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Dehalogenation of Organic Halides using the $NiCl_2 \cdot 2H_2O$-Li-DTBB (cat.) Combination[1]

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Abstract

The reaction of different chlorinated, brominated or iodinated materials, bearing or without a functional group, with a mixture of nickel(II) chloride dihydrate, an excess of lithium powder and a catalytic amount of 4,4'-di-*tert*-butylbiphenyl (DTBB) (5 mol%) in THF at room temperature, leads to the formation of the corresponding products resulting from a halogen/hydrogen exchange. The use of deuterium oxide instead of water in the nickel salt allows the corresponding deuteration. This methodology does not work with fluorinated materials.

Keywords: Reduction; Dehalogenation; Nickel; Arene-catalysis

I. Introduction

Dehalogenation of organic halides is accomplished in general by using hydrogen and a transition metal as well as with metal hydrides. Alkali metals, alumina, magnesium and especially zinc and some metal compounds such as chromous sulfate and samarium diiodide have also been used for the same purpose [1-15].[2,3,4] On the other hand, chlorinated organic molecules, especially aromatic compounds, represent a major environmental problem because they are extremely persistent due to their slow degradation by reductive or oxidative enzymatic pathways [15,17], so efficient ways to dehalogenate these recalcitrant compounds are welcome.

Recently we have applied an arene-catalysed lithiation process [18,19][5] for the activation of dihydrated nickel(II) chloride. This combination has shown to be very effective for the hydrogenation of alkenes [21], alkynes [22] or carbonyl compounds and their imine derivatives [23]. In this paper we describe the application of this methodology to the dehalogenation of organic halides, especially studying the corresponding chlorinated compounds.

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[1] Part 4 in the series "The $NiCl_2 \cdot 2H_2O$-Li-arene combination as reducing system". For part 3 see reference [23].

[2] For general information see references [1-6].

[3] For recent reports see references [7-13].

[4] For the reduction of organic halides with magnesium and isopropyl alcohol, see references [14,15].

[5] For the last paper from our laboratory on the application of this methodology, see reference [20].

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II. Results and discussion

The reaction of 1-chlorodecane with a mixture of nickel(II) chloride dihydrate (1:1 molar ratio), an excess of lithium powder (1:8 molar ratio, referred to the nickel salt) and a catalytic amount of 4,4'-di-*tert*-butylbiphenyl (DTBB) (0.1 mol/mol of nickel salt, 10 mol%) in tetrahydrofuran at room temperature, led to decane as the only reaction product (Table 1, entry 1). The same procedure applied to different aliphatic or aromatic chlorinated materials bearing or without a functional group led to the expected products (Table 1, entries 3, 4, 6, 8, 9 and 11), even when the molecule contained more than one chlorine atom (Table 1, entry 10). The use of $NiCl_2{\cdot}2D_2O$ instead of the corresponding dihydrate afforded the expected deuterated materials (Table 1, entries 2, 5, and 7), this methodology being very convenient for the preparation of deuterium labelled compounds taking into account the deuterium source used.

Even considering that chlorinated materials are more accesible, stable, and cheap than the corresponding brominated ones, the method can be applied to this last type of compounds as illustrated in Table 1, entries 12-15, for aliphatic or aromatic starting materials. In addition, the methodology described above is also applicable to iodinated compounds, so as an example 2-iodoethylbenzene was reduced to ethylbenzene in good yield (Table 1, entry 16). Finally, it is worthy to note that fluorinated materials (for instance 1-fluorononane) are inert to the procedure describe here. It should be pointed out that when the above experiments were carried out in the absence of the hydrated nickel salt or using the anhydrous nickel salt, the yields obtained were much lower due to the formation of byproducts, among them coupling products.

Concerning a possible mechanism for the reduction of halogenated compounds, the nickel salt is reduced to nickel(0) (a black precipitate is always formed) and at the same time molecular hydrogen (or deuterium) is formed and probably adsorbed on the surface of the metal (no gas evolution was observed in any case), affording the halogen/hydrogen exchange. As an alternative, the formation of nickel hydride species acting as intermediates in the reduction step can not be ruled out [24].

III. Conclusion

As a conclusion, we think that the methodology describe herein can be useful for halogen/hydrogen exchange under very mild reaction conditions, one noteworthy remark being the introduction of deuterium by using deuterium oxide as a cheap and easily accessible isotopic source.

IV. Experimental section

IV.1. General

Melting points were obtained with a Reichert Thermovar apparatus. NMR spectra were recorded on a Bruker AC-300 (300 MHz for ^{1}NMR and 75 MHz for ^{13}C) using $CDCl_3$ as solvent and TMS as internal standard; chemical shifts are given in δ (ppm) and coupling constants (*J*) in Hz. Mass spectra (EI) were obtained at 70 eV on a Shimadzu QP-5000 spectrometer, fragment ions in m/z with relative intensitites (%) in parenthesis. The purity of volatile and the chromatographic analyses (GLC) were determined with a Hewlet Packard HP-5890 instrument equipped with a flame ionization detector and a 12 m capillary column (0.2 mm diam, 0.33 mm film thickness), using nitrogen (2 ml/min) as carrier gas, $T_{injector}$ = 275°C,

Table 1
Reduction of halogenated compounds

$$\mathrm{RHal} \xrightarrow[\text{Li, DTBB (cat.)}]{NiCl_2{\cdot}2H_2O} \mathrm{RH}$$

Entry	Starting material	Product[a]	Yield (%)[b]
1	$CH_3(CH_2)_8CH_2Cl$	$CH_3(CH_2)_8CH_3$	80 (55)[c]
2[d]	$CH_3(CH_2)_8CH_2Cl$	$CH_3(CH_2)_8CH_2D$	98 (53)[c,e]
3	$HO(CH_2)_5CH_2Cl$	$HO(CH_2)_5CH_3$	98 (51)[f]
4	$PhCH_2CH_2Cl$	$PhCH_2CH_3$	99 (50)[f]
5[d]	$PhCH_2CH_2Cl$	$PhCH_2CH_2D$	99 (56)[f,g]
6	Ph_3CCl	Ph_3CH	94 (66)[c]
7[d]	Ph_3CCl	Ph_3CD	93 (60)[c,h]
8	$4\text{-}ClC_6H_4CH_2OH$	$PhCH_2OH$	84 (53)[c]
9	$4\text{-}ClC_6H_4OH$	PhOH	98 (73)[i]
10	$3,5\text{-}Cl_2C_6H_3OH$	PhOH	99 (90)[i]
11	$4\text{-}ClC_6H_4NH_2$	$PhNH_2$	92 (65)[c]
12	$CH_3(CH_2)_{14}CH_2Br$	$CH_3(CH_2)_{14}CH_3$	99 (75)[c]
13	$HO(CH_2)_5CH_2Br$	$HO(CH_2)_5CH_3$	98 (57)[f]
14	$4\text{-}BrC_6H_4Me$	PhMe	99
15	$4\text{-}BrC_6H_4Ph$	PhPh	89 (65)[c,j]
16	$PhCH_2CH_2I$	$PhCH_2CH_3$	89 (54)[f]

[a] All products were >95% pure (GLC). [b] GLC yield based on the starting organic halide; isolated yields are given in parenthesis. [c] Purified by column chromatography (silica gel, hexane/ethyl acetate). [d] $NiCl_2{\cdot}2D_2O$ was used instead of $NiCl_2{\cdot}2H_2O$. [e] 74% deuterium incorporation (mass spectrometry, 300 MHz ^1H NMR). [f] Purified by distillation. [g] 70% deuterium incorporation (mass spectrometry, 300 MHz ^1H NMR). [h] 58% deuterium incorporation (mass spectrometry, 300 MHz ^1H NMR). [i] Purified by acid/base work-up. [j] 55% isolated yield (71%, GLC) was obtained in the absence of the catalyst.

T_{column} = 60°C (3 min) and 60-270°C (15°C/min). Column chromatography was performed using silica gel 60 of 40-60 microns. All starting compounds were of the best available grade (Acros, Aldrich, Fluka) and were used without further purification. THF was dried over benzophenone ketyl under an argon atmosphere and distilled before use. Dihydrated nickel(II) chloride was prepared from commercially available nickel(II) chloride hexahydrate by heating *in vacuo* (*ca.* 0.5 torr) at 100°C in Kugelrohr during 2 h; its deuterated derivative was prepared by treating commercially available anhydrous nickel(II) chloride with an excess of deuterium oxide and then the same thermal treatment as for the hydrated salt.

IV.2. Reduction of halogenated compounds using the $NiCl_2{\cdot}2H_2O$-Li-DTBB combination.

General procedure.- To a mixture of $NiCl_2{\cdot}2H_2O$ (166 mg, 1.0 mmol) or its deuterated salt, lithium powder (56 mg, 8.0 mmol) and DTBB (27 mg, 0.1 mmol), was a added a solution of the halogenated compound (1.0 mmol) in THF (10 ml) at room temperature under an argon atmosphere. The reaction mixture, which was initially dark green, changed to black, indicating the formation of nickel(0). After total conversion of the starting material (GLC; all the reaction times were less than 4 h), the resulting suspension was diluted with ether (20 ml) and filtered off through a pad containing silica gel and celite (*ca.* 3:1). The filtrate was dried with anhydrous sodium sulfate, evaporated (760 or 15 Torr) and the resulting residue purified as noted in Table 1. Acidic work-up with diluted HCl was employed for phenolic products. Reduced products were fully characterised by comparison of their chromatographic and spectral data with those of the corresponding commercially available pure samples (decane, hexan-1-ol, ethylbenzene, triphenylmethane, benzyl alcohol, phenol, aniline, hexadecane, toluene, and biphenyl). For the rest of compounds included in Table 1, physical and spectroscopic data, as well as literature references for known compounds follow:

1-Deuteriodecane [25]: Colorless oil; t_r 6.51; δ_H 0.89 (5H, m, CH_3, CH_2D), 1.23-1.30 (16H, m, 8xCH_2); δ_C 13.8 (t, J = 19.5, CH_2D), 14.1 (CH_3), 22.6, 22.7, 29.4, 29.65, 29.7, 31.35, 31.4, 31.95 (8xCH_2); *m/z* 143 (M^+, 2%), 85 (14), 72 (12), 71 (26), 58 (33), 57 (78), 56 (20), 55 (16), 44 (38), 43 (100), 42 (34), 41 (67).

2-Deuterioethylbenzene [26]: Colorless oil; t_r 4.07; δ_H 1.20-1.28 (2H, m, CH_2D), 2.63-2.70 (2H, m, CH_2CH_2D), 7.15-7.32 (5H, m, ArH); δ_C 15.3 (t, J = 19.5, CH_2D), 28.8 (t, J = 6.1, CH_2), 125.6, 127.85, 128.3, 144.25 (ArC); *m/z* 108 (M^++1, 13%), 107 (M^+, 29), 106 (12), 93 (27), 92 (85), 91 (100), 78 (15), 65 (14), 52 (16), 51 (28).

Deuteriotriphenylmethane [27, 28]: Colorless solid; t_r 16.07; m.p. 93.5-94.5°C (ethanol) (lit. [29] 93.0-94.5°C, ethanol); δ_H 7.08-7.17 (6H, m, ArH), 7.20-7.31 (9H, m, ArH); δ_C 56.89 (CD), 126.3, 128.35, 129.5, 143.95 (ArC); *m/z* 246 (M^++1, 19%), 245 (M^+, 100), 244 (81), 243 (22), 168 (60), 167 (80), 166 (86), 165 (93), 153 (18), 152 (21), 114 (15), 51 (14).

V. Acknowledgments

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VI. References

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