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Regiospecific synthesis of 5-silyl azoles

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Abstract—5-Silylisoxazoles bearing other silyl groups different to the more usual trimethylsilyl have been prepared by condensation of silylalkynones with hydroxylamine hydrochloride. The reaction with hydrazines is more complex and leads to 5-silylpyrazoles or the corresponding hydrazones, which can be cyclized by reaction with electrophiles. This has allowed us to synthesize 5-silylpyrazoles functionalized at C-4 by groups impossible to introduce by electrophilic substitution of the pyrazole nucleus.

1. Introduction

Recently,[1] we have reported the synthesis of regioisomeric silicon and tin 4- or 5-metalated pyrazoles by silyl or stannylcupration of 4-halopyrazoles or lithiation with LDA of 5-unsubstituted pyrazoles and the subsequent treatment with chlorosilanes or chlorostannanes, respectively. Moreover, starting from 5-unsubstituted 4-halopyrazoles using both procedures and beginning with 5-metalation followed by coupling with silyl or stannylcuprates, we have been able to synthesize a variety of 4,5-dimetalated pyrazoles bearing different silyl and stannyl groups.

This methodology can be applied to the preparation of 4-silyl and 4-stannylisoxazoles, but not to the synthesis of 5-silyl or 5-stannylisoxazoles, because the 5-lithio intermediate is opened by fission of N–O and C_3–C_4 bonds.[2] Previously, Birkofer et al.[3] synthesized 5-trimethylsilyl isoxazoles by reaction of trimethylsilylalkynones with hydroxylamine hydrochloride. Using this procedure we have synthesized 5-silylisoxazoles bearing dimethylphenyl and *tert*-butyldiphenylsilyl groups. Furthermore, we have prepared 5-silylpyrazoles starting from differently silylated acetylenic ketones by condensation with hydrazines. In some cases, the cyclization step was difficult or did not take place. Fortunately, the hydrazone intermediates were cyclized in the presence of acids or other electrophiles. This allowed us to obtain 5-silylpyrazoles functionalized at C-4 by groups impossible to introduce directly in the heterocycle.

2. Results and discussion

2.1. Synthesis of 5-silylisoxazoles

We have obtained 5-dimethylphenylsilyl- and 5-*tert*-butyldiphenylsilyl-3-methylisoxazoles according to the procedure described by Birkofer.[3] The necessary silylalkynones have been prepared by us starting from trimethylsilylacetylene through the following sequence:

The reaction of the disilylacetylene **1b** with acetyl chloride was regiospecific and afforded the *tert*-butyldiphenylsilyl ketone **2c**, in accordance with the results obtained previously by us[4] in the desilylative acetylation of vinylsilanes bearing two silyl groups (trimethyl and *tert*-butyldiphenyl) of very different electrofugacity. However, the acetylation of **1a** gave a mixture of the two possible silylacetylenes **2a** and **2b**, the dimethylphenylsilyl derivative **2b** being the major product (Scheme 1).

The reaction of **2b** and **2c** with hydroxylamine hydrochloride led to 5-dimethylphenylsilyl **4b** and 5-*tert*-butyldiphenylsilyl-3-methylisoxazole **4c**. The cyclization of the oxime bearing the hindered *tert*-butyldiphenylsilyl group **3c** was not complete and together with the 5-silylisoxazole **4c** we isolated **3c** as a mixture of *Z* and *E* isomers (Scheme 2).

2.2. Synthesis of 5-silylpyrazoles

The reaction of silylated acetylenic ketones with hydrazines is more complicated. The cyclization to the 5-silylpyrazole or the exclusive formation of the corresponding hydrazone depends on the nature of the substituents of the hydrazine and silyl group.

When free hydrazine or methylhydrazine were used, only the 4-dimethylphenylsilyl-3-butyn-2-one **2b** led to

Keywords: 5-silyl azoles; condensation; electrophiles.

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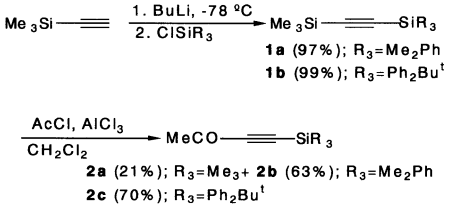
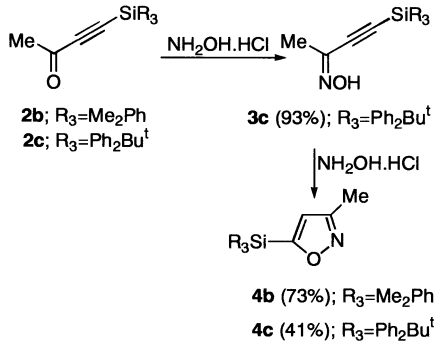
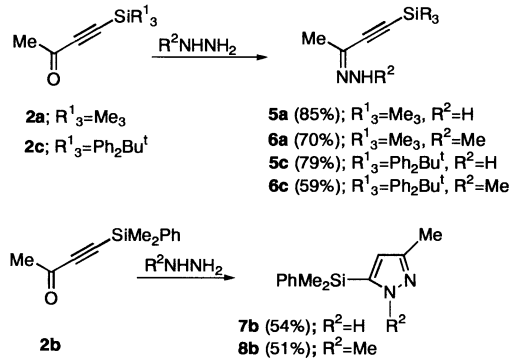


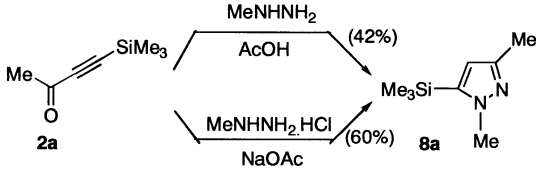
Scheme 1.



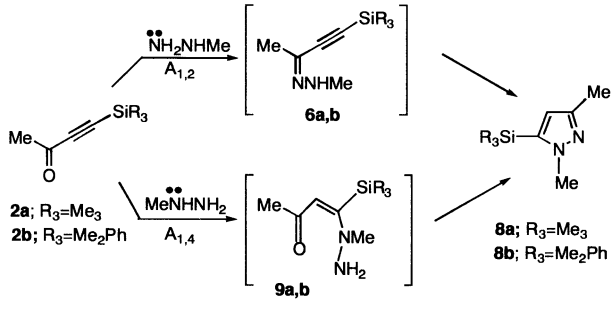
Scheme 2.



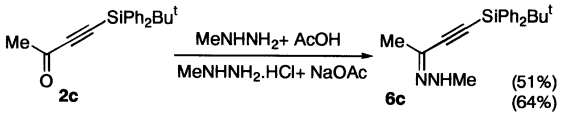
Scheme 3.



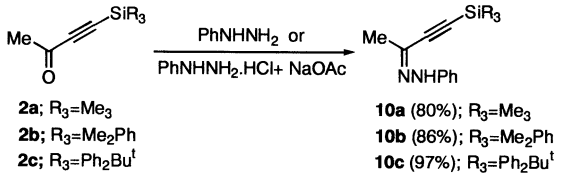
Scheme 4.



Scheme 5.



Scheme 6.



Scheme 7.

3(5)-dimethylphenylsilyl-5(3)-methylpyrazole **7b** or the 1,3-dimethyl-5-dimethylphenylsilylpyrazole **8b**. On the contrary, when the silyl group is trimethyl or *tert*-butyldiphenyl substituted the respective hydrazones **5a** and **6a** or **5c** and **6c** were isolated (Scheme 3).

Nevertheless, when the 4-trimethylsilyl-3-butin-2-one **2a** reacted with an excess of methylhydrazine in the presence of acetic acid we obtained the 5-trimethylsilylpyrazole **8a** together with a 1.1 mixture of the 1,3-dimethyl and 1,5-dimethylpyrazole. The latter are the result of the reaction with methylhydrazine of the desilylated acetylenic ketone formed in the acid medium necessary for the cyclization. Better yields of **8a** were obtained using methylhydrazine hydrochloride and sodium acetate (Scheme 4).

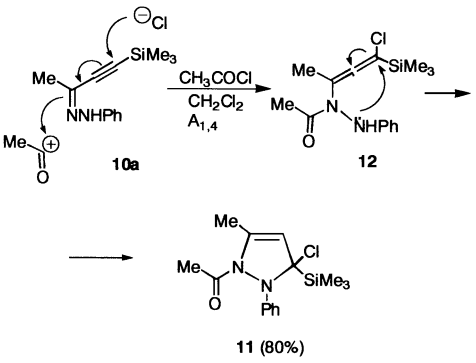
The formation of the 5-silyl-1,3-dimethylpyrazoles **8a** and **8b** can occur by the cyclization from either the hydrazone intermediates **6a**,**b** resulting from 1,2-addition of methylhydrazine by the NH_2 group or through the intermediates **9a**,**b** obtained by 1,4-addition of the NMe group (Scheme 5).

The ketone **2c** which bears the hindered *tert*-butyldiphenylsilyl group did not cyclize when it was heated with methylhydrazine in the conditions previously cited. In all cases, the methylhydrazone **6c** was exclusively isolated (Scheme 6).

When phenylhydrazine was used as a 1,2-dinucleophile (free, in the form of hydrochloride or with acid catalysis) the cyclization did not take place. The reaction with the three silylated ketones **2a**–**c** afforded only the corresponding phenylhydrazones **10a**–**c** (Scheme 7).

Fortunately, the trimethylsilyl and the dimethylphenylsilylhydrazone **10a** and **10b** could be cyclized to pyrazole derivatives by reaction with other electrophiles.Thus, when the phenylhydrazone **10a** was treated with acetyl chloride in methylene chloride at room temperature we obtained with an excellent yield the 2-acetyl-5-chloro-3-methyl-5-trimethylsilyl-1-phenyl-3-pyrazoline **11** resulting from cyclization of the allenic intermediate **12** formed by 1,4-addition (Scheme 8).

The highly functionalized pyrazoline **11** is an interesting synthon. It contains an allylsilane moiety susceptible of electrophilic substitution.[5,6] Moreover, it bears a chloro α



Scheme 8.

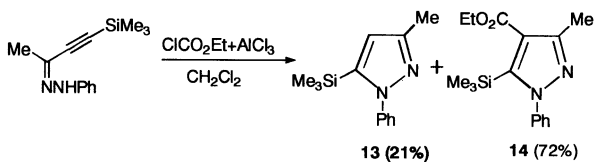
to the silyl group, and these groups are expected to undergo α-elimination affording a carbene intermediate whose addition to olefins[7] could give heterocyclic spiranes.

When we used ethyl chloroformate in the same conditions as described for the acetyl chloride, the starting product **10a** was recovered. Nevertheless, in the presence of aluminum chloride a 1:3 mixture of the corresponding 5-silylpyrazole **13** and the 4-ethoxycarbonyl-5-silylpyrazole **14** was obtained (Scheme 9).

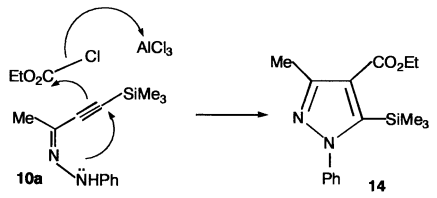
This result is noteworthy because the 4-ethoxycarbonylation of the pyrazole nucleus has not been described. In fact, we recovered untransformed the 3,5-dimethyl-1-phenyl pyrazole and also the 3-methyl-5-trimethylsilyl-1-phenyl-pyrazole **13** after refluxing with ethyl chloroformate and aluminum chloride in chloroform for 24 h. Therefore, the introduction of the ethoxycarbonyl group has to be simultaneous with the cyclization (Scheme 10).

Other electrophiles, like iodine, were showed to be more reactive. When the hydrazones **10a**,**b** were stirred at room temperature with one equivalent of iodine, the 4-iodo-5-silylpyrazoles **15a**,**b** were isolated (Scheme 11).

In conclusion, we have prepared isoxazoles bearing at C-5 other silyl groups more stable than the usual trimethylsilyl, which on occasions proved to be more convenient. For example, we have recently described the reductive cleavage of 4- and 5-silyl isoxazoles and their homologues to give silyl β-enaminones of great interest in the construction of silylated penta- and hexaheterocycles. On occasions, the trimethylsilyl derivatives were unstable in the acidic conditions neccessary for cyclization to take place and desilylated heterocycles were obtained. Nevertheless, β-enaminones bearing more stable silyl groups such as dimethylphenyl, diphenylmethyl and *tert*-butyldiphenyl, yielded pyrazoles, pyrimidines, 2-pyridones and pyrroles, which retain the silyl group.[8] Moreover, we have prepared for the first time



Scheme 9.



Scheme 10.

5-silyl pyrazoles by condensation of silylalkynones with hydrazines. Especially interesting is the addition of electrophiles to the hydrazone intermediates to give in one step highly functionalized 3-pyrazolines or 5-silylpyrazoles bearing at C-4 groups which are impossible to introduce by electrophilic substitution.

3. Experimental

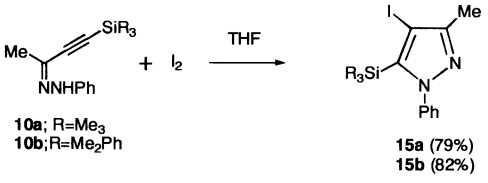
3.1. General

THF was distilled from sodium benzophenone ketyl in a recycling still. CH_2Cl_2 was distilled from P_2O_5. All chromatographic and workup solvents were distilled prior to use. All reactions involving organometallic reagents were carried out under N_2. The 4-trimethylsilyl-3-butyn-2-one was purchased from Aldrich. ^1H and ^{13}C NMR spectra were recorded at 300 and 75 MHz, respectvely in $CDCl_3$ as an internal standard. Carbon multiplicities were assigned by DEPT experiments. Reactions were monitored by TLC on a precoated plate of silica gel 60 (nano-SIL-20, Macheray–Nagel). Flash chromatography was performed on silica gel 60 (230–240 mesh, M–N).

3.2. Preparation of silylalkynones 2a–c

To a stirred solution of trimethylsilylacetylene (12 mmol) in dry THF (10 mL) at −78°C under N_2, BuLi (12 mmol, 7.5 mL of a solution 1.6 M in hexane) was added. Then, the chlorosilane (12 mmol) was added dropwise and the mixture was allowed to warm to 0°C and stirred for 3 h. Quenching with an aq. NH_4Cl solution, workup with ether, drying of the Et_2O layer ($MgSO_4$) and chromatography of the residue obtained after evaporation of Et_2O gave the following products.

3.2.1. 1-Dimethylphenylsilyl-2-trimethylsilylacetylene 1a. (97%); R_f=0.87 (hexane–AcOEt, 20:1); IR (film) 2100, 1250, 1100 cm^{-1}; ^1H NMR δ 7.67 (m, 2H), 7.41 (m, 3H), 0.44 (s, 6H), 0.22 (s, 9H); ^{13}C NMR δ 136.87, 133.70, 129.38, 127.85, 115.97, 11.37, −0.08, −0.76; MS (EI) *m/z* (%) 232 (M^+, 22%), 217 (100), 159 (40), 135 (23),



Scheme 11.

73 (60).Anal. Calcd for $C_{13}H_{20}Si_2$: C, 67.17; H, 8.67. Found: C, 66.83; H, 8.42.

3.2.2. 1-*tert*-Butyldiphenylsilyl-2-trimethylsilylacetylene 1b. (99%); R_f=0.85 (hexane–AcOEt, 20:1); IR (film) 2120, 1390, 1100 cm^{-1}; ^1H NMR δ 7.86 (m, 4H), 7.45 (m, 6H), 1.14 (s, 9H), 0.32 (s, 9H); ^{13}C NMR δ 135.56, 133.14, 129.63, 127.75, 119.00, 108.98, 26.98, 18.44, −0.10; MS (EI) *m/z* (%) 336 (M^+, 2%), 279 (100), 73 (2), 57 (14). Anal. Calcd for $C_{21}H_{28}Si_2$: C, 74.93; H, 8.38. Found: C, 75.15; H, 8.16.

To a solution of **1a** or **1b** (11.8 mmol) in CH_2Cl_2 (10 mL) cooled at −20°C for **1a** and 0°C for **1b** was added acetyl chloride (11.8 mmol, 0.83 mL) and freshly sublimed aluminum chloride (11.8 mmol, 1.584 g). The reaction was stirred at this temperature until TLC indicated complete reaction (2–3 h). The mixture was hydrolyzed with aq. NH_4Cl and the organic layer washed with a sodium hydrogen carbonate solution and brine, dried ($MgSO_4$) and distilled to isolate **2a** and **2b** or chromatographed to purify **2c**.

3.2.3. 4-Trimethylsilyl-3-butin-2-one 2a. (21%); bp 156°C.

3.2.4. 4-Dimethylphenylsilyl-3-butin-2-one 2b. (63%); bp 79–81°/0.5 mmHg;; R_f=0.40 (hexane–AcOEt,20:1); IR (film) 2150, 1670, 1260, 1100 cm^{-1}; ^1H NMR δ 7.66 (m, 2H), 7.48 (m, 3H), 2.40 (s, 3H), 0.50 (s, 6H); ^{13}C NMR δ 184.20, 139.72, 133.64, 129.20, 127.65, 103.44, 95.22, 32.51, −1.69; MS (EI) *m/z* (%) 202 (M^+, 8%), 201 (24), 187 (100), 159 (84), 145 (84), 129 (35),77 (19). Anal. Calcd for $C_{12}H_{14}OSi$: C, 71.24; H, 6.97. Found: C, 70.97; H, 7.12.

3.2.5. 4-*tert*-Butyldiphenylsilyl-3-butin-2-one 2c. (70%); R_f=0.42 (hexane–AcOEt, 20:1); mp 48°C (from hexane); IR (film) 2060, 1680, 1100 cm^{-1}; ^1H NMR δ 7.75 (m, 4H), 7.41 (m, 6H), 2.46 (s, 3H), 1.12 (s, 9H); ^{13}C NMR δ 183.92, 135.46, 131.34, 130.01, 127.94, 105.72, 92.96, 32.76, 29.00, 26.90; MS (EI) *m/z* (%) 249 ($M^+-{}^t$Bu, 36%), 207 (20), 57 (100), 43 (46). Anal. Calcd for $C_{20}H_{22}OSi$: C, 78.38; H, 7.24. Found: C, 78.65; H, 6.95.

3.3. Reaction of 2a–c with hydroxylamine or hydrazines. Typical procedure

A mixture of the silylalkynone **2a–c** (3 mmol) and hydroxylamine hydrochloride or hydrazine hydrochlorides (6 mmol) and sodium acetate (9 mmol) or free hydrazines (6 mmol), was refluxed in ethanol (12 mL) until TLC indicated complete reaction. The solvent was evaporated under reduced pressure and the residue was extracted with CH_2Cl_2/H_2O. The organic layer was dried ($MgSO_4$) and concentrated and the residue was chromatographed to give the following products.

3.3.1. 3-Methyl-5-dimethylphenylsilylisoxazole 4b. (73%); R_f=0.42 (CH_2Cl_2); IR (film) 1590, 1250, 1100 cm^{-1}; ^1H NMR δ 7.60 (m, 2H), 7.35 (m, 3H), 6.29 (s, 1H), 2.33 (s, 3H), 0.64 (s, 6H); ^{13}C NMR δ 176.09, 157.67, 139.94, 129.21, 127.76, 114.66, 10.73, −0.05; MS(EI) *m/z* (%) 217 (M^+, 4%), 202 (30), 174 (46), 161 (48), 135 (100). Anal. Calcd for $C_{12}H_{15}NOSi$: C, 66.31; H, 6.96; N, 6.44. Found: C, 66.73; H, 7.19; N, 6.31.

3.3.2. *Z* and *E*-4-*tert*-Butyldiphenylsilyl-3-butyn-2-one oxime 3c. (93%); R_f=0.36 (CH_2Cl_2); IR (KBr) 3300, 2190, 1100 cm^{-1}; ^1H NMR of the ***Z*-3c**:δ 8.47 (s br, 1H), 7.84–7.79 (m, 4H), 7.43 (m, 6H), 2.16 (s, 3H), 1.14 (s, 9H); ^1H NMR of the ***E*-3c**: δ 9.08 (s br, 1H), 7.84–7.79 (m, 4H), 7.43–7.37 (m, 6H), 2.14 (s, 3H), 1.13 (s, 9H). The mixture of ***Z*/*E*-3c** was cyclized by heating at 190°C/0.1 mm Hg to give the following.

3.3.3. 3-Methyl-5-*tert*-butyldiphenylsilylisoxazole 4c. (41%); mp 96–97°C (from hexane) R_f=0.43 (CH_2Cl_2); IR (film) 1590, 1550, 1450, 1100 cm^{-1}; ^1H NMR δ 7.62 (m, 4H), 7.35 (m, 6H), 6.20 (s, 1H), 2.32 (s, 3H), 1.17 (s, 9H); ^{13}C NMR δ 174.30, 157.59, 136.04, 132.01, 129.92, 127.88, 117.92, 27.48, 18.52, 10.81; MS (EI) *m/z* (%) 321 (M^+, 7%), 264 (100), 223 (45), 57 (8). Anal. Calcd for $C_{20}H_{23}NOSi$: C, 74.72; H, 7.21; N, 4.36. Found: C, 74.56; H, 7.08; N, 4.50.

3.3.4. 4-Trimethylsilyl-3-butyn-2-one hydrazone 5a. (84%);R_f=0.54 (CH_2Cl_2); IR (film) 3350, 3200, 2140, 1250 cm^{-1}; ^1H NMR δ 7.47 (s, 1H), 6.06 (s, 1H), 2.32 (s, 3H), 0.27 (s, 9H); ^{13}C NMR δ 128.76, 107.27, 88.90, 21.80, −0.32; MS (EI) *m/z* (%) 154 (M^+, 30%), 139 (100), 98 (47), 81 (6), 73 (8). Anal. Calcd for $C_7H_{14}N_2Si$: C, 54.49; H, 9.15; N, 18.16. Found: C, 54.23; H, 8.97, N, 18.29.

3.3.5. 4-Trimethylsilyl-3-butyn-2-one methylhydrazone 6a. (70%); R_f=0.50 (CH_2Cl_2); ^1H NMR δ 3.02 (s, 3H), 2.00 (s, 3H), 0.24 (s, 9H); ^{13}C NMR δ 128.31, 104.96, 90.71, 38.47, 18.39, 1.33; MS (EI) *m/z* (%) 168 (M^+, 28%), 153 (100), 97 (4), 95 (5), 73 (15), 59 (22). Anal. Calcd for $C_8H_{16}N_2Si$: C, 57.09; H, 9.58; N, 16.64. Found: C, 56.89; H, 9.26; N, 16.42.

3.3.6. 4-*tert*-Butyldiphenylsilyl-3-butyn-2-one hydrazone 5c. (79%); R_f=0.43 (CH_2Cl_2); IR (film) 3400, 3250, 2110, 1100 cm^{-1}; ^1H NMR δ 7.80 (m, 4H), 7.38 (m, 6H), 6.03 (s, 2H), 2.18 (s, 3H), 1.14 (s, 9H); ^{13}C NMR δ 135.50, 132.25, 129.8, 128.49, 127.70, 102.70, 99.22, 27.04, 21.98, 18.40; MS (EI) *m/z* (%) 320 (M^+, 14%), 263 (100), 222 (51), 185 (15), 77 (3), 57 (8). Anal. Calcd for $C_{20}H_{24}N_2Si$: C, 74.95; H, 7.55; N, 8.74. Found: C, 75.12; H, 7.33; N, 8.56.

3.3.7. 4-*tert*-Butyldiphenylsilyl-3-butyn-2-one methylhydrazone 6c. (59%); R_f=0.42 (CH_2Cl_2); IR (film) 3300, 2150, 1100 cm^{-1}; ^1H NMR δ 7.80 (m, 4H), 7.46 (m, 6H), 6.06 (s, 1H), 3.05 (d, *J*=4.8 Hz, 3H), 2.13 (s, 3H), 1.13 (s, 9H); ^{13}C NMR δ 135.50, 131.37, 130.03, 127.97, 123.31, 105.73, 93.04, 32.83, 26.94, 22.67, 18.50; MS (EI) *m/z* (%) 334 (M^+, 32%), 277 (52), 236 (35), 183 (9), 95 (8), 77 (18), 57 (100). Anal. Calcd for $C_{21}H_{26}N_2Si$: C, 75.40; H, 7.83; N, 8.37. Found: C, 75.24; H, 7.96; N, 8.12.

3.3.8. 3-Methyl-5-dimethylphenylsilylpyrazole 7b. (54%); R_f=0.42 (CH_2Cl_2); IR (film) 3200, 1260, 1120 cm^{-1}; ^1H NMR δ 9.63 (s, 1H), 7.61 (m, 2H), 7.39 (m, 3H), 6.10 (s, 1H), 2.36 (s, 3H), 0.34 (s, 6H); ^{13}C NMR δ 143.25, 140.13, 133.02, 132.93, 129.14, 127.64, 104.49, 11.95, 0.86. Anal. Calcd for $C_{12}H_{16}N_2Si$: C, 66.62; H, 7.45; N, 12.95. Found: C, 66.39; H, 7.62; N, 13.06.

3.3.9. 1,3-Dimethyl-5-trimethylsilylpyrazole 8a. (60%); R_f=0.27 (hexane–AcOEt, 10:1); spectroscopic data were the same as those described by Effenberger.[9]

3.3.10. 1,3-Dimethyl-5-dimethylphenylsilylpyrazole 8b. (51%); R_f=0.28 (hexane–AcOEt, 10:1); IR (film) 1580, 1500, 1470, 1270, 1100 cm^{-1}; ^1H NMR δ 7.73 (m, 2H), 7.39 (m, 3H), 6.21 (s, 1H), 3.68 (s, 3H), 2.29 (s, 3H), 0.58 (s, 6H); ^{13}C NMR δ 147.38, 141.22, 136.24, 133.80, 129.54, 127.99, 115.24, 39.23, 12.90, 0.87. MS (EI) *m/z* (%) 230 (M^+, 19%), 215 (38), 135 (46), 95 (5), 77 (100). Anal. Calcd for $C_{13}H_{18}N_2Si$: C, 67.77; H, 7.88; N, 12.16. Found: C, 67.56; H, 7.59; N, 12.31.

3.3.11. 4-Trimethylsilyl-3-butyn-2-one phenylhydrazone 10a. (80%); R_f=0.44 (hexane–CH_2Cl_2, 10:1); IR (film) 3320, 2160, 1630, 1250 cm^{-1}; ^1H NMR δ 8.33 (s, 1H), 7.84 (t, *J*=7 Hz, 2H), 7.10 (d, *J*=7 Hz, 2H), 6.92 (t, *J*=7 Hz, 1H), 2.18 (s, 3H), 0.35 (s, 9H); ^{13}C NMR δ 143.91, 129.23, 123.29, 120.25, 112.84, 107.80, 96.00, 21.65, −0.19; MS (EI) *m/z* (%) 230 (M^+, 46%), 215 (15), 185 (3), 105 (35), 77 (100), 73 (15). Anal. Calcd for $C_{13}H_{18}N_2Si$: C, 67.77; H, 7.88; N, 12.16. Found: C, 67.92; H, 7.63; N, 11.98.

3.3.12. 4-Dimethylphenylsilyl-3-butyn-2-one phenylhydrazone 10b. (86%); R_f=0.61 (hexane–AcOEt, 20:1); IR (film) 3300, 2110, 1260, 1100 cm^{-1}; ^1H NMR δ 8.32 (s, 1H), 7.62 (m, 2H), 7.40 (m, 3H), 7.29 (t, *J*=8 Hz, 2H), 7.00 (d, *J*=8 Hz, 2H), 6.89 (t, *J*=8 Hz, 1H), 2.19 (s, 3H), 0.59 (s, 6H); ^{13}C NMR δ 143.79, 139.77, 133.60, 129.87, 129.22, 128.17, 123.03, 120.29, 112.82, 106.04, 97.75, 21.56, −1.13; MS (EI) *m/z* (%) 292 (M^+, 25%), 277 (8), 199 (10), 159 (18), 135 (27), 105 (52), 77 (100). Anal. Calcd for $C_{18}H_{20}N_2Si$: C, 73.92; H, 6.89; N, 9.58. Found: C, 74.08; H, 7.03; N, 9.34.

3.3.13. 4-*tert*-Butyldiphenylsilyl-3-butyn-2-one phenylhydrazone 10c. (97%); R_f=0.90 (hexane–AcOEt, 20:1); IR (film) 3300, 2110, 1390, 1370, 1100 cm^{-1}; ^1H NMR δ 8.55 (s, 1H), 7.91 (m, 4H), 7.52 (m, 6H), 7.32 (t, *J*=8 Hz, 2H), 7.04 (d, *J*=8 Hz, 2H), 6.92 (t, *J*=8 Hz, 1H), 2.32 (s, 3H), 1.36 (s, 9H); ^{13}C NMR δ 143.77, 135.47, 132.22, 129.92, 129.25, 127.98, 122.97, 120.36, 112.76, 103.41, 100.11, 27.09, 21.60, 18.5; MS (EI) *m/z* (%) 396 (M^+, 21%), 339 (16), 298 (25), 220 (75), 181 (42), 105 (100), 57 (64). Anal. Calcd for $C_{26}H_{28}N_2Si$: C, 78.74; H, 7.12; N, 7.06. Found: C, 78.47; H, 7.32; N, 6.97.

3.4. Cyclization of *N*-phenylhydrazones by reaction with electrophiles

(a) To a solution of the hydrazone **10a** (5 mmol) in dry CH_2Cl_2 (20 mL) was added at room temperature acetyl chloride (7.5 mmol, 0.67 mL). After stirring for 24 h at this temperature, the mixture was diluted with CH_2Cl_2, washed with sodium bicarbonate aq. solution and the organic layer dried ($MgSO_4$) and evaporated under reduced pressure. The residue was purified by flash chromatography (SiO_2, CH_2Cl_2) to give the following.

3.4.1. 2-Acetyl-5-chloro-3-methyl-1-phenyl-5-trimethylsilyl-3-pyrazoline 11. (81%);R_f=0.42 (CH_2Cl_2); IR (film) 1660, 1590, 1250 cm^{-1}; ^1H NMR δ 7.37–7.26 (m, 5H), 5.36 (s, 1H), 2.15 (s, 3H), 1.92 (s, 3H), 0.17 (s, 9H); ^{13}C NMR δ 174.73, 149.94, 139.42, 135.00, 129.66, 129.31, 119.88, 95.98, 31.72, 20.73, −2.69; MS (EI) *m/z* (%) 293 (M^+−Me, 4%), 265 (6), 231 (18), 216 (94), 215 (10), 200 (10), 174 (7), 105 (6), 93 (100), 73 (72). Anal. Calcd for $C_{15}H_{21}ClN_2OSi$: C, 58.33; H, 6.85; N, 9.07. Found: C, 58.52; H, 6.73; N, 8.91.

(b) Ethyl chloroformate (2.2 mmol, 0.22 mL) and the phenylhydrazone **10a** (2 mmol) were added successively to freshly sublimed aluminum chloride (2.2 mmol, 0.293 g), in CH_2Cl_2 (5 mL) at room temperature. The stirred mixture was refluxed until TLC indicated complete reaction, neutralised with an ice-cooled 1 M solution of $NaHCO_3$, and extracted with CH_2Cl_2. The combined organic layers were dried ($MgSO_4$), the solvent evaporated and the residue chromatographed (SiO_2, CH_2Cl_2) to give the following compounds:

3.4.2. 3-Methyl-5-trimethylsilyl-1-phenylpyrazole 13. (21%), whose spectroscopic data are identical to those earlier reported by us.[8.]

3.4.3. 4-Ethoxycarbonyl-3-methyl-5-trimethylsilyl-1-phenylpyrazole 14. (73%); R_f=0.36 (CH_2Cl_2); IR (film) 1710, 1250 cm^{-1}; ^1H NMR δ 7.20–7.33 (m, 5H), 4.24 (q, *J*=7 Hz, 2H), 2.27 (s, 3H), 1.29 (t, *J*=8 Hz, 3H), 0.09 (s, 9H); ^{13}C NMR δ 167.66, 153.47, 151.41, 141.62, 136.16, 132.31, 130.79, 126.01, 68.01, 24.55, 14.41, −0.08. MS (EI) *m/z* (%) 302 (M^+, 85%), 258 (5), 229 (50), 225 (10), 105 (22), 97 (30), 77 (100), 73 (50). Anal. Calcd for $C_{16}H_{22}N_2O_2Si$: C, 63.54; H, 7.33; N, 9.26. Found: C, 63.34; H, 7.14; N, 9.38.

(c) To a solution of the phenylhydrazones **10a**,**b** (3 mmol) in dry THF (10 mL) at room temperature was slowly added iodine (3 mmol, 0.750 g). The reaction mixture was stirred at this temperature until the total disappearance of the starting product (TLC). After adding a solution of concentrated sodium thiosulfate, the mixture was stirred until it became colourless. The aq. layer was separated and extracted with ether and the combined organic phases were dried ($MgSO_4$) and evaporated. The residue was chromatographed to give:

3.4.4. 4-Iodo-3-methyl-5-trimethylsilyl-1-phenylpyrazole 15a. (79%); R_f=0.29 (hexane–AcOEt, 10:1); IR (film) 1580, 1250 cm^{-1}; ^1H NMR δ 7.43 (m, 3H), 7.36 (m, 2H), 2.33 (s, 3H), 0.16 (s, 9H); ^{13}C NMR δ 151.23, 144.23, 142.96, 128.84, 127.18, 126.20, 57.42, 13.73, 0.08. MS (EI) *m/z* (%) 356 (M^+, 100%), 341 (75), 229 (5), 214 (24), 127 (5), 105 (7), 77 (5), 73 (15). Anal. Calcd for $C_{13}H_{17}IN_2Si$: C, 43.83; H, 4.81; N, 7.86. Found: C, 44.01; H, 4.56; N, 7.62.

3.4.5. 4-Iodo-3-methyl-5-dimethylphenylsilyl-1-phenylpyrazole 15b. (84%); colourless crystals; mp 86–88°C (from hexane).[1]

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