

A Novel Route for the Synthesis of Six- and Seven- Membered 6-Trimethylsilylspiro[4,n]alk-6-enes

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A novel route for the synthesis of 6-trimethylsilylspiro[4,5]dec-6-ene and 6-trimethylsilylspiro[4,6]undec-6-ene by the Wurtz-Fittig type coupling reaction of 6-iodospiro[4,5]dec-6-ene and 6-iodospiro[4,6]undec-6-ene with alkali metals and chlorotrimethylsilane in good yields is reported. The compounds serve as a new class of spiranyl cyclic vinylanionic synthons.

Key words: spiranes, cyclic vinylsilanes, anionic synthons, Wurtz-Fittig reaction.

1. INTRODUCTION

Cyclic vinylsilanes are an important class of compounds in organic synthesis [1]. The compounds serve as masked vinylanionic synthons [2]. Spirocyclics on the other hand, are important compounds with diverse properties, which are found to occur as subunits in many natural products [3]. To our knowledge, there is only one report on the preparation of spiranyl cyclic vinylsilanes in the literature by Paquette [4]. Substitution of the trimethylsilyl group in simple spirocyclic compounds alters the electronic properties of the molecules, thereby providing a route for easy functionalization with diverse functional groups [5].

We had earlier prepared a wide variety of simple and substituted cyclic vinylsilanes by the Wurtz-Fittig coupling reaction of the corresponding cyclic vinyl bromides/chlorides with sodium and chlorotrimethylsilane in different anhydrous solvents [6].

The most recent of the substituted cyclic vinylsilanes synthesized by us are the 2-trimethylsilylcycloalkanones [7]. The compounds are α -acylvinyl anionic synthons [8].

During our study on the synthesis of the 2-trimethylsilylcycloalkanones, we found 6-trimethylsilyl-7-methyl-1,4-dioxaspiro[4,5]dec-6-ene to be highly unstable even in the mildest acidic medium [9]. The 6-trimethylsilyl-7-methyl-1,4-dioxaspiro[4,5]dec-6-ene could not be isolated under the conditions of our work, even though the

compound has been isolated by Yus [10]. Therefore, we chose to prepare the corresponding carbon equivalents, which are the spiranyl-compounds. These novel spiranyl cyclic vinyl silanes are expected to be very stable.

2. EXPERIMENTAL

IR spectra were recorded on a Shimadzu FT-IR 8400S spectrometer. NMR spectra were recorded on a Bruker AMX 400 MHz spectrometer. GC was run on a Shimadzu 14-B/Mayura 9800 Gas Chromatograph using a SE-30 SS 2m \times 1/8" column. Yields refer to the isolated yields of the products. GC-MS spectra were obtained using a Shimadzu GC-MS QP 5050A.

General procedure for the preparation of spiro[4, n]alkanones

Spiro[4,n]alkanones (3 and 4): To a magnetically stirred suspension of potassium *tert*-butoxide (2.2 mol equivalents) in 100 mL refluxing anhydrous benzene was added a mixture of cycloalkanone (10 g) and 1,4- dibromobutane (1.2 mol equivalents) over a period of 40 min. After completion of the addition, the mixture was further refluxed for 10 hrs. The reaction mixture was cooled, diluted with 50 mL ether and added to 100 mL of ice cold water. The organic layer was separated, and the aqueous layer was extracted with ether (3 \times 50 mL). The combined organic extracts were washed with water (2 \times 50 mL), brine (2 \times 30 mL) and dried over anhydrous potassium carbonate. The solvent was removed on a rotary evaporator and distilled *in vacuo* to isolate spirocyclic ketones **3** and **4** in yields as reported in the literature.

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Spiro[4,5]decan-6-one (3) [13]: IR (Neat); 2937, 2864, 1708, 1448, 1342, 1311, 1236, 1193, 1126, 1060, 954, 904, 852, 800 ; **¹H NMR (CDCl₃):** δ 1.27-1.28 (m, 2H), 1.30-1.31 (m, 4H), 1.46-1.49 (m, 4H), 1.70-1.71 (m, 2H), 1.91-1.96 (m, 2H), 2.21-2.31 (m, 2H). **GC-MS:** m/e (rel. intensity): 152 (36), 123 (11), 111 (100), 95 (35), 81 (22), 67 (93), 55 (29), 41 (44).

Spiro[4,6]undecan-6-one (4) [12]: IR (Neat) ; 2931, 2858, 1703, 1446, 1346, 1313, 1141, 1076, 1029, 979, 937, 840 ; **¹H NMR (CDCl₃):** δ 1.27-1.33 (m, 2H), 1.39-1.41 (m, 2H), 1.51-1.57 (m, 10H), 1.69-1.72 (m, 2H), 1.82-1.91 (m, 2H). **¹³C NMR (DMSO):** δ 25.4, 26.0, 26.3, 30.1, 36.5, 37.9, 59.0, 216.4. **GC-MS:** m/e (rel. intensity); 166 (10), 148 (3), 125 (26), 95 (37), 81 (29), 67 (100), 55 (38), 41 (68).

6-Iodospiro[4,n]alk-6-enes (5 and 6): Triethylamine (1.5 mol equivalents) and hydrazine monohydrate (18 mol equivalents) were added to a solution of spiro[4,n]alkanones in absolute ethanol (25 mL) and the mixture was refluxed for 12 hours. Ethanol was evaporated *in vacuo*. The residue was extracted with ether (3×20 mL), the organic layers were combined, dried over anhydrous sodium sulfate, and evaporated *in vacuo* to get the hydrazones of **3** and **4**.

A solution of iodine (2.2 mol equivalents) in dry ether (50 mL) was added dropwise to a solution of spiro[4,n]alkanone hydrazones (4 g) and 1,5-diazabicyclo[4.3.0]non-5-ene (6 mol equivalents) in dry ether (50 mL). After the reaction mixture was stirred for 3.5 hours, it was quenched with saturated sodium bicarbonate solution (20 mL). The layers were separated and the aqueous layer was extracted with ether (3×40 mL). The organic layers were combined, dried over anhydrous sodium sulfate, and evaporated *in vacuo*. The residue was chromatographed using silica gel to isolate **5** and **6**. Further distillation gave the pure compounds.

6-Iodospiro[4,5]dec-6-ene (5): B.p. 80-82°C/1 mm **IR (Neat) ;** 2933, 2864, 1618, 1444, 1319, 1180, 1085, 1024, 954, 877, 804, 738, 688 cm⁻¹; **¹H NMR (CDCl₃):** δ 1.47 (m, 2H), 1.67 (m, 4H), 1.75 (m, 4H), 1.83 (m, 2H), 2.07 (m, 2H), 6.43 (1H, t, *J*=4 MHz), **¹³C NMR (CDCl₃):** δ 19.8, 25.2, 29.9, 36.5, 40.8, 49.7, 117.9, 138.9 ; **GC-MS:** m/e (rel. intensity): 262 (36), 135 (83), 107 (26), 93 (81), 79 (72), 66 (100), 54 (20), 40 (42).

6-Iodospiro[4,6]undec-6-ene (6) B.p. 80-82°C/0.6mm **IR (Neat):** 2929, 2862, 1699, 1608, 1446, 1359, 1330, 1220, 1101, 1024, 995, 937, 844, 815, 715, 676 cm⁻¹; **¹H NMR (CDCl₃):** δ 1.57-1.58 (m, 4H), 1.64-1.65 (m, 4H), 1.73-1.74 (m, 4H),

1.83-1.85 (m, 2H), 2.03-2.07 (m, 2H), 6.54 (t, 1H, *J*=6.8 Hz); **¹³C NMR (CDCl₃):** δ 23.6, 25.0, 26.3, 29.4, 33.1, 41.6, 55.6, 123.0, 142.9. **GC-MS:** m/e (rel. intensity): 276 (0.9), 149 (8), 126 (16), 107 (10), 91 (31), 79 (31), 67 (33), 41 (100); **Anal. calcd. for C₁₁H₁₇I:** C, 47.84%; H, 6.20%. **Found:** C, 48.13%; H, 6.34%.

Synthesis of 6-trimethylsilylspiro[4,n]alkenes (7 and 8):

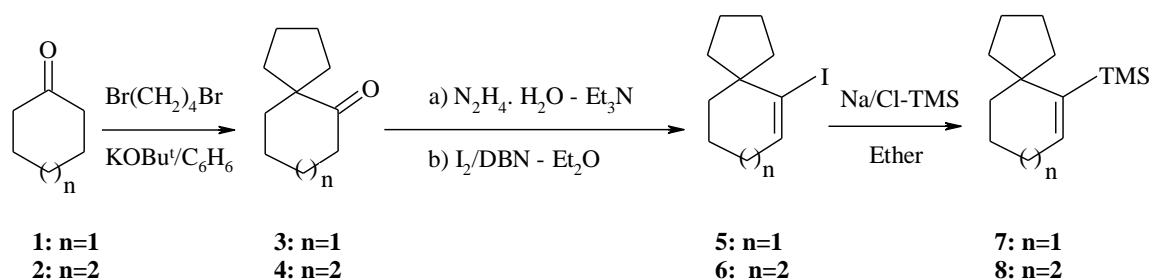
To a suspension of finely cut metal pieces (5 mol equivalents) and chlorotrimethylsilane (3 mol equivalents) in 10 mL of anhydrous ether, 6-iodospiro[4,n]alkene (1g) in 5 mL of dry ether was added. The mixture was refluxed with efficient stirring on an oil bath at 45^o- 50^oC. The completion of the reaction was followed by GC. The mixture was cooled; the precipitated solids and remaining metal pieces were removed by filtering on a plug of glass wool and washed with ether (2×10 mL). The combined organic extract was washed with saturated sodium bicarbonate (15 mL), saturated sodium chloride (10 mL) and dried (anhydrous Na₂CO₃). Concentration *in vacuo* and distillation yielded **7** and **8**.

6-Trimethylsilylspiro[4,5]dec-6-ene (7): B.p. 75-78°C/1 mm; **IR (neat):** 2952, 2929, 2871, 1595, 1445, 1406, 1249, 1054, 1002, 943, 836, 754, 684, 634 cm⁻¹; **¹H NMR (CDCl₃):** δ 0.10 (s, 9H), 1.37 – 1.39 (m, 2H), 1.40 -1.44 (m, 2H), 1.56 – 1.59 (m, 2H), 1.65 - 1.66 (m, 6H), 1.90 - 2.03 (m, 2H), 6.03 (t, 1H, *J*=3.6Hz); **¹³C NMR (CDCl₃):** δ 19.2, 24.0, 27.1, 35.2, 39.0, 46.4, 137.5, 146.1; **GC-MS:** m/e (rel. intensity): 208 (2), 193 (9), 165 (3), 134 (100), 119 (9), 105 (10), 91 (22), 73 (86), 59 (35), 44 (17)

6-Trimethylsilylspiro[4,6]undec-6-ene (8): B.p.: 72-75°C/0.8mm **IR (Neat):** 2921, 2858, 1645, 1446, 1247, 1151, 1099, 960, 931, 837, 754 cm⁻¹; **¹H NMR (CDCl₃):** δ 0.096 (s, 9H), 1.42-1.48 (m, 4H), 1.54-1.68 (m, 8H), 1.82-1.86 (m, 2H), 2.16-2.21 (m, 2H), 6.13(t, 1H, *J* = 6.4 Hz); **¹³C NMR (CDCl₃):** δ 2.16, 3.53, 26.60, 27.33, 30.54, 36.51, 37.65, 51.72, 141.76, 153.51 ; **GC-MS:** m/e (rel. intensity): 222 (0.3), 207 (0.8), 179 (0.5), 148 (30), 133 (6), 91 (13), 73 (100), 59 (33.36), 45 (28) **Anal. calcd. for C₁₄H₁₇Si:** C, 75.59%; H, 11.78%. **Found:** C, 75.92%, H, 12.38%

3. RESULTS AND DISCUSSION

In expansion of the scope of the Wurtz-Fittig coupling reaction, we now report for the first time the successful synthesis of six- and seven-membered 6-trimethylsilylspiro[4,n]alk-6-enes: 6-trimethylsilylspiro[4,5]dec-6-ene (**7**) [4] and 6-trimethylsilylspiro[4,6]undec-6-ene (**8**) by the route



Scheme-1: Synthesis of Novel Spiranyl Cyclic Vinylsilanes

shown in **Scheme 1**. This route expands the scope and utility of the Wurtz-Fittig coupling reaction. The starting spiro[4,5]decan-6-one (**3**) [11] and spiro[4,6]undecan-6-one (**4**) [12] were prepared by alkylating cyclohexanone (**1**) and cycloheptanone (**2**) with 1,4-dibromobutane using potassium *tert*-butoxide in benzene solvent. The compounds **3** and **4** were reacted with hydrazine hydrate and triethylamine for their conversion to corresponding hydrazones. Monitoring the reaction by GC-MS indicated the formation of bis-spiro[4,*n*]alk-6-ylidene-hydrazine along with the required hydrazones of **3** and **4**. The mixture of azines and hydrazones without further purification was reacted with I_2 / DBN according to the Barton vinyl iodination method to their corresponding 6-iodospiro[4,5]dec-6-ene (**5**) and 6-iodospiro[4,6]undec-6-ene (**6**) [13]. 6-Iodospiro[4.5]dec-6-ene (**5**) is not reported in literature. However, for the vinyl bromide equivalent of **5** see [14]. The literature survey indicates that there are no precedents for the conversion of spiranyl cyclic vinyl iodides to spiranyl cyclic vinylsilanes through the Wurtz-Fittig reaction, even though Yus has employed lithium metal for the synthesis of 6-trimethylsilyl-1,4-dioxaspiro[4,5]-6-decene [10].

We have screened the alkali metals Li, Na and K as electron sources for the formation of a cyclic vinyl anion. The comparative reactivity of **5** and **6** with alkali metals is given in Table 1.

Table 1. Comparative reactivity of spiranyl cyclic vinyl iodides with alkali metals

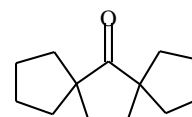
Compound	Metal	Product	Yield, %
5	Lithium	7	81-84
5	Sodium	7	67-72
5	Potassium	7	63-67
6	Lithium	8	84-88
6	Sodium	8	71-75
6	Potassium	8	69-73

The reactions were repeated 10 times for each substrate and the range of isolated yields is

indicated in Table 1. We have found that metallic lithium gave better yields over sodium and potassium.

The best results with lithium metal can be attributed to the greater solubility of the spiranyl vinyl lithium ion pairs in anhydrous ether solvent and also to the controlled reactivity due to their covalent nature originating from the polarizing power of the lithium ion. This observation is also in good conformity with the HSAB theory [15].

We have also tried to extend the methodology to prepare the five- and eight- membered spiranyl cyclic vinylsilanes. Reaction of cyclopentanone with 1,4-dibromobutane and potassium *tert*-butoxide gave the dispiro[4.1.4.2]tridecan-6-one as the major product. In case of cyclooctanone, though we have isolated the spiro[4,7]dodecanone and its hydrazone, the corresponding 6-iodospiro[4,7]dodec-6-ene could not be isolated in the conditions employed. The structure of the dispiro[4.1.4.2]tridecan-6-one was found to be:



To our knowledge, this is the first instance where spiranyl cyclic vinyl iodides are being used for the synthesis of spiranyl cyclic vinylsilanes using the Wurtz-Fittig coupling reaction. The compound **7** has been reported by Paquette through the tosyl hydrazone route [4]. To our knowledge the compound **8** has not been reported. The method we hereby report is simple and with a high yield. The spiranyl cyclic vinylsilanes **7** and **8** may serve as starting materials in the synthesis of the muscone related group of compounds [16].

4. CONCLUSIONS

A novel route for the synthesis of six- and seven- membered 6-trimethylsilylspiro[4,*n*]alk-6-enes by the Wurtz-Fittig type coupling reaction of the corresponding spiranyl iodides with alkali metals lithium/sodium/potassium and chloro-

trimethylsilane in good yields is reported. The compounds could serve as novel spiranyl anionic synthons.

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НОВ МАРШРУТ ЗА СИНТЕЗ НА ШЕСТ И СЕДЕМ АТОМНИ ПРЪСТЕНИ НА 6-ТРИМЕТИЛ-СИЛИЛ-СПИРО [4,N] АЛК-6-ЕНИ

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(Резюме)

Съобщава се за нов маршрут за синтезата на 6-триметил-силил-спиро [4,6] дек-6-ен и 6-триметил-силил-спиро[4,n] ундек-6-ен по реакцията на Wurtz-Fittig между 6-йодоспиро[4,5]дек-6-ен and 6-йодоспиро[4,6]ундек-6-ен с алкални метали and хлор-триметил-силан с добри добиви. Съединенията служат за нов клас от спиралилни циклени жинил-йонни синтони.