Tele vs. Oxidative Substitution of Hydrogen in *meta* Monochloromethyl, Dichloromethyl, and Trichloromethyl Nitrobenzenes in the Reaction with Grignard Reagents

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Grignard reagents add to nitrobenzene derivatives containing trichloromethyl, dichloromethyl, and monochloromethyl groups in the *meta* position to form σ^H adducts, which are either further converted through departure of a chloride anion, giving products of *tele* substitution, or oxidized to products of oxidative nucleophilic substitution of hydrogen.

Introduction

Nucleophilic substitution of hydrogen in nitroarenes proceeds through addition of anionic nucleophiles in positions occupied by hydrogen *ortho* and *para* to the nitro group. The formed anionic σ^H adducts are further converted into products of nucleophilic substitution of hydrogen in a variety of ways.[1,2] Perhaps the most general of these is vicarious nucleophilic substitution (VNS), when nucleophiles contain leaving groups X at the nucleophilic centre. Anionic σ^H adducts formed by such nucleophiles undergo base-induced β-elimination, giving products of VNS in the form of anions.[3,4] Of great importance is oxidation of σ^H adducts with a variety of oxidants, giving products of oxidative nucleophilic substitution of hydrogen (ONSH).[1,2,5,6] Oxidation of some σ^H adducts with dimethyldioxirane proceeds in a different way, the oxidant reacting with the negatively charged nitro groups, and these thus being replaced by hydroxy groups.[7]

When the starting electrophilic arene contains a nucleofugal group suitably located in a position remote from the addition site, the intermediate σ^H adducts can lose such groups, giving products of so-called *tele* substitution.[8] This process can proceed in electrophilic arenes containing leaving groups in a variety of positions. Perhaps the most interesting cases are nitroarenes or heteroarenes containing trichloromethyl substituents, which not only provide leaving groups suitably located for the *tele* substitution, but also significantly increase the electrophilic activity of the rings. Thus, treatment of 1-nitro-3-(trichloromethyl)benzene (**1**) with sodium methoxide in methyl alcohol gave the dimethylacetal of 4-methoxy-3-nitrobenzaldehyde.[9] There are many reported examples of similar processes.[8]

To the best of our knowledge, though, there are no examples in the literature of *tele* substitution between 1-nitro-3-(trichloromethyl)benzene (**1**) and carbon nucleophiles. Since the Grignard reagents represent an interesting class of carbon nucleophiles able to add to nitroaromatic rings to produce relatively stable σ^H adducts,[10] we decided to study the reactions of these nucleophiles with 1-nitro-3-(trichloromethyl)benzene (**1**).

Results and Discussion

Alkylmagnesium halides add to the electron-deficient rings of nitroarenes *ortho* and *para* to the nitro group, giving σ^H adducts that can be oxidized with a variety of oxidants, particularly $KMnO_4$, to produce alkylated nitroarenes.[10,11] This oxidative nucleophilic alkylation of nitroarenes with the Grignard reagents has substantial value in organic synthesis. We expected that the Grignard reagent should add to 1-nitro-3-(trichloromethyl)benzene (**1**) to produce a σ^H adduct that would lose Cl^- anion according to the *tele* substitution scheme to give ring-alkylated 1-nitro-3-(dichloromethyl)benzenes.

Indeed, treatment of **1** with methylmagnesium chloride in a ratio of 1:1, followed by the addition of liquid ammonia, gave the expected 3-(dichloromethyl)-1-nitro-6-

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methylbenzene (**2**) in a moderate yield of 21%. This product of *tele* substitution was accompanied with another product, **2b**, of the same $C_8H_7Cl_2NO_2$ composition. The ^1H NMR spectrum of **2b** indicated that it was not a simple positional isomer of **2**. The signal of the methyl group in the ^1H NMR spectrum of **2b** is shifted upfield and appears at δ = 1.30 ppm as a doublet with J = 7 Hz, while the signals of the ring protons are also shifted upfield (δ = 7.4, 6.85, 6.22, and 4.4 ppm, the last of these appearing as a quadruplet with J = 7 Hz). From these data it can be concluded that the compound does not contain an aromatic ring and is most probably 5-dichloromethylene-1-nitro-6-methylcyclohexa-1,3-diene (**2b**). It appears that **2a** and **2b** are produced by addition of MeMgCl to the electron-deficient ring of **1** in positions 6 and 2, respectively, to give two isomeric σ^H adducts that undergo further elimination of Cl^- anions to form isomeric *exo*-dichloromethylene cyclohexadienes **2a** and **2b**. The first, **2a**, undergoes re-aromatization through a 1,5-hydrogen shift to give **2**, whereas no similar conversion of **2b** occurs, most probably because of unfavourable stereochemistry. When an excess of MeMgCl (2 mol) was used in the reaction with **1** it added to **2a** and **2b** to give two isomeric cyclohexene derivatives **2c** and **2d**. It thus appears that addition of MeMgCl to **2a** proceeds more rapidly than its rearomatization to **2**. Since a second molecule of MeMgCl adds to intermediates **2a** and **2b** before their rearomatization to *tele* products, and not to the initially formed σ^H adducts, we can assume that rearomatization is facilitated by liquid ammonia.

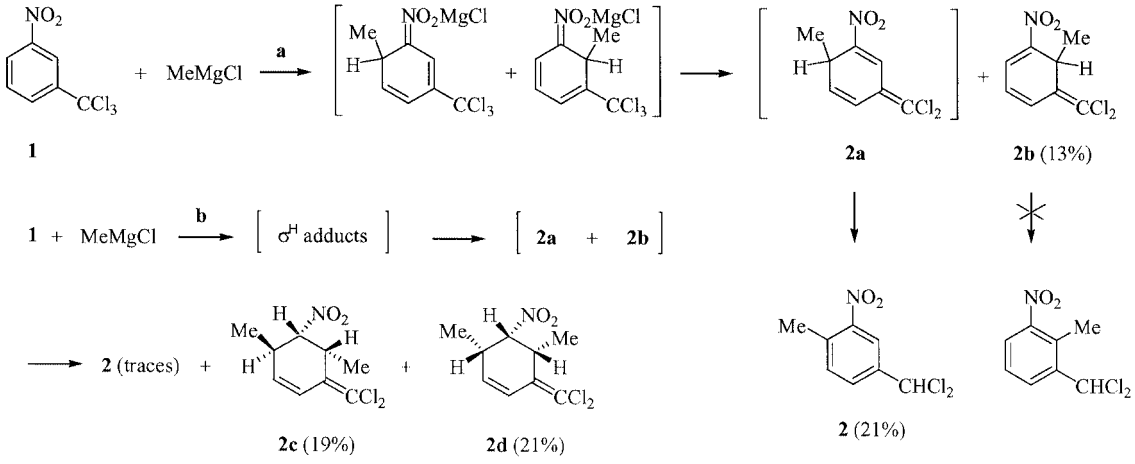
A ^1H NMR investigation of **2c** and **2d** showed that hydrogen atoms 4-H, 5-H, and 6-H of compound **2d** are located on the same side of the cyclohexene ring (J_{4H-5H} = 2.8, J_{6H-5H} = 2.0 Hz). In compound **2c**, hydrogen atoms 4-H and 5-H are located on the same side of the cyclohexene ring (J_{4H-5H} = 4.4 Hz) whereas 6-H is located on the opposite side (J_{6H-5H} = 10.5 Hz). The structures of compounds **2c** and **2d** were confirmed by ^1H NMR, NOE, COSY, and by selective decoupling techniques.

When compound **1** was treated with an equimolar amount of butylmagnesium chloride, followed by the addition of liquid ammonia, the expected products of *tele* substitution, 6-butyl-3-(dichloromethyl)-1-nitrobenzene (**3**) and 4-butyl-3-(dichloromethyl)-1-nitrobenzene (**4**), were formed in a ratio of 3.5:1. The overall yield of the mixture of positional isomers **3** and **4** was 51%. It is noteworthy that although the formation of product **3** can be explained by a mechanism analogous to that given for compound **2** (Scheme 1), which is similar to the formation of **4** in the first two steps, there is an important difference in the last step, in which a 1,3-hydrogen shift takes place in order to effect aromatization (Scheme 2). This is the first time that a 1,3-hydrogen shift has been reported for a *tele* nucleophilic aromatic substitution. On the other hand, when compound **1** was treated with an excess of the Grignard reagent in a ratio of 1:2, followed by the addition of liquid ammonia, the main product was the double adduct **3b**. We assume that **3b** was produced through the addition of the second molecule of BuMgCl to the intermediate **3a**. Apparently this addition proceeds more rapidly than the 1,5-hydrogen shift and rearomatization of **3a** to afford product **3**.

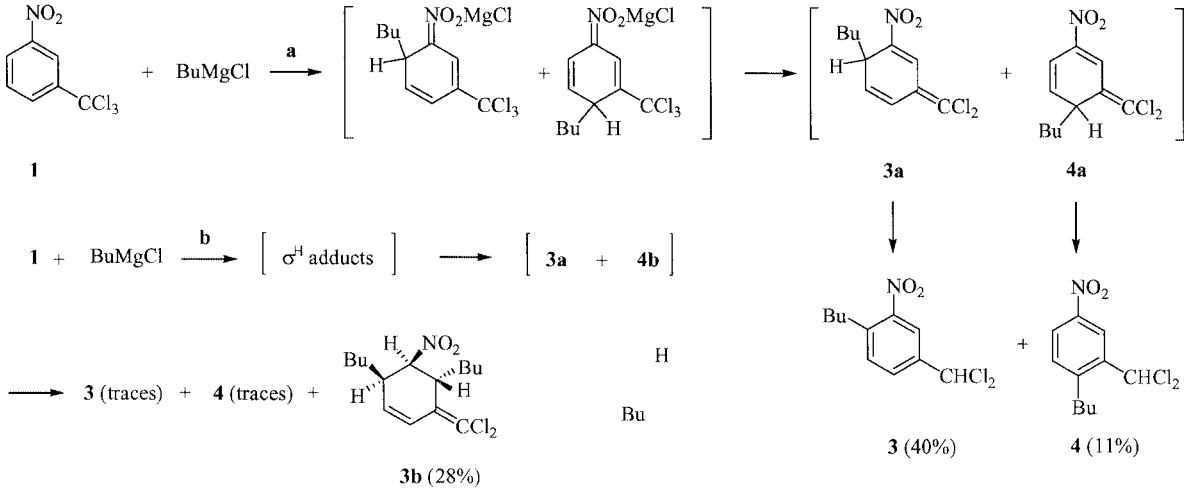
It should be stressed that when a mixture of **1** with BuMgCl was treated at −70 °C with $KMnO_4$ in liquid ammonia or with DDQ we were unable to isolate any defined product. Apparently the Grignard reagent adds to the compound **1** to form a σ^H adduct that undergoes rapid elimination of chloride anion to produce compounds **3a** and **4a**, which are unstable in the presence of oxidants. We therefore conclude that elimination of chloride anion from the σ^H adducts of Grignard reagents to **1** is a very fast process, so it is impossible to trap them by oxidation, whereas hydrogen shift and rearomatization are a slow processes under the reaction conditions.

The reaction between compound **1** and 2-phenylethylmagnesium chloride in a ratio of 1:1, followed by the addition of liquid ammonia, proceeded smoothly and gave 3-(dichloromethyl)-1-nitro-6-(2-phenylethyl)benzene (**5**) and 3-(dichloromethyl)-1-nitro-4-(2-phenylethyl)benzene (**6**) in a ratio of 3.7:1, overall yield 42% (Scheme 3).

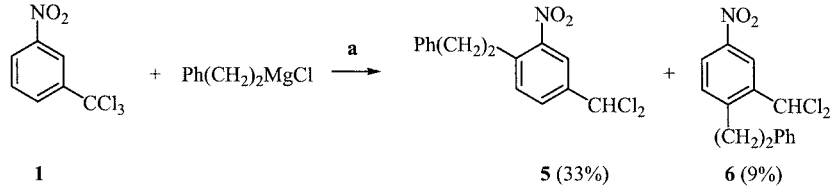
In the reactions described so far it was observed that all of starting material **1** was consumed when treated with 1



Scheme 1. Conditions: (a) THF, −70 °C, (ratio of **1** to MeMgCl, 1:1), then $NH_{3(liq.)}$, −70 °C to room temp.; (b) THF, −70 °C, (ratio of **1** to MeMgCl, 1:2), then $NH_{3(liq.)}$, −70 °C to room temp.

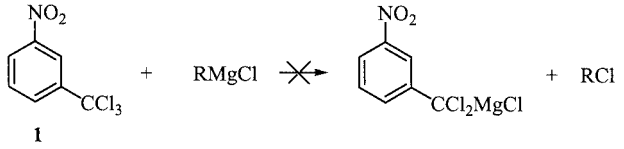


Scheme 2. Conditions: (a) THF, −70 °C, (ratio of **1** to BuMgCl, 1:1), then $NH_{3(liq.)}$, −70 °C to room temp.; (b) THF, −70 °C, (ratio of **1** to BuMgCl, 1:2), then $NH_{3(liq.)}$, −70 °C to room temp.



Scheme 3. Conditions: (a) THF, −70 °C [ratio of **1** to $Ph(CH_2)_2MgCl$, 1:1], then $NH_{3(liq.)}$, −70 °C to room temp.

equivalent of the Grignard reagents. It should be stressed that in our previous studies we have found that 1.5 equivalents of RMgX are needed for complete conversion of nitroarenes.[11] In the reactions of **1** with RMgX, yields of the products were moderate, although starting **1** was completely consumed. Obviously the reaction between the Grignard reagents and compound **1** was accompanied by competing reactions. The main competing process appears to be the halophilic attack of the Grignard reagents on the CCl_3 group, resulting in formation of alkyl chlorides and dichloromethylmagnesium chloride. These products have not been observed in any of the reactions. (Scheme 4).



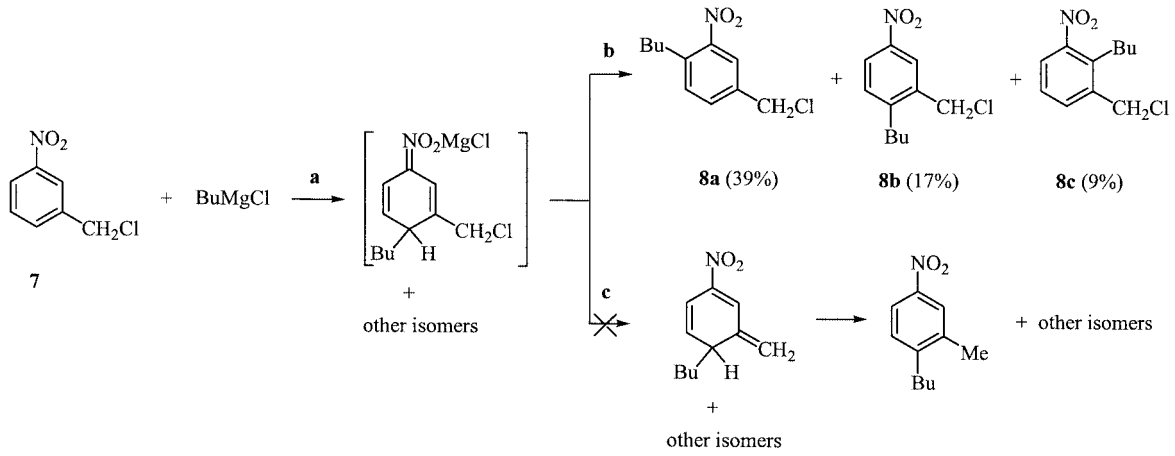
Scheme 4. Formation of these products has not been observed

Indeed, substantial amounts of *n*-butyl chloride and 2-phenylethyl chloride were found by gas chromatography in the reaction mixtures of **1** with BuMgCl and $PhCH_2CH_2MgCl$. We were unable, however, to find 3-(dichloromethyl)-1-nitrobenzene, or any other products resulting from the breakdown of 3-dichloromethylmagnesium(nitrophenyl) chloride. A plausible explanation is that it is unstable and decomposes rapidly.

The isolation and stability of compounds **2b**, **2c**, **2d**, and **3b** merits further comment. It appears that the rate of the rearomatization of the cyclohexadiene derivative **2b** produced after elimination of the chloride anion from the σ^H adduct is slow due to steric hindrance, whereas **2a**, **3a**, and **4a** do not experience steric difficulties for rearomatization through 1,5- and 1,3-hydrogen shifts. Even in these cases, however, the rates of rearomatization are not very high, and so when the Grignard reagent is present in excess its addition to the nitroethylene moiety of **2a**, **2b**, and **3a** proceeds more rapidly, so **2c**, **2d**, and **3b** are produced.

Looking for a better model for observation of the *tele* substitution and oxidation of σ^H adducts, we have chosen 3-(chloromethyl)-1-nitrobenzene (**7**). Bartoli[10] has found that Grignard reagents add to the ring of 4-(chloromethyl)nitrobenzene and that the σ^H adduct thus formed could be oxidized so the ONSH proceeded satisfactorily. We have found that *n*-butylmagnesium chloride also adds to **7** to give σ^H adducts, which do not lose chloride anion according to the *tele* substitution pattern, even when kept for long period at 0 °C. On the other hand, these σ^H adducts can be efficiently oxidized with tetrabutylammonium permanganate to give a mixture of isomers of butyl(chloromethyl)nitrobenzenes **8**, with an overall yield of 65% (Scheme 5).

Compounds **1** and **7** reacted with the Grignard reagents in different ways: through *tele* substitution and through the ONSH process. We reasoned that 3-(dichloromethyl)-1-nitrobenzene should occupy an intermediate position and



Scheme 5. Conditions: (a) THF, −70 °C (ratio of **7** to BuMgCl, 1:1.5), then (b) Bu_4NMnO_4, −70 °C to room temp., or (c) aq. HCl, 0 °C

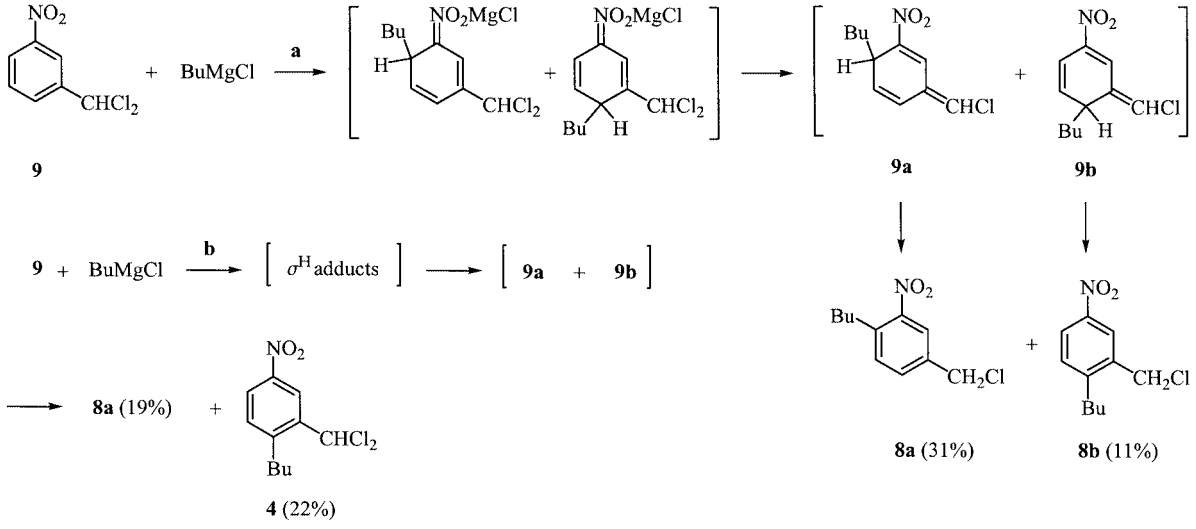
expected that competition between *tele* substitution and the ONSH process should be observable in reactions between Grignard reagents and 3-(dichloromethyl)-1-nitrobenzene (**9**).

When compound **9** was treated with *n*BuMgCl in THF at −70 °C, followed by addition of liquid ammonia, it was postulated to give two isomeric σ^H adducts resulting from addition at positions 6 and 4 (Scheme 6). These σ^H adducts lose chloride anion and then undergo 1,5- or 1,3-hydrogen shifts in the presence of the liquid ammonia to form products of *tele* substitution **8a** and **8b** in 31% and 11% yields, respectively (Scheme 6). When the reaction was repeated and DDQ was added in place of liquid ammonia, *tele* substitution product **8a** was isolated in 19% yield and the ONSH product **4** was obtained in 22% yield.

On the basis of the results shown in Scheme 6, we can propose that the σ^H adduct resulting from addition to position 6 of **9** undergoes rapid loss of chloride anion to give intermediate **9a**, followed by a 1,5-hydrogen shift and rearomatization to give **8a**. On the other hand, similar conversion of the σ^H adduct to **9b**, resulting from addition to position 4 of **9**, proceeds more slowly, so it can be oxidized to **4**.

Conclusions

Methyl-, 2-phenylethyl-, and *n*-butylmagnesium chloride react with 1-nitro-3-(trichloromethyl)benzene by addition to the positions *ortho* or *para* to the nitro group to produce σ^H adducts, which lose chloride anion from the CCl_3 group and give relatively stable cyclohexadiene intermediates. Addition of liquid ammonia to the reaction mixture induces 1,3- or 1,5-hydrogen shifts to give products of *tele* nucleophilic substitution. In the case of methylmagnesium chloride, 5-(dichloromethylene)-6-methyl-1-nitrocyclohexa-1,3-diene was isolated. If a second equivalent of the Grignard reagent is present in the reaction mixture, further addition of methyl and *n*-butyl anion occurs to the cyclohexadienes, which leads to cyclohexene derivatives.



Scheme 6. Conditions: (a) THF, −70 °C (ratio of **9** to BuMgCl, 1:1.5), then $NH_{3(liq.)}$, −70 °C to room temp.; (b) THF, −70 °C (ratio of **9** to BuMgCl, 1:1.5), then DDQ, −70 °C to room temp.

The addition of *n*-butylmagnesium chloride to 3-(chloromethyl)-1-nitrobenzene, followed by treatment with *n*-tetrabutylammonium permanganate, afforded three isomeric ONSH products. The reaction pattern of 3-(dichloromethyl)-1-nitrobenzene with *n*-butylmagnesium chloride can be controlled to give *tele* substitution products when addition of liquid ammonia follows, or an ONSH product, together with a *tele* substitution product, when addition of DDQ follows.

Experimental Section

General Remarks: Melting points are uncorrected. Infrared spectra were recorded on a Perkin−Elmer FT-IR spectrometer, solids as Nujol mulls and liquids as thin films between sodium chloride discs. Nuclear magnetic resonance spectra were measured at 400 MHz on Mercury-400BB or Bruker AMKS (500 MHz) spectrometers. Chemical shifts are reported in ppm relative to tetramethylsilane as internal standard. Mass spectra were obtained by use of an AMD 604 Inectra GmbH EI instrument. Data are given for ions containing ^{35}Cl or ^{37}Cl. Appropriate isotope patterns were observed. Analytical TLC was carried out on Merck Alufolien Kieselgel 60 F_{254} sheets, while Lachema silica gel was used for preparative TLC. For preparative HPLC, Merck-Hitachi equipment was used with a L-7100 detector VL-7400 pump, and with hexane as a solvent.

Solvents and reagents were used as received from the manufacturers, except for tetrahydrofuran, which was distilled from over potassium benzophenone ketyl before use

General Procedure for Treatment of 1-Nitro-3-(trichloromethyl)benzene (1) with Grignard Reagents: A solution of alkylmagnesium halide (1.0 or 2.0 mmol) in tetrahydrofuran was added dropwise over ca. 1 min to a stirred solution of **1** (241 mg, 1 mmol) in tetrahydrofuran (10 mL), cooled to −70 °C under argon. After 5 min, liquid ammonia (5 mL) was added and the reaction mixture was stirred for 15 min. Ammonium chloride (100 mg, 2 mmol) was added, and the cooling bath was then removed. When the ammonia had evaporated, the reaction mixture was filtered through silica gel, which was then washed with dichloromethane (4 × 10 mL). After evaporation of the solvent, the products were purified either by preparative thin layer chromatography with hexane as an eluent to give a mixture of 3-dichloromethyl-6-methyl-1-nitrobenzene (**2**) and 5-dichloromethylene-6-methyl-1-nitrocyclohexa-1,3-diene (**2b**), which was separated further by preparative HPLC, or directly by HPLC to give pure compounds: 3-(dichloromethylene)-4,6-dimethyl-5-nitrocyclohex-1-ene isomers **2c** and **2d**, 6-butyl-3-(dichloromethyl)-1-nitrobenzene (**3**), 4-butyl-3-(dichloromethyl)-1-nitrobenzene (**4**), 3,5-dibutyl-6-dichloromethylene-4-nitrocyclohexene (**3b**), 3-(dichloromethyl)-1-nitro-6-(2-phenylethyl)benzene (**5**), or 3-(dichloromethyl)-1-nitro-4-(2-phenylethyl)benzene (**6**).

3-(Dichloromethyl)-6-methyl-1-nitrobenzene (2): Yield 0.047 g, 21%, pale yellow oil. ^1H NMR (400 MHz, $CDCl_3$) δ: 2.64 (s, 3 H, Me), 6.74 (s, 1 H, $CHCl_2$), 7.43 (d, J = 8 Hz, 1 H, 5-H), 7.74 (dd, J = 8, J = 2 Hz, 1 H, 5-H), 8.19 (d, J = 2 Hz, 1 H, 4-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.3, 69.7, 122.5, 130.5, 133.5, 135.4, 139.6, 148.9 ppm. MS (EI): *m*/*z* (%) = 221 (5.7), 219 (8.5), 204 (28.9), 202 (44.3), 186 (32.9), 184 (100.0). HRMS (EI) $(M)^+$ found 220.98307. $C_8H_7NO_2{}^{35}Cl^{37}Cl$ requires 220.98243. IR (liquid film): 1623, 1532, 1351, 823, 733 cm^{-1}. UV (abs): 253 (0.131), 217 (0.481), 198 nm (0.345). $C_8H_7Cl_2NO_2$: calcd. C 43.67, H 3.21, N 6.37, Cl 32.22%; found C 43.49, H 3.40, N 6.25, Cl 32.48%.

5-(Dichloromethylene)-6-methyl-1-nitrocyclohexa-1,3-diene (2b): Yield 0.029 g, 13%, yellow oil. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.30 (d, J = 7 Hz, 3 H, Me), 4.40 (q, J = 10 Hz, 1 H, 6-H), 6.22 (dd, J = 10, J = 6 Hz, 1 H, 3-H), 6.85 (d, J = 10 Hz, 1 H, 4-H) 7.42 (d, J = 6 Hz, 1 H, 2-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 18.3, 34.3, 120.8, 122.7, 126.0, 129.5, 136.3, 151.0 ppm. MS (EI): *m*/*z* (%) = 221 (11.4), 219 (17.4), 204 (100.0), 202 (8.5), 175 (12.7), 173 (18.5), 160 (22.9), 158 (35.5). HRMS (EI) $(M)^+$ found 220.98281. $C_8H_7NO_2{}^{35}Cl^{37}Cl$ requires 220.98243. IR (liquid film): 1534, 1510, 1324, 915, 733 cm^{-1}. UV (abs): 383 (0.223), 255 (0.323), 201 nm (0.577). $C_8H_7Cl_2NO_2$: calcd. C 43.67, H 3.21, N 6.37, Cl 32.22%; found C 43.56, H 3.31, N 6.32, Cl 32.42%.

(±)-3-(Dichloromethylene)-4,6-dimethyl-5-nitrocyclohex-1-ene Isomer (2c): Yield 0.045 g, 19%, orange oil. ^1H NMR (500 MHz, $CDCl_3$) δ: 1.04 (d, J = 6.9 Hz, 3 H, Me-4), 1.14 (d, J = 6.8 Hz, 3 H, Me-6), 3.10−3.19 (m, 1 H, 6-H), 3.64 (dq, J = 6.9, J = 4.4 Hz, 1 H, 4-H), 4.33 (dd, J = 10.5, J = 4.4 Hz, 1 H, 5-H), 5.67 (dd, J = 10.1, J = 2.4 Hz, 1 H, 1-H), 6.39 (ddd, J = 10.1, J = 2.8, J = 1.0 Hz, 1 H, 2-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 12.2, 18.1, 29.6, 36.9, 90.9, 118.9, 121.7, 133.5, 134.4 ppm. ^{13}C NMR DEPT (100 MHz, $CDCl_3$) δ: 12.2, 18.1, 29.6, 36.9, 90.9, 121.7, 133.5 ppm. MS (EI): *m*/*z* (%) = 237 (7.7), 235 (12.5), 220 (4.0), 218 (6.1), 189 (39.3), 188 (33.0), 175 (65.2), 173 (100.0), 153 nm (78.5). HRMS (EI) found 235.01657. $C_9H_{11}NO_2{}^{35}Cl_2$ requires 235.01668. $C_9H_{11}NO_2Cl_2$: calcd. C 45.79, H 4.70, N 5.93%; found C 45.80, H 4.76, N 6.00%.

(±)-3-(Dichloromethylene)-4,6-dimethyl-5-nitrocyclohex-1-ene Isomer (2d): Yield 0.050 g, 21%, orange oil. ^1H NMR (500 MHz, $CDCl_3$) δ: 1.29 (d, J = 7.2 Hz, 3 H, Me-4), 1.30 (d, J = 7.6 Hz, 3 H, Me-6), 3.06−3.13 (m, 1 H, 6-H), 3.71 (dq, J = 7.4, J = 2.8 Hz, 1 H, 4-H), 4.46−4.48 (m, J = 2.8, J = 2.0, J = 0.8 Hz, 1 H, 5-H), 5.85 (dd, J = 10.3, J = 4.3, J = 0.7 Hz, 1 H, 1-H), 6.47 (dd, J = 10.3, J = 2.1, J = 0.6 Hz, 1 H, 2-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 17.9, 19.6, 33.0, 35.9, 90.0, 119.3, 121.3, 131.8, 131.9 ppm. ^{13}C NMR DEPT (100 MHz, $CDCl_3$) δ: 17.9, 19.6, 33.0, 35.9, 90.0, 121.3, 131.8 ppm. $C_9H_{11}NO_2Cl_2$: calcd. C 45.79, H 4.70, N 5.93%; found C 45.74, H 4.55, N 5.80%.

6-Butyl-3-(dichloromethyl)-1-nitrobenzene (3): Yield 105 mg, 40% yellow oil. ^1H NMR (400 MHz, $CDCl_3$) δ: 0.95 (t, J = 7 Hz, 3 H, Me), 1.36−1.48 (m, 2 H, CH_2), 1.59−1.69 (m, 2 H, CH_2), 2.89 (t, J = 8 Hz, 2 H, CH_2), 6.74 (s, 1 H, $CHCl_2$), 7.43 (d, J = 8 Hz, 1 H, 6-H), 7.74 (dd, J = 8, J = 2 Hz, 1 H, 5-H), 8.08 (d, J = 2 Hz, 1 H, 3-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.8, 22.6, 32.5, 32.6, 69.8, 122.4, 130.2, 132.6, 139.3, 139.6, 149.1 ppm. MS (EI): *m*/*z* (%) = 263 (6.9), 261 (10.6), 246 (63.1), 244 (100.0), 228 (14.6), 226 (35.9). $C_{11}H_{13}Cl_2NO_2$: calcd. C 50.40, H 5.00, N 5.34, Cl 27.05%; found C 50.28, H 5.28, N 5.13, Cl 27.43%.

4-Butyl-3-(dichloromethyl)-1-nitrobenzene (4): Yield 30 mg, 11%, yellow oil. ^1H NMR (400 MHz, $CDCl_3$) δ: 0.98 (t, J = 7 Hz, 3 H, Me), 1.36−1.51 (m, 2 H, CH_2), 1.58−1.69 (m, 2 H, CH_2), 2.80 (t, J = 8 Hz, 2 H CH_2), 6.97 (s, 1 H, $CHCl_2$), 7.37 (dd, J = 8, J = 0.4 Hz, 1 H, 6-H), 8.14 (dd, J = 8, J = 2 Hz, 1 H, 5-H), 8.72 (d, J = 2 Hz, 1 H, 3-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.8, 22.6, 32.2, 32.9, 67.3, 120.7, 123.2, 124.3, 130.8, 139.7, 145.7 ppm. $C_{11}H_{13}Cl_2NO_2$: calcd. C 50.40, H 5.00, N 5.34%; found C 50.13, H 5.00, N 5.46%.

(±)-3,5-Dibutyl-6-(dichloromethylene)-4-nitrocyclohexene (3b): Yield 0.090 g, 28%, orange oil. ^1H NMR (400 MHz, $CDCl_3$) δ:

0.82−0.92 (m, 6 H, 2 × Me), 1.18−1.56 (m, 12 H, 6 × CH_2), 3.05−3.14 (m, 1 H, 6-H), 3.57−3.63 (m, 1 H, 4-H), 4.47 (dd, J = 10, J = 4 Hz, 1 H, 5-H), 5.78 (dd, J = 10, J = 3 Hz, 1 H, 2-H), 6.39 (ddd, J = 10, J = 3, J = 1 Hz, 1 H, 1-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.9, 22.6, 22.8, 27.8, 27.9, 28.8, 31.5, 34.9, 42.3, 89.0, 119.1, 122.3, 131.8, 133.5 ppm. MS (EI): *m*/*z* (%) = 321 (0.7), 319 (1.2), 295 (0.6), 274 (4.8), 272 (7.1), 239 (3.7), 237 (9.8), 217 (63.7), 215 (100.0), 161 (20.6), 159 (24.5). $C_{15}H_{23}Cl_2NO_2$: calcd. C 56.26, H 7.24; N 4.37%; found C 56.13, H 7.29, N 4.42%.

3-(Dichloromethyl)-1-nitro-6-(2-phenylethyl)benzene (5): Yield 0.104 g, 33%, orange oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.94−3.00 (m, 2 H, CH_2), 3.18−3.25 (m, 2 H, CH_2), 6.75 (s, 1 H, $CHCl_2$), 7.34 (d, J = 8 Hz, 1 H, 6-H), 7.18−7.40 (m, 5 H, Ph), 7.72 (dd, J = 8, J = 2 Hz, 1 H, 5-H), 8.14 (d, J = 2 Hz, 1 H, 3-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): 35.1, 36.7, 69.7, 122.6, 126.3, 128.4, 128.5, 130.3, 132.8, 138.3, 139.6, 140.4, 148.9 ppm. MS (EI): *m*/*z* (%) = 311 (2.0), 309 (2.9), 294 (1.2), 292 (1.9), 274, 256, 238, 91 (100.0). HRMS (EI) found 309.03175. $C_{15}H_{13}NO_2{}^{35}Cl_2$ requires 309.03233.

3-(Dichloromethyl)-1-nitro-4-(2-phenylethyl)benzene (6): Yield 0.030 g, 9%, orange oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.94−3.02 (m, 2 H, CH_2), 3.11−3.17 (m, 2 H, CH_2), 6.82 (s, 1 H, $CHCl_2$), 7.09−7.35 (m, 6 H Ph and 6-H), 8.12 (dd, J = 8, J = 2 Hz, 1 H, 5-H), 8.71 (d, J = 2 Hz, 1 H, 3-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 34.3, 36.8, 67.3, 123.0, 124.3, 126.7, 128.3, 128.8, 131.1, 139.6, 139.8, 144.5, 146.9 ppm. MS (EI): *m*/*z* (%) = 311 (2.8), 309 (4.3), 294 (26.6), 292 (39.8), 276 (5.8), 274 (15.6), 264 (4.5), 258 (4.1), 256 (11.8), 91 (100.0). HRMS (EI) found 309.03254. $C_{15}H_{13}NO_2{}^{35}Cl_2$ requires 309.03233.

Treatment of 3-(Chloromethyl)-1-nitrobenzene (7) with *n*-Butylmagnesium Chloride: A solution of *n*-butylmagnesium chloride (1.5 mmol) in tetrahydrofuran (0.5 mL) was added dropwise over ca. 1 min to a stirred solution of **7** (172 mg, 1 mmol) in dry tetrahydrofuran (10 mL), cooled to −70 °C under argon. After 5 min, *n*-tetrabutylammonium permanganate (362 mg, 1 mmol) dissolved in acetone (10 mL) was added at −70 °C, or 3 drops of hydrochloric acid (38%) was added at 0 °C. In the case of oxidation with *n*-tetrabutylammonium permanganate the mixture was stirred for 15 min, the cooling bath was removed, and then 3 drops of hydrochloric acid (38%) were added at 0 °C. The reaction mixture was filtered through silica gel, which was washed with dichloromethane (4 × 10 mL). After evaporation of the solvent the products were purified by preparative thin layer chromatography with hexane/ethyl acetate (50:1) as the eluent to give a mixture of 2-butyl-5-(chloromethyl)-1-nitrobenzene (**8a**), 4-butyl-3-(chloromethyl)-1-nitrobenzene (**8b**), and 2-butyl-3-(chloromethyl)-1-nitrobenzene (**8c**), yield 148 mg, 65% (in a ratio of 60:26:14) as an orange oil. MS (EI): *m*/*z* (%) = 229 (15), 227 (54), 212 (34), 210 (100), 192 (23). $C_{11}H_{14}ClNO_2$: calcd. C 58.03, H 6.20, N 6.15, Cl 15.57%; found C 58.41, H 6.53, N 5.77, Cl 14.92%.

2-Butyl-5-(chloromethyl)-1-nitrobenzene (8a): ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.97 (t, J = 7 Hz, 3 H, Me), 1.52−1.34 (m, 2 H, CH_2), 1.57−1.69 (m, 2 H, CH_2), 2.79 (t, J = 8 Hz, 2 H, CH_2), 4.67 (s, 2 H, CH_2Cl), 7.38 (d, J = 8 Hz, 1 H, 6-H), 8.12 (dd, J = 8, J = 2 Hz, 1 H, 5-H), 8.24 (d, J = 2 Hz, 1 H, 3-H) ppm. MS (EI): *m*/*z* (%) = 229 (15.1), 227 (54.1), 212 (33.9), 210 (100.0), 192 (23.4), 174 (58.2), 168 (61.7). HRMS (EI) found 227.07120. $C_{11}H_{14}NO_2{}^{35}Cl$ requires 227.07131.

4-Butyl-3-(chloromethyl)-1-nitrobenzene (8b): Orange oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.94 (t, J = 7 Hz, 3 H, Me), 1.34−1.52 (m, 2 H, CH_2), 1.57−1.69 (m, 2 H, CH_2), 2.88 (t, J = 8 Hz, 2 H, CH_2), 4.60 (s, 2 H, CH_2Cl), 7.35 (d, J = 8 Hz, 1 H, 6-H), 7.54 (dd, J = 8, J = 2 Hz, 1 H, 5-H), 7.90 (d, J = 2 Hz, 1 H, 3-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.8, 22.6, 32.4, 44.5, 124.5, 132.4, 132.6, 136.5, 137.9, 149.3 ppm. MS (EI): *m*/*z* (%) = 229 (1.1), 227 (3.1), 212 (21.4), 210 (64.0), 192 (9.2), 168 (31), 154 (100.0). HRMS (EI) found 227.07120. $C_{11}H_{14}NO_2{}^{35}Cl$ requires 227.07131. $C_{11}H_{14}ClNO_2$: calcd. C 58.03, H 6.20, N 6.15%; found C 58.20, H 6.39, N 6.03.

2-Butyl-3-(chloromethyl)-1-nitrobenzene (8c): ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.97 (t, J = 7 Hz, 3 H, Me), 1.34−1.52 (m, 2 H, CH_2), 1.57−1.69 (m, 2 H, CH_2), 2.88 (t, J = 8 Hz, 2 H, CH_2), 4.67 (s, 2 H, CH_2Cl), 7.31−7.37 (m, 1 H, 5-H), 7.60 (dd, J = 8, J = 1 Hz, 1 H, 6-H), 7.72 (dd, J = 8, J = 1 Hz, 1 H, 4-H) ppm.

Treatment of 3-(Dichloromethyl)-1-nitrobenzene (9) with *n*-Butylmagnesium Chloride: The reactions were performed according to the General Procedure for treatment of 1-nitro-3-(trichloromethyl)-benzene (**1**) with Grignard reagents [compound **9** (206 mg, 1 mmol) and *n*-butylmagnesium chloride (175 mg, 1.5 mmol), to give 2-butyl-5-(chloromethyl)-1-nitrobenzene (**8a**), yield 70 mg, 31% and 4-butyl-3-(chloromethyl)-1-nitrobenzene (**8b**) yield 25 mg, 11%], and according to the treatment of 3-(chloromethyl)-1-nitrobenzene (**7**) with *n*-butylmagnesium chloride [compound **9** (206 mg, 1 mmol), *n*-butylmagnesium chloride (175 mg, 1.5 mmol) and DDQ (227 mg, 1 mmol) being used instead of *n*-tetrabutylammonium permanganate, to give 2-butyl-5-(chloromethyl)-1-nitrobenzene (**8a**), yield 43 mg, 19% and 4-butyl-3-(dichloromethyl)-1-nitrobenzene (**4**) yield 57 mg, 22%].

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