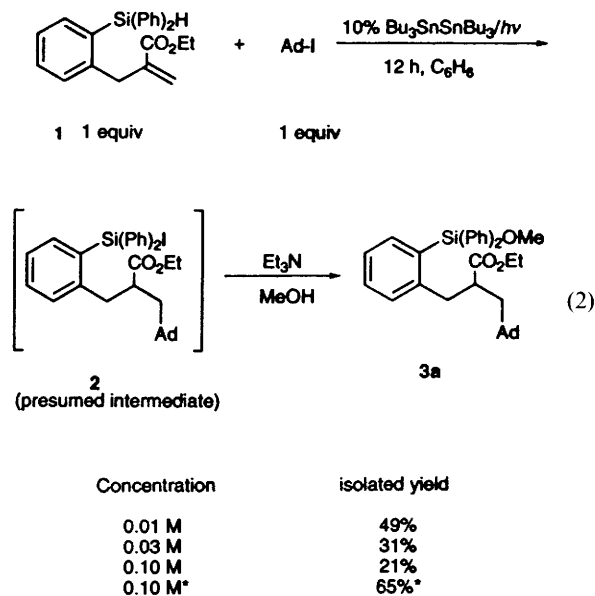
*Et_3N/MeOH present from the beginning, 9% silanol 3c also isolated

this combined with the unexpected decrease in the yield of 3a with increasing reaction concentration led us to speculate that there might be stability problems with the presumed intermediate silicon iodide 2.

Addition of a trap for the silicon iodide 2 to the reaction mixture during (rather than after) the radical addition resulted in significant improvements in yield. For example, addition of 2 equiv. each of methanol and triethylamine to the mixture at 0.1 M resulted in the formation of 3a in an improved yield of 65%. Furthermore, an additional 9% on the silanol 3c (see Table 1) was isolated, presumably due to adventitious water in either the benzene or the methanol. This raises the combined yield of radical adducts to 74%.

This last experiment suggested that benzene could be advantageously replaced by a nucleophilic solvent. Table 1 summarizes this line of experimentation, which led to the discovery of practical reaction conditions. Addition of adamantyl iodide to 1 in *tert*-butyl alcohol containing 2 equiv. of triethylamine (0.1 M, hv, 12 h, 10% $Bu_3SnSnBu_3$) provided 42% of the *tert*-butyl silyl ether 3b and 21% of the silanol 3c (entry 1). By using carefully dried *tert*-butyl alcohol. the yield of 3b could increase at the expense of 3c. However. it proved much simpler to increase the yield of 3c at the expense of 3b; addition of 2% water to the reaction mixture provided only 3c. Reactions under these conditions showed the expected increase in yield as a function of concentration, with the yield levelling off at higher concentrations (entries 2–6).

A number of other radical additions were conducted under these standard conditions, and the results are summarized in Table 2. In the interest of solvent economy, the highest concentration (0.5 M) was chosen for these additions, and the
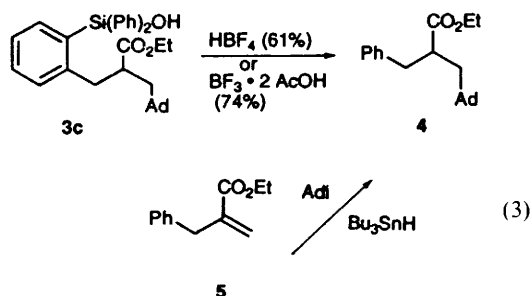
Table 1 Addition of adamantyl iodide to 1

1	+	Ad–I
1 equiv		1 equiv

10% $Bu_3SnSnBu_3$/hv
---
t-BuOH, 80°C/12 h
2 equiv Et_3N

$Si(Ph)_2OR$
CO_2Et

Ad

3b, R = t-Bu
3c, R = H

Entry	Additive	Concentration/M	Products (% yields)
1	2 equiv. Et_3N	0.10	**3b** (42), **3c** (21)
2	2% H_2O	0.01	**3c** (57)
3	2% H_2O	0.04	**3c** (81)
4	2% H_2O	0.08	**3c** (83)
5	2% H_2O	0.20	**3c** (79)
6	2% H_2O	0.50	**3c** (83)

Table 2 Additions of alkyl halides to 1

R–X	+	1
1 equiv		1 equiv

t-BuOH/2% H_2O/hv
---
2 equiv Et_3N/80°C/12 h
0.50 M

$Si(Ph)_2OH$
CO_2Et

R

Entry	R–X	Initiator	Yield (%)
1a	Ad–I	$Bu_3SnSnBu_3$	83
1b	Ad–I	$(TMS)_4Si$	80
2a	c-C_6H_{11}I	$Bu_3SnSnBu_3$	77
2b	c-C_6H_{11}I	$(TMS)_4Si$	80
3a	$PhCH_2CH_2$I	$Bu_3SnSnBu_3$	75
3c	$PhCH_2CH_2$I	$(TMS)_4Si$	72
4	$I(CH_2)_4Cl$	$Bu_3SnSnBu_3$	70
5	Ad–Br	$Bu_3SnSnBu_3$	70
6	c-C_6H_{11}Br	$Bu_3SnSnBu_3$	57
7	Me_2BrCCO_2Et	$Bu_3SnSnBu_3$	69

halide and **1** were always used in a 1:1 stoichiometry. Isolated yields of silanol adducts were uniformly good (57–83%), though bromides appear to give somewhat lower yields than iodides in these reactions (compare entries 1 with 5 and 2 with 6). To develop tin-free conditions for this reaction, we substituted 10% tetrakis(trimethylsilyl)silane[6] for hexabutyldi-tin in several of the examples. Pleasingly, the yields of these pairs of reactions were comparable (compare entries 1a–3a with 1b–3b), so the silane appears to be a viable substitute for ditin.
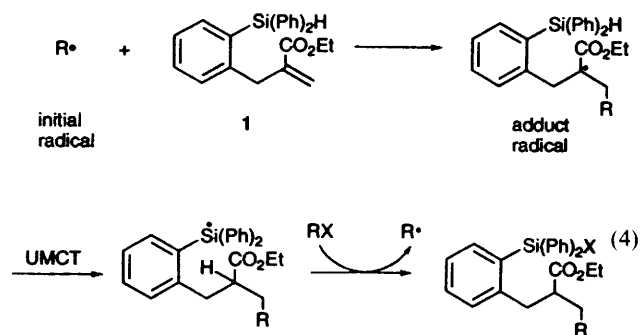
Desilylation of adduct **3c** can be accomplished with HBF_4 or $BF_3\cdot2AcOH$ in reasonable (unoptimized) yields [eqn. (3)] to

$Si(Ph)_2OH$
CO_2Et

Ad

3c

HBF_4 (61%)
or
$BF_3\cdot2$ AcOH
(74%)

CO_2Et
Ph

Ad

4

CO_2Et Ad
Ph

Bu_3SnH

5

(3)

provide **4**, so reagent **1** can be viewed as the UMCT equivalent of the standard acceptor **5**. Control experiments with **5** clearly demonstrated the UMCT advantage. Reduction of **5** in the presence of 1 equiv. tributyltin hydride and 1 equiv. adamantyl iodide (a simulation of the standard conditions in Table 1). provided only traces of **4**. As expected at these high tin hydride concentrations, the major product was adamantane. Syringe pump addition of 1 equiv. of tributyltin hydride to a 0.05 M

solution of adamantyl iodide and **5** provided **4** in 34% isolated yield. To match the UMCT reaction would require both low tin hydride concentration and a significant excess of **5**. Little or no reaction occurred when a solution of **5** and adamantyl iodide was treated with Ph_3SiH.

The experimental observations to date are consistent with the UMCT chain mechanism shown in eqn. (4). Radical addition is

R• +

$Si(Ph)_2H$
CO_2Et

initial radical

1

$Si(Ph)_2H$
CO_2Et

R

adduct radical

UMCT

$Si(Ph)_2$
H CO_2Et

R

RX   R•

$Si(Ph)_2X$
CO_2Et

R

(4)

followed by intramolecular hydrogen transfer and bimolecular iodine (or bromine) transfer. The fundamental problem of the Giese reaction conducted by bimolecular chain transfer methods is the difficulty in establishing selectivity between the initial and adduct radicals. Giese reactions can be accomplished by reacting structurally different initial and adduct radicals, and by choosing appropriate reactions conditions to minimize the metal hydride concentration (slow addition of hydride or high dilution) and maximize the concentration of alkene (excess alkene used). The UMCT reactions described in this paper bypass both the fundamental selectivity problem and the attendant limitations in reaction conditions—good yields of adducts are obtained at high reaction concentrations on a stoichiometric basis.

The ability to bypass the standard selectivity problem with bimolecular chain transfer reactions is best illustrated by the result in Table 2, entry 7. In this reaction, the initial and adduct radical are both tertiary radicals α to esters, so they could not be differentiated by bimolecular chain transfer methods and a good yield of the 1:1 adduct could not be obtained. But differentiation by UMCT occurs smoothly because the initial radical does not have a rapid unimolecular option and the adduct radical does. Indeed, there is a general impression that ester-substituted radicals cannot be used in addition reactions to electron-poor alkenes because the electronic pairing is not correct. However, rate constant measurements show that such reactions are reasonably rapid,[7] and substituent effects show that such radicals are only weakly 'electrophilic', and might better be termed 'enthalpic' radicals.[8] The successful UMCT result in Table 2, entry 7 shows that the problem with adding ester-substituted radicals to electron-poor alkenes by bimolecular chain transfer is one of selectivity. not electronic mismatching in the radical addition step.

The benefits of the UMCT method do not come without a price—the connection and disconnection of the silicon hydride to the reagent. However. the potential to conduct difficult radical reactions on a stoichiometric basis under practical experimental conditions suggests that the development and study of new types of UMCT reagents is worthwhile. In this regard, we view reagent **1** as a prototype for electron-poor UMCT radical acceptors. We are currently studying other methods of connectivity of the silicon hydride to the radical acceptor, and these should provide different classes of products.

Acknowledgements

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