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Dimetallation of *N*-ethynylpyrrole and subsequent regiospecific derivatization

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Abstract

The dilithium derivative *N*-lithioethynyl-2-lithiopyrrole generated from *N*-ethynylpyrrole or *N*-1,2-dichlorovinylpyrrole and two mol equivalents of *n*-butyllithium has been used for regiospecific substitution in the 2-position by reaction with *n*-butyl iodide, *N,N*-dimethylformamide, sulfur, selenium and tellurium. The intermediate thiolates, selenolates and tellurolates have been converted into bicyclic compounds by addition of a mixture of *t*-butyl alcohol and hexamethylphosphoric triamide.

Keywords: Lithium; Silicon; Sulfur; Tellurium; Dilithiation; Dimetallation

1. Introduction

It has been shown [1,2] that interaction between phenylacetylene or 1-naphthylacetylene and two equivalents of a 1 : 1 molar combination of *n*-butylithium (BuLi) and potassium *tert*-butoxide leads to metallation at the acetylenic carbon and at the *ortho*-position. The dimetallic derivatives were used for the synthesis of some *ortho*-functionalized arylacetylenes and condensed bi- or tricyclic compounds containing sulfur, selenium or tellurium. The present paper deals with analogous conversions with *N*-ethynylpyrrole, a compound which has become readily available starting from pyrrole and trichloroethene [3,4].

2. Results and discussion

It is known [4] that treatment of *N*-1,2-dichlorovinylpyrrole **1** with two equivalents of alkyllithium produces *N*-lithioethynylpyrrole. We found that if three equivalents of ^{n}BuLi are used a second lithiation takes place at the 2-position of the ring. This reaction proceeds readily at temperatures in the range 20–35°C in THF–hexane mixtures. The reagent ^{n}BuLi — tetramethylethane diamine (TMEDA) — hexane can also be used.

The efficiency of the dimetallation was demonstrated by treatment with trimethylchlorosilane, which afforded the disilyl derivative **4a** in ca. 80% yield. When only one equivalent of *n*-butyl iodide was used 2-butyl-1-ethynylpyrrole **4b** was obtained in ca. 62% yield. A similar regiospecificity was found in the reaction (at temperatures < -40°C) with *N,N*-dimethylformamide. The unstable aldehyde **4c** was obtained in moderate yields after acid hydrolysis.

In the reactions leading to **4a–c** the intermediate **3** was generated from the dichloro compounds **1**. For the syntheses of **4d–f** (X = S, Se or Te) we used *N*-ethynylpyrrole **2**, though its preparation from **1** involves a time-consuming separation from diethyl ether by distillation [3,4].

The reason for not generating the metallated ethynylpyrrole from **1** was the formation of the side product, *n*-butyl chloride, which might react with the chalcogenates formed in the reactions with sulfur, selenium and tellurium.

Compounds **4d** were formed upon addition of a mixture of *t*-butyl alcohol and hexamethylphosphoric triamide after the reactions with the elements were

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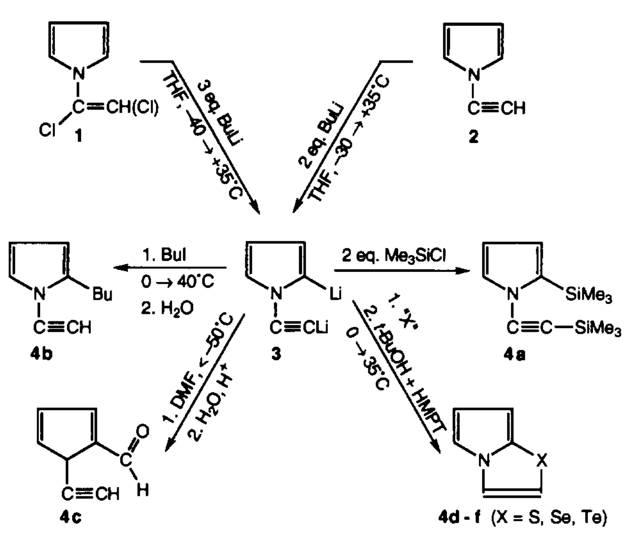


complete. After flash chromatography on neutral Al_2O_3 the pure bicyclic compounds **4d** were isolated in reasonable yields.

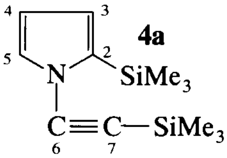
3. Experimental section

The ^1H and ^{13}C NMR spectra were recorded on a Bruker AC 300 machine (ca. 20% solution (v/v) in $CDCl_3$). The exact masses of the products **4a–d** obtained by high-resolution mass spectroscopy corresponded with the calculated values.

N-(1,2-Dichlorovinyl)pyrrole and *N*-ethynylpyrrole were obtained by the procedure described in [4]. The *n*-butyllithium used for the dimetallations was the commercially available solution (ca. 1.6 M) in hexane. The THF was purified by shaking with machine-powdered KOH (200 g for 2 l) and distilling the filtered liquid under N_2 from $LiAlH_4$ (2 g for 2 l). The distillate was stored under nitrogen. The TMEDA was dried by shaking with machine-powdered KOH and subsequently distilling the filtered liquid from $LiAlH_4$. The *tert*-butyl alcohol was dried by distilling it from commercially ^{t}BuOK (5 g for 1 l). Dry HMPT was obtained by distilling the commercial solvent (purity ca. 99%) at 0.1–0.5 mm Hg from ^{t}BuOK; the distillate was redistilled at water pump pressure. The GLC analyses were carried out with a Varian 3400 gas chromatograph with a 15 m capillary column (internal diameter 0.53 mm) with a 1.5 μm DB-5 coating.

3.1. *1-Trimethylsilylethynyl-2-trimethylsilylpyrrole 4a*

A 1-l round-bottomed, three-necked flask, fitted with an efficient mechanical stirrer a gas inlet and a thermometer-gas outlet combination, was flushed with nitrogen, and *N*-(1,2-Dichlorovinyl)-pyrrole (0.05 mol) and 70 ml of THF was introduced. The mixture was coded to −80°C, and a solution of 100 ml of 1.6 M BuLi was added during a few minutes without external cooling. The mixture was kept for 1 h at 30°C, during which a suspension was formed. This was cooled to −50°C and 6.11 g of trimethylchlorosilane was added in one portion without further cooling. After 30 min the mixture was treated with 200 ml of ice-water. The organic layer and one ethereal extract were dried over $MgSO_4$ and the solution was concentrated under reduced pressure. Distillation through a 20 cm Vigreux column afforded **4a**, b.p. 114°C/15 mm Hg, n_D^{20} 1.4930, yield 78%.

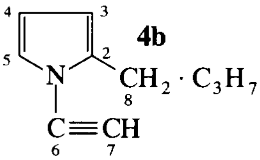


4a

^1H NMR: 6.21 (m, H_3); 6.38 (m, H_4); 7.10 (m, H_5); 0.31 and 0.39 (Me_3Si groups). ^{13}C NMR: 137.48 (C_2); 110.36 (C_3); 120.08 (C_4); 128.88 (C_7).

3.2. *2-Butyl-1-ethynylpyrrole 4b*

A suspension of dilithiated ethynylpyrrole was prepared as described above. Butyl iodide (0.05 mol) was added at 0°C and the temperature allowed to rise to room temperature. After an additional 2 h at 40°C the mixture was treated with water and the product **4b** isolated as described above, b.p. 78°C/15 mm Hg, n_D^{20} 1.4960, yield 62%.

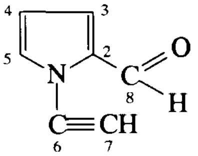


4b

^1H NMR: 5.96 (m, H_3); 6.15 (m, H_4); 6.89 (m, H_5); 2.97 (s, H_7); 2.76 (t, H_8). ^{13}C NMR: 137.62 (C_2); 106.92 (C_3); 109.78 (C_4); 123.27 (C_5); 75.17 (C_6); 57.17 (C_7); 30.93, 26.13, 22.38, 13.91 (C_4H_9 group).

3.3. *2-Formyl-1-ethynylpyrrole 4c*

The suspension of dilithiated *N*-ethynylpyrrole was cooled to −80°C and 5 g (excess) of *N*,*N*-dimethylformamide was added in one portion with vigorous stirring as the temperature was allowed to rise to −40°C. The cold mixture was then transferred by syringe into a vigorously stirred and cold (−20°C) mixture of 17 g of 30% hydrochloric acid and 150 ml of water containing 30 g of ammonium chloride. The cold mixture was immediately extracted four times with a 1 : 1 mixture of ether and pentane. The combined extracts were washed once with water, dried over $MgSO_4$ and concentrated under reduced pressure. The residue was subjected to flash chromatography on neutral Al_2O_3 using a hexane–ether (9 : 1) mixture as solvent. Concentration in vacuo left a yellow oil, which rapidly turned brown, even in the refrigerator. Yield 33% (after flash chromatography on neutral Al_2O_3).

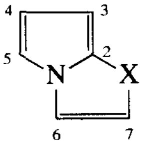


4c

^{1}H NMR: 6.16 (m, H_3); 6.85 (m, H_4); 7.02 (m, H_5); 9.60 (s, H_8); 3.06 (s, C_7). ^{13}C NMR: 134.33 (C_2); 111.94 (C_3); 120.82 (C_4); 132.69 (C_5); 73.05 (C_6); 59.23 (C_7); 178.39 (C_8).

*3.4. Reaction of dilithiated N-ethynylpyrrole with sulfur, selenium or tellurium and subsequent cyclization to give **4d–f***

A mixture of 0.025 mol of *N*-ethynylpyrrole and 20 ml of THF was cooled to −40°C and a solution of 0.06 mol of BuLi in 36 ml of hexane was added within a few seconds. The mixture was kept at 40°C for 30 min and then cooled to −40°C, −20°C or 0°C in the case of reaction with S, Se and Te, respectively. Finely powdered sulfur, selenium (red) or tellurium (grey powder) (0.025 mol) was added in several small portions during 20 min to the efficiently stirred suspension, while the indicated temperature was maintained. After complete dissolution of the elements (in the case of Te the mixture was stirred for an additional 45 min at 20°C) the mixture was cooled to −20°C and a mixture of 4 g of *t*-butylalcohol and 15 ml of HMPT was added in one portion. The dark solution was kept at 30°C for 40 min and 250 ml of water were added. The aqueous layer was extracted four times with ether and the extract washed four times with water. After drying of the extract over $MgSO_4$ and removal of the solvent in vacuo, the products were purified by flash chromatography on neutral Al_2O_3, with hexane–ether (9 : 1) as solvent. Crystallization (from hexane) of the products remaining after evaporation of the solvent afforded the pure compounds.



4d–f

X = S, m.p. 26–27°C (hexane), yield 49%. ^{1}H NMR: 6.23 (d, H_3); 6.57–6.67 (m, $H_4 + H_7$); 7.21 (dd, H_5); 7.33 (d, H_6). ^{13}C NMR: 129.85 (C_2); 110.94 (C_3); 111.30 (C_4); 120.44 (C_5); 114.65 (C_6); 97.13 (C_7).
X = Se, m.p. 49–50°C (hexane), yield 52%. ^{1}H NMR: 6.42 (d, H_3); 6.62 (m, H_4); 6.97 (dd, H_7); 7.34 (m, H_5); 7.42 (d, H_6). ^{13}C NMR: 124.96 (C_2); 113.75 (C_3); 114.19 (C_4); 122.18 (C_5); 109.69 (C_6); 102.52 (C_7).
X = Te, m.p. 43–44°C (hexane), yield 45%. ^{1}H NMR: 6.37 (m, H_3); 6.42 (m, H_4); 7.33 (d, H_7); 7.39–7.45 (m, H_5 and H_6). ^{13}C NMR: 127.30 (C_2); 111.85 (C_3); 113.10 (C_4); 118.32 (C_5); 105.98 (C_6); 94.65 (C_7).

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