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Hydro-dediazoniation of diazonium salts using trichlorosilane: new cleavage conditions for the T_1 traceless linker[1]

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Abstract

An efficient, selective cleavage of triazenes and in situ hydro-dediazoniation of the intermediately formed diazonium salts with trichlorosilane ($HSiCl_3$) in liquid as well on solid phase is reported. Starting from anilines, attachment to solid support and subsequent cleavage gives rise to the corresponding unsubstituted arenes. This cleavage reagent is compatible with various functionalities (esters, amides, nitro groups, halides, aliphatic double and triple bonds). © 2000 Elsevier Science Ltd. All rights reserved.

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The reduction of anilines to the corresponding unsubstituted arenes is a well-known[2] process in organic synthesis[3] and has been widely used for the synthesis of various compounds. In general, an intermediate diazonium salt is reduced using various reductants. Among the most successful examples are phosphinic acid derivatives,[4–6]which have become the standard, and sodium borohydride.[7] Various solvents such as methanol (with[8] or without copper salts), ethanol,[9] THF,[10] or DMF[11] are suitable hydrogen donors. Some transition-metal catalysts or mediators (copper,[12] iron,[11] and rhodium salts) are also applicable. However, most of the methods are not general and give only moderate yields especially for electron-rich arenes. In particular, formation of haloarenes or phenol/phenolether as by-products has been observed.

Recently, we have demonstrated the use of triazenes as linker moieties in solid phase organic synthesis to detach arenes in a traceless manner.[13–15] The cleavage conditions used (THF, HCl, and ultrasound), however, were not suitable for automation. In addition, we observed various amounts of polymeric by-products due to ring opening of THF. Therefore, we looked for alternatives for this cleavage/reduction protocol, which avoid the use of toxic materials, high-boiling reagents (bp >120°C) and complicated work-up procedures. Although methanol or ethanol are in principle suitable reductants, we observed various amounts of ether formation with less electron-poor arenes. Triethylsilane in dichloromethane is a suitable reductant, however, in some cases, the formation of triethylsilylarenes was observed.[16]

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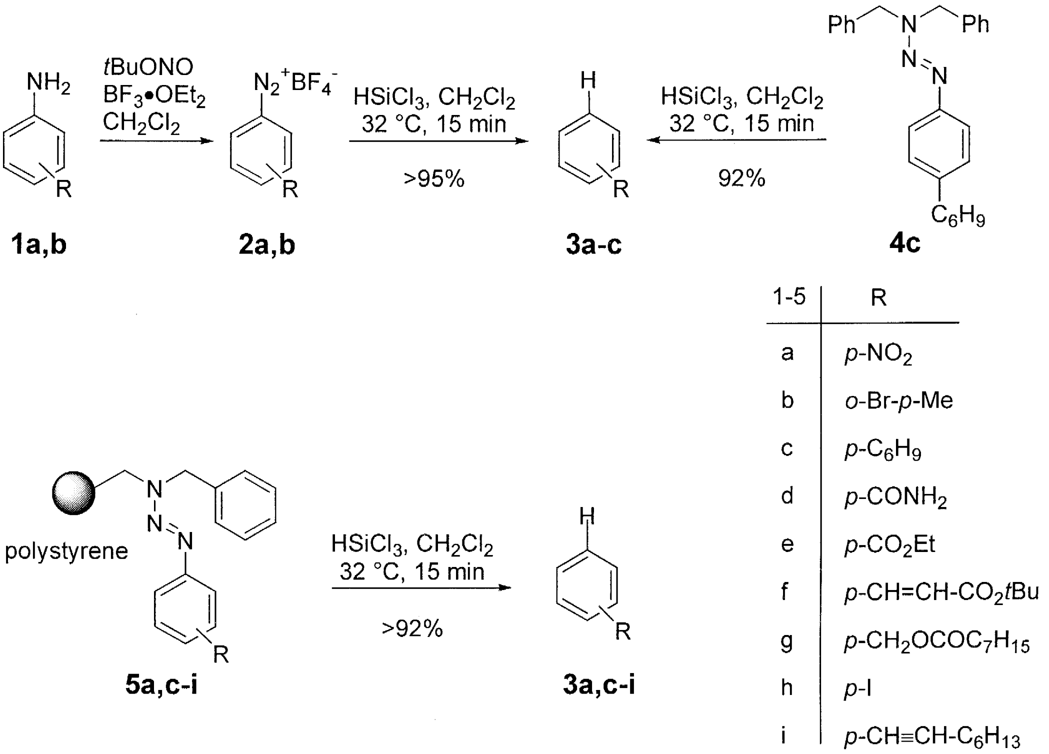
Trichlorosilane is an economical, volatile reagent (bp 32°C) with selective reducing properties (e.g. phosphine oxides to phosphines,[17] benzyl carbamate cleavage,[18] and reductive enolization of α-chloroketones[19]), which does not attack ketones,[18] triple bonds,[18] and double bonds[20] under metal-free conditions and in the absence of radical initiators. Furthermore, the by-products after hydrolysis (silicones) are readily removable. To best of our knowledge, the reduction of diazonium salts with this reagent has not been reported before.

Therefore, the use of trichlorosilane in the reduction of diazonium salts **2** was examined. The latter were readily prepared from the corresponding anilines (*t*BuONO, $BF_3 \cdot OEt_2$, CH_2Cl_2). Treatment of the crude salts **2** as a slurry with three equivalents of trichlorosilane in dichloromethane at room temperature, addition of silica gel after 15 min to remove the excess of trichlorosilane, filtration, and evaporation of the solvent gave rise to the arenes **3** in excellent yields.

Subsequently, the cleavage and reduction of a triazene in liquid phase was examined. The reaction of the triazene **4c** (Scheme 1) [mixture of 3-cyclohex-1-enyl and 4-cyclohex-1-enyl (ca. 70:30)] with trichlorosilane in dichloromethane proceeds cleanly to give the required hydrocarbons **3c** in excellent purity (>95%) and the corresponding amines as the hydrochloride salts, which were removed by filtration.



1-5	R
a	*p*-NO_2
b	*o*-Br-*p*-Me
c	*p*-C_6H_9
d	*p*-$CONH_2$
e	*p*-CO_2Et
f	*p*-CH=CH-CO_2*t*Bu
g	*p*-$CH_2OCOC_7H_{15}$
h	*p*-I
i	*p*-CH≡CH-C_6H_{13}

Scheme 1.

The execution of the solid phase synthesis was accomplished using the T_1 linker.[13,14,21] Starting from benzylaminomethyl polystyrene[22] (1–2% cross-linked with DVB, 100–200 mesh), the required diverse arylresins **5** were prepared from substituted anilines in good yields. Modifications of the triazenes [Heck reaction[13,21,23] (entries 3, 6, 7, 11) and acylation (entry 8)] were carried out to install various functionalities. The cleavage of the resin in the presence of trichlorosilane was conducted as above. Filtration and evaporation afforded the products **3** in 70 to 95% yield and over 90% purity without any further purification (NMR-, GC, and GC–MS spectroscopy).[24]

General procedure for the traceless cleavage of the T_1 linker: A suspension of the resin (200 mg) in dichloromethane was treated with 4 equiv. of trichlorosilane (Caution: corrosive and low boiling material) and the mixture was stirred at 40°C (external) for 15 min or at room temperature for 60 min. After being cooled to room temperature, silica gel (100 mg) was added, the mixture was filtered and the solvent was removed (Table 1).

Table 1
Cleavage and reduction conducted with trichlorosilane

Entry	Triazene/Diazonium salt	Product	Purity[a] [%]
1	**2a**	**3a**	96
2	**2b**	**3b**	95
3	**4c**[b]	**3c**[b]	92
4	**5d**	**3d**	95
5	**5e**	**3e**	93
6	**5c**[b]	**3c**[b]	92
7	**(*E*)-5f**	**(*E*)-3f**	93[c]
8	**5g**	**3g**	96
9	**5a**	**3a**	96
10	**5h**	**3h**	95
11	**(*E*)-5i**	**(*E*)-5i**	91

[a] The yields of the solution phase reactions exceed 90%. The yields of the solid phase reactions are higher than 70% based on the loading of the aminoresin.

[b] Mixture of 3-cyclohex-1-enyl and 4-cyclohex-1-enyl (ca. 70:30).

[c] The formation of *tert*.-butyl *p*-chlorocinnamate (2.2%) was also detected.

The compatibility with functional groups is in the expected range (Scheme 1). Alkenes, alkynes, *tert*-butyl and other esters, nitro groups, and halides are tolerated. Both electron withdrawing and electron-donor substituents can be present in the target molecule.

In conclusion, a novel technique for the hydro-dediazoniation of diazonium salts was developed, giving rise to products in high yield and purity. The method was also successfully applied in the traceless cleavage of the T_1 triazene linker.

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24. The polymeric compounds were characterized by IR and elemental analysis; the deaminated products **3** were characterized by NMR methods, GC–MS, and comparison with authentic samples. The purity and yields were determined by GC and GC–MS measurements.