Pergamon

Tetrahedron Letters 39 (1998) 1449–1452

TETRAHEDRON LETTERS

Reactions of pyrazolium salts with silyllithium reagents. Regioselective synthesis of 5-silylated 3-pyrazolines

Purificación Cuadrado and Ana M. González-Nogal*

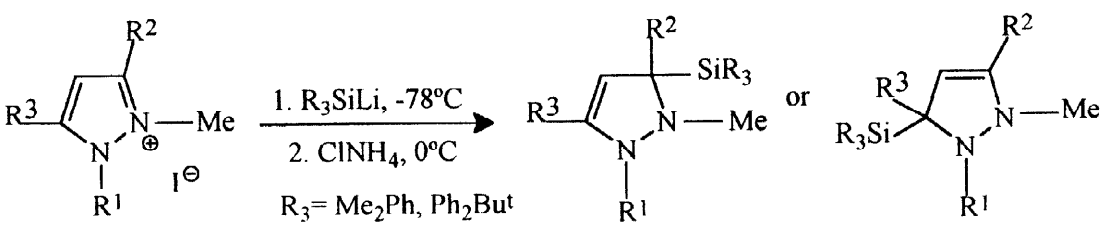
Departamento de Química Orgánica, Universidad de Valladolid, 47011, Spain.

Received 10 November 1997; accepted 12 December 1997

Abstract: 1,3,5-trisubstituted-2-methylpyrazolium iodides react with dimethylphenylsilyl- and *tert*-butyldiphenylsilyllithium leading, in general, to one of the corresponding 5-silyl-3-pyrazolines. The silyl group is easily substituted by electrophiles to give 5-functionalized 3-pyrazolines. Moreover, 5-silyl-3-pyrazolines undergo thermic ring opening with silicon-rearrangement affording α-silylated β-diimines.

Pyrazolium salts are not reactive toward organometallic reagents. Elguero *et al.*[1] studied the reaction of methylmagnesium iodide with 1-phenyl-2,3,5-trimethyl- and 1-phenyl-2,3-dimethylpyrazolium iodide in ether and they obtained unsuccessful results even after refluxing for 20 hours. Recently[2], we have found that the presence of a nitro group at C-4 in pyrazolium salts satisfactorily activates the ring toward organolithium or Grignard reagents, leading to 4-nitropyrazolidines together with 4-nitro-3-pyrazolines. Pyrazolium rings bearing electron-withdrawing groups at C-4, other than nitro, do not react with organometallic compounds.

We now report that 1,3,5-trisubstituted-2-methylpyrazolium iodides **1-5** react easily with dimethylphenylsilyl- and *tert*-butyldiphenylsilyllithium giving, in general, 5-silyl-3-pyrazolines **6** or **7** regioselectively. (Scheme 1).



1-5 **6** **7**

Scheme 1

The results obtained are summarized in Table 1.

PII: S0040-4039(97)10825-5

Table 1. Reactions of 2-methylpyrazolium iodides with silyllithium reagents[a]

Substrate	R^1	R^2	R^3	R_3Si	Products and yields (%)
1	Ph	Me	Me	$PhMe_2$	6a (89)
				$^tBuPh_2$	7a (57)
2	Ph	Me	Ph	$PhMe_2$	6b (52) + 7b (41)
				$^tBuPh_2$	7c (35)
3	Me	Me	Me	$PhMe_2$	——[b]
				$^tBuPh_2$	6d (67)
4	Me	Me	Ph	$PhMe_2$	6e (91)
				$^tBuPh_2$	6f (73)
5	Me	Ph	Ph	$PhMe_2$	6g (84)
				$^tBuPh_2$	6h (38)

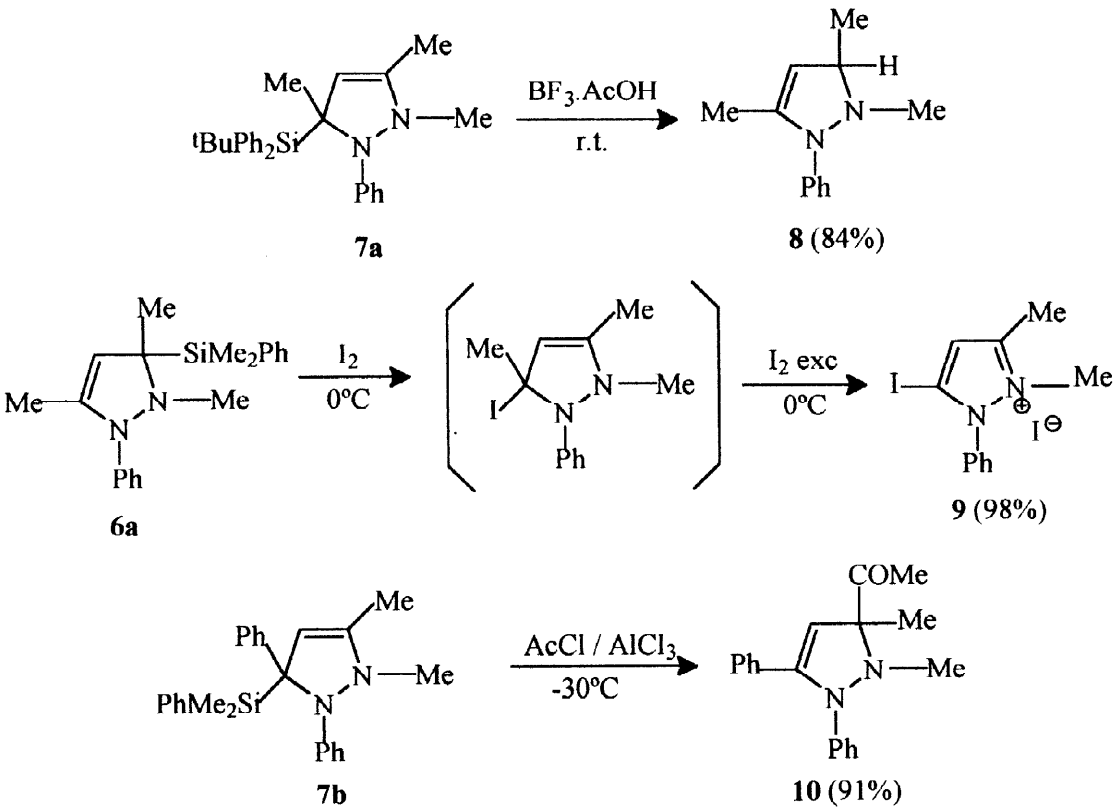
[a] Reactions were carried out using a molar ratio pyrazolium/R_3SiLi = 1:1 in THF as a solvent. [b] Only traces of 1,2,3,5-tetramethyl-5-dimethylphenylsilyl-3-pyrazoline were detected by ^{1}H-NMR.

When R^1=Ph, the C-3 and C-5 positions of 2-methylpyrazolium salts are different. The attack of silyl anion at C-3 or C-5 would lead to regioisomers 5-silyl-3-pyrazolines. The reaction of the 2-methyl-pyrazolium iodide **1** (R^1=Ph, R^2=R^3=Me) with dimethylphenylsilyllithium only gave the 3-pyrazoline **6a** resulting from the attack of silyl anion at the more electron-deficient C-3. However, the voluminous *tert*-butyl-diphenylsilyllithium attacked the less hindered C-5 to give the 3-pyrazoline **7a**. In addition, when $R^2 \neq R^3$, the selective formation of either of the 3-pyrazolines also depends on the nature of the 3- and 5-substituents. Thus, the 5-phenyl group in the pyrazolium salt **2** (R^2=Me, R^3=Ph) enhances the electrophilicity of C-5. In its reaction with dimethylphenylsilyllithium it afforded a 1.25:1 mixture of 3-pyrazolines **6b** and **7b**, respectively. Nevertheless, the *tert*-butyldiphenylsilyllithium attacked at C-5 exclusively, although in this case the yield of the corresponding 3-pyrazoline was lower than in its reaction with **1**. Probably the presence in C-5 of phenyl, a larger group than methyl, increases the steric hindrance[3] and the approach of the bulky *tert*-butyldiphenylsilyl group is more difficult.

On the other hand, although the C-3 and C-5 positions in the 1,2-dimethylpyrazolium salts are interchangeable, if the substituents are different, the attack of silyl anion may take place at either positions to give two different 5-silyl-3-pyrazolines. The reactions of 1,2-dimethylpyrazolium iodide **4** (R^2=Me, R^3=Ph) with dimethylphenylsilyl- and *tert*-butylphenylsilyllithium afford, in both cases, selectively the 5-silyl-3-pyrazoline in which the double bond C=C is conjugated with the phenyl group, **6e** and **6f**, respectively.

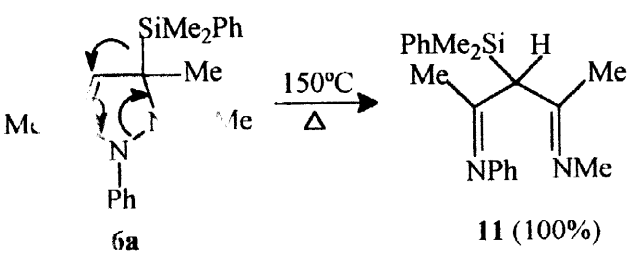
In general, the dimethylphenylsilyllithium is showed a more reactive and suitable reagent than its *tert*-butyldiphenylsilyl counterpart.All new compounds showed satisfactory spectral and analytical data[4].

Two additional features of this methodology should be pointed out: in the first place, the allylsilane unit of these 5-silyl-3-pyrazolines is easily substituted by electrophiles with double bond rearrangement to give new 5-functionalized 3-pyrazolines. The protodesilylation, the substitution by iodine and by acetyl chloride have been proved. The iododesylilation is rapid and quantitative. In the presence of iodine, the resulting 5-iodo-3-pyrazoline was quickly oxidated to 5-iodopyrazolium iodide **9** (Scheme 2).



Scheme 2

On the other hand, although 5-silyl-3-pyrazolines are stable at room temperatura, when they were heated to about 150°C, the ring was opened with silicon-rearrangement to give α-silyl-β-diimines (Scheme3)



Scheme 3.

The bis-imine structure for **11**, rather than an enamino-imine, was assigned by ^{1}H- and ^{13}C-NMR spectroscopy (proton attached at carbon). Moreover, the silyl group can not be attached at N because the relatively weak N-Si bond would be easily hydrolyzed by H_2O or MeOH. When **11** was stirred with aqueous NH_4Cl for 30 min. it remained unchanged.

In conclusion, we have developed a simple and suitable method to prepare 5-silylated 3-pyrazolines for the first time. Furthermore, we have been able to prove the easy substitution of the silyl groups by some electrophiles. This methodology will be extended to other pyrazolium salts and to the use of a wide variety of electrophiles, with the aim of synthesizing new 5- functionalized 3-pyrazolines. Finally, it is important to emphasize that α-silyl-β-diimines, resulting from the pyrolytic opening of 5-silyl-3-pyrazolines are interesting synthons in organic chemistry, because they are synthetic equivalents of α-silylated-β-diketones.

ACKNOWLEDGEMENTS: We thank the Junta de Castilla y León for financial support. (Grant VA26/95).

REFERENCES and NOTES

1. Elguero, J.; Jacquier, R.; Tizané, D. *Bull. Soc. Chim. France* **1970,**1121 and 1129.
2. Cuadrado, P.; González-Nogal, A.M.; Martínez, S. *Tetrahedron* **1997,** 8585.
3. In a previous paper we have reported similar steric effects in the reaction of 4-nitro-1,5-diphenylpyrazole with $LiAlH_4$ (reference 2).
4. Selected spectroscopy data: **6a :** ^{1}H-NMR ($CDCl_3$) δ 7.69-7.08 (10H, m, PhN and PhSi), 4.63 (1H, s, 4-H), 2.33 (3H, s, MeN), 1.66 (3H, s, 3-Me), 1.24 (3H, s, 5-Me), 0.58 and 0.56 (total 6H, s, $SiMe_2$); ^{13}C-NMR($CDCl_3$) δ 146.76 (=*C*Me), 140.98 (=C, PhSi), 137.33 (=C, PhN), 133.94, 127.48 and 126.14 (=CH, PhSi), 132.74, 130.81 and 128.67 (=CH, PhN), 108.24 (=CH), 59.74 (C-5), 37.02 (MeN), 17.59 (3-Me), 13.99 (5-Me), -4.82 and -5.01 ($SiMe_2$). **7a:** ^{1} H-NMR ($CDCl_3$) δ 7.76-7.32 (15H, m, PhN and Ph_2Si), 3.90 (1H, s, 4-H), 2.54 (3H, s, MeN), 2.26 (3H, s, 3-Me), 1.41 (3H, s, 5-Me), and 1.21 (9H, s, ^{t}BuSi). **9**: ^{1}H-NMR ($CDCl_3$) δ 7.79-7.61 (5H, m, Ph), 6.64 (1H, s, 4-H), 3.82 (3H, s, MeN) and 2.70 (3H, s, 3-Me). **10**: ^{1}H-NMR ($CDCl_3$) δ 7.67-7.32 (10H, m, PhN and PhC), 5.44 (1H, s, 4-H), 2.64 (3H, s, MeN), 2.24 (3H, s, COMe) and 1.32 (3H, s, 5-Me). **11**: ^{1}H-NMR ($CDCl_3$) δ 7.62-7.48 (2H, m, PhSi), 7.46-7.39 (3H, m, PhSi), 7.33 (2H, dd, J 7.1 and 8.4, NPh H_s *meta),* 7.05 (1H, tt, J 7.1 and 1.2, NPh H_s *para),* 6.87 (2H, dd, J 8.3 and 1.2, NPh H_s *orto),* 4.74 (1H, s, 3-H), 2.97 (3H, s, MeN), 2.03 (3H, s, 2-Me), 1.89 (3H, s, 4-Me), 0.40 and 0.39 (total 6H, s, $SiMe_2$). ^{13}C-NMR ($CDCl_3$) δ 166.36 (*C*=NPh), 156.81 (*C*=NMe), 151.75 (=C, PhN), 139.65 (=C, PhSi), 133.72, 128.4 and 128.30 (=CH, PhSi), 132.85, 127.5 and 121.44 (=CH, PhN), 93.63 (HC-3), 29.43 (MeN), 20.9 (2-Me), 19.1 (4-Me) and -4.03 ($SiMe_2$).