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Reactions of Lithium Silylcuprates with Pyrazolium and Indazolium Salts

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Although pyrazolium salts have been shown to be unreactive toward lithium carbocuprates, these substrates were opened by lithium silylcuprate reagents to give versatile *N*-silylated β-enaminoimines stabilized by coordination of the silyl group with both nitrogen atoms. In contrast, the behaviour of indazolium salts on treatment with the same reagents is more complex. Depending on the substitution patterns of the indazolium salts, the nature of the silylcuprate and even on the temperature, we obtained 3-silylindazolines and other interesting products resulting either from the opening of the heterocyclic ring or from modification by its opening/closing.

Introduction

Pyrazolium salts are not reactive toward organolithium and Grignard reagents,[1,2] except when they bear a nitro group at C-4. Nevertheless, in previous papers[3] we have reported the regioselective synthesis of silylated pyrazolines and indazolines by treatment of pyrazolium and indazolium salts with silyllithium reagents. On the other hand, we have not found any descriptions of the behaviour of these substrates toward lithium carbocuprates, but have verified their lack of reactivity. 2,3,5-Trimethyl-1-phenylpyrazolium iodide was recovered unchanged after treatment with lithium dimethylcuprate.

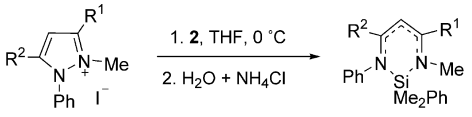
In contrast, however, this pyrazolium salt was shown to be reactive toward lithium dimethylphenylsilylcuprate. In this paper we describe in full the results obtained relating to the reactions of lithium silylcuprates with pyrazolium and benzopyrazolium salts.

Results and Discussion

Reactions of Pyrazolium Salts with Lithium Silylcuprates

With the aim of identifying the scope and limitations of this reaction, without counterpart in carbon chemistry, as substrates we used differently substituted and functionalized pyrazolium salts and as reagents two mixed higher-order lithium alkylsilylcuprates[4] of different size and reactivity: $Bu(Me_2PhSi)Cu(CN)Li_2$ (**2**) and $Bu(tBuPh_2Si)Cu(CN)Li_2$ (**3**), which selectively transfer a silyl group and consequently behave like lithium bis(silyl)cuprates, but are more advantageous because they substantially cheapen the synthesis and simplify the isolation process.

3,5-Alkyl- or -aryl-substituted 2-methyl-1-phenylpyrazolium iodides **1a**–**c** react with the mixed higher-order lithium butyl(dimethylphenylsilyl)cuprate **2**, but not with the bulky lithium butyl(*tert*-butyldiphenylsilyl)cuprate **3**, to give *N*-silylated β-enaminoimines **4a**–**c** (Scheme 1).



1a: $R^1 = R^2 = Me$ — **4a**: $R^1 = R^2 = Me$ (48%)
1b: $R^1 = Me$, $R^2 = Ph$ — **4b**: $R^1 = Me$, $R^2 = Ph$ (73%)
1c: $R^1 = R^2 = Ph$ — **4c**: $R^1 = R^2 = Ph$ (76%)

Scheme 1.

The high affinity of Cu towards N and the presence of a good leaving iminium group could explain the easy formation of a copper(III) amidocuprate intermediate, which selectively transfers the silyl ligand to the nitrogen atom, affording the *N*-silyl derivatives **A** upon reductive elimination (Scheme 2). Because of the easy metalotropy of the silyl groups, the β-enaminoimines **A** should exist in tautomeric equilibrium with the β-enaminoimines **B**. Nevertheless, in all the cases tested the ^1H NMR spectra of the reaction mixture showed single signals for the NMe and =CH protons. Moreover, although the silicon–nitrogen bond is very weak and easily hydrolysed with water or methanol, **4a**–**c** surprisingly retain their silyl groups after hydrolysis of their reaction mixtures with saturated aqueous ammonium chloride. These facts could justify admitting a stabilized chelated structure **C**, in which the silyl group is coordinated with both nitrogen atoms.

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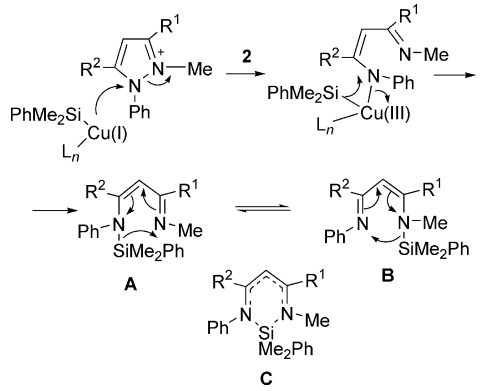
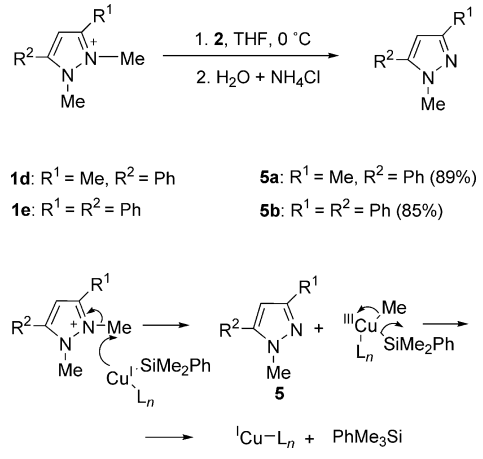


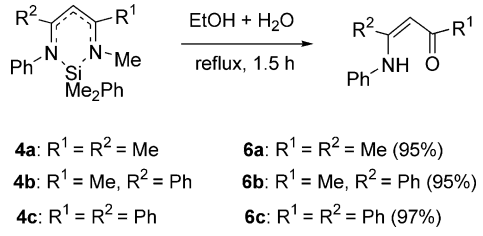
Scheme 2.

In contrast, when 1,2-dimethylpyrazolium salts **1d** and **1e** were treated with the dimethylphenylsilylcuprate **2**, dequaternization of the pyrazolium ring took place, leading to pyrazoles **5a** and **5b**. This behaviour, which is different from that observed with silyllithium reagents,[3] may be explained in terms of coordination of the Cu at the *N*-methylpyrazolium ion, elimination of the corresponding pyrazoles **5a** and **5b** and subsequent transfer of the silyl ligand at the Me group and reductive elimination to give $PhSiMe_3$[5] (Scheme 3).



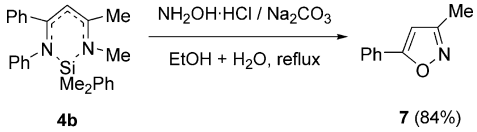
Scheme 3.

These *N*-silyl-β-enaminoimines **4a**–**c** may be regarded as synthetic equivalents of the corresponding β-enaminoketones **6a**–**c**, obtained by heating at reflux with a mixture of EtOH/H_2O 1.5:1 (Scheme 4).



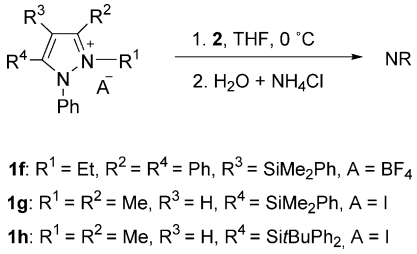
Scheme 4.

Moreover, the *N*-silyl-β-enaminoimines **4a**–**c** are interesting synthons, as they exhibit reactivity analogous to that already known from the β-enaminoketones.[6] Thus, **4b** was regioselectively[7] converted into 3-methyl-5-phenylisoxazole (**7**) by treatment with hydroxylamine hydrochloride (Scheme 5).



Scheme 5.

We have extended this reaction to differently functionalized pyrazolium salts. With the object of preparing synthetic equivalents of silylated β-enaminones, the applications of which to the synthesis of silyl heterocycles (pyrroles, pyrazoles, pyrimidines and pyridinones) have been established by us,[8] we studied the behaviour of differently silylated *N*-phenylpyrazolium salts with lithium butyl(dimethylphenylsilyl)cuprate. Unfortunately the presence of an electron-donating silyl group in the heterocyclic ring prevents the addition of the silylcuprate. The 4- or 5-silylpyrazolium salts **1f** or **1g/1h** were shown to be unreactive towards lithium butyl(dimethylphenylsilyl)cuprate **2** (Scheme 6).

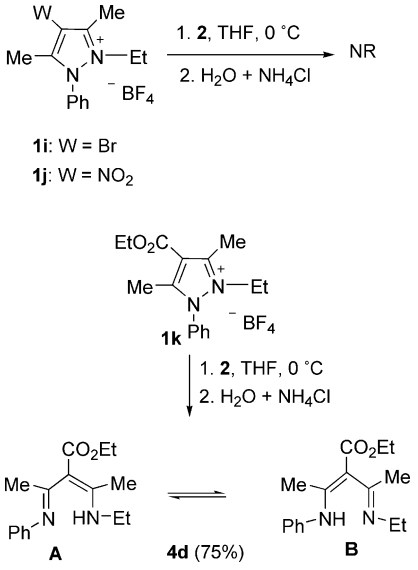


Scheme 6.

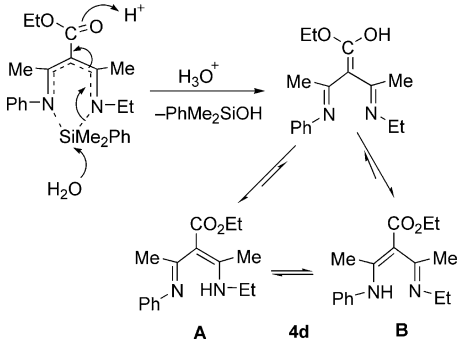
Although the presence of electron-withdrawing groups increases the electron deficiency of the pyrazolium ring and therefore the reactivity of this system toward silylcuprates, the 4-nitro- and 4-bromo-2-ethyl-3,5-dimethyl-1-phenylpyrazolium salts **1i** and **1j** were shown to be unreactive toward the silylcuprate reagent **2**. The same lack of reactivity was observed by us on treatment of **1i** and **1j** with silyllithium reagents.[3b] Nevertheless, the 4-ethoxycarbonylpyrazolium tetrafluoroborate **1k** reacted with the silylcuprate **2** to give a mixture of the two tautomeric desilylated β-enaminoimines **4d** (Scheme 7).

The hydrolytic lability of the initially formed *N*-silylated α-ethoxycarbonyl-β-enaminoimine may be attributed to the conjugative stabilization of the enol form of the ester group by the C=N functionalities (Scheme 8).

The behaviour of ethoxycarbonylpyrazolium salts toward lithium dimethylphenylsilylcuprate depends on the position of the ester group in the ring. Treatment of 5-ethoxycarbonylpyrazolium salt **1l** with the silylcuprate **2** gave the 5-ethoxycarbonyl-3-pyrazoline **8** (Scheme 9). This result could be satisfactorily explained in terms of a single-electron-transfer (SET) mechanism. Nevertheless, we think that



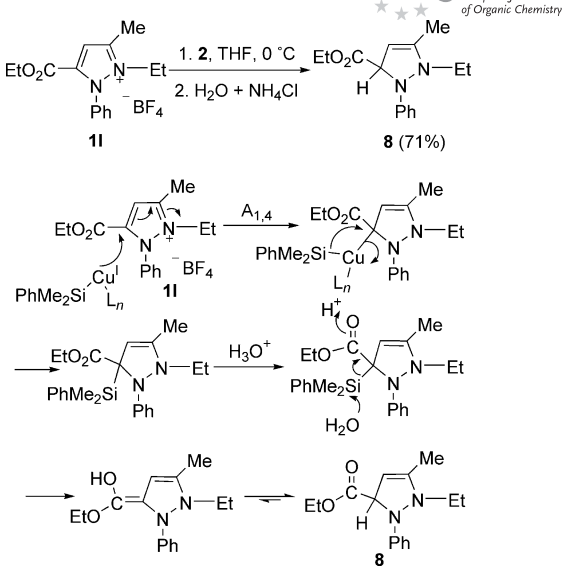
Scheme 7.



Scheme 8.

the compound **8** could also arise through desilylation of the initially formed 5-silylated 5-ethoxycarbonyl-3-pyrazoline, because we obtained the same result when we carried out the reaction with the silyllithium reagent.[3b] The withdrawing ester group at C-5 increases the electronic deficiency in this position, facilitating the conjugated addition of the silylcuprate **2** to the α,β-unsaturated iminium system and giving a coordinated copper(III) intermediate, which transfers the silicon at C-5 with concomitant reductive elimination of copper(I) to afford the corresponding 5-silyl-3-pyrazoline. Sensitivity to desilylation in this compound may be attributed to conjugative stabilization of the enol form by the *gem*-ester functionality.

When the ethoxycarbonyl group is attached at C-3 instead of at C-4 or C-5, the activity of the pyrazolium salt toward the nucleophilic attack is less, as was also previously observed by us[3b] in the reactions of these substrates with silyllithium reagents. When we treated the 2-ethyl-3-ethoxycarbonyl-5-methyl-1-phenylpyrazolium salt **1m** with the silylcuprate **2**, no reaction took place at –78 °C, whereas at 0 °C a complex mixture (of no synthetic interest) resulting from the attack of the reagent at the ring and the ester group was obtained.



Scheme 9.

Reactions of Indazolium Salts with Lithium Silylcuprates

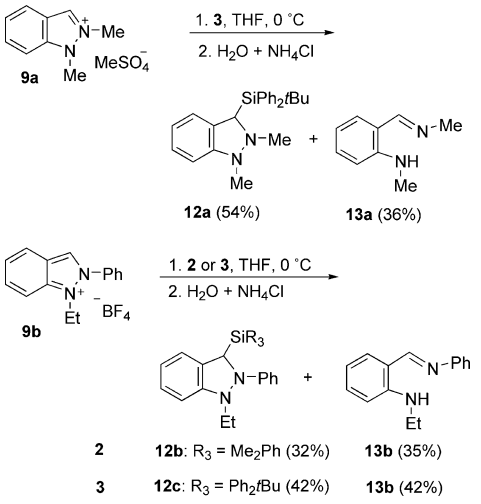
We were also interested in the behaviour of benzopyrazolium salts with silylcuprate reagents. We started from 3-unsubstituted (**9a** and **9b**), 3-substituted (**9c**) and 3-functionalized (**9d**) indazolium salts, as the natures of the products obtained depend on the substitution patterns of the substrates. Furthermore, we have been able to establish different behaviour relating to the structures of the silylcuprate reagents. In this case we used the mixed lithium silylcuprates **2** or **3** and the corresponding lithium bis(silyl)-cuprates $(Me_2PhSi)_2Cu(CN)Li_2$ (**10**) and $(t\text{BuPh}_2Si)_2Cu(CN)Li_2$ (**11**).

The reactivity of benzopyrazolium salts toward silylcuprates is complex and difficult to explain. In general, the organocuprates, besides being interesting nucleophilic reagents, are capable of electron transfer processes, and on occasions they can also behave as basic reagents. This can explain the different results obtained in the reactions between indazolium salts and silylcuprates depending on the structure of the benzopyrazolium salt, the nature of the silylcuprate and the reaction conditions.

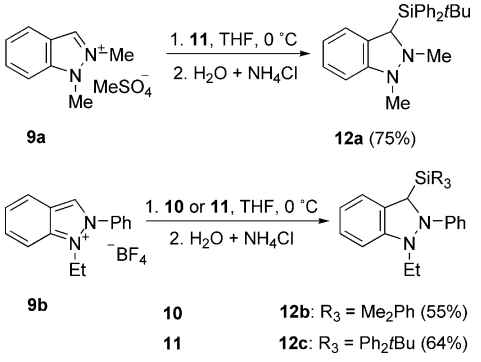
Thus, 3-unsubstituted indazolium and isoindazolium salts **9a** and **9b** underwent nucleophilic addition of mixed silylcuprates **2** and **3** to give the corresponding 3-silylindazolines **12a–c** and reductive ring opening, possibly through a single-electron-transfer mechanism, leading to the β-enaminoimines **13a** and **13b** (Scheme 10).

The use of lithium bis(silyl)cuprates increases regioselectivity. Both indazolium salts **9a** and **9b**, on treatment with higher-order bis(silyl)cuprates **10** and **11**, yielded 3-silylindazolines **12a–c** exclusively (Scheme 11).

The lack of regioselectively when **9a** and **9b** were treated with the mixed silylcuprates **2** and **3** at 0 °C could be due to the presence of lithium dibutylcuprate in dynamic equilibrium with the lithium silylcuprates. As we did not find any references concerning the reactivity of these substrates with lithium organocuprates, we initially studied the reac-

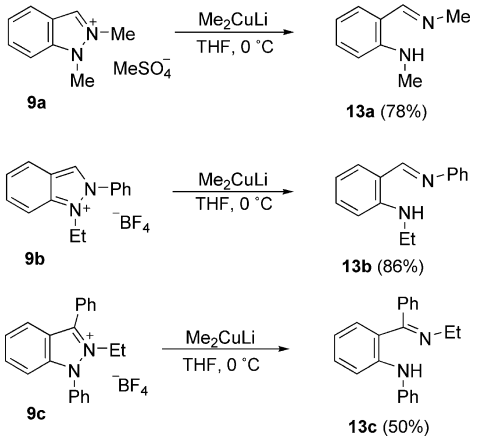


Scheme 10.



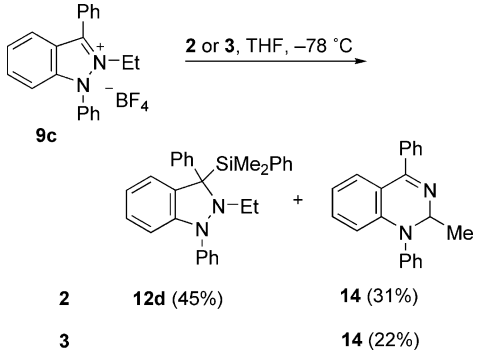
Scheme 11.

tion of the indazolium tetrafluoroborates **9a**–**c** toward lithium dimethylcuprate. These indazolium salts underwent reductive ring opening, probably through an electron-transfer process, giving the benzo-β-enaminoimines **13a**–**c** (Scheme 12).



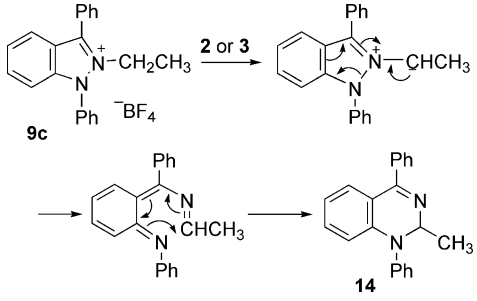
Scheme 12.

Nevertheless, the behaviour of the 3-phenylpyrazolium salt **9c** with lithium silylcuprates was more complex and temperature dependent. Thus, **9c** reacted at –78 °C with the mixed lithium butyl(dimethylphenylsilyl)cuprate (**2**) to afford a mixture of 3-silylindazoline **12d** and 2-methyl-1,4-diphenyldihydroquinazoline **14**. Meanwhile, the bulky *tert*-butyldiphenylsilylcuprate **3** (less nucleophilic and more basic than **2**) did not add to this indazolium salt, and the hydroquinazoline **14** was the only isolable product (Scheme 13). This behaviour by the *tert*-butyldiphenylsilyl cuprate as a base was observed by us in its reactions with phenylallenes. In contrast with dimethylphenylsilylcuprate, which is added to phenylallenes to afford vinylsilanes,[9] the basic *tert*-butyldiphenylsilylcuprate (*tert*-butyl alcohol inactivates it) induces the isomerization of the phenylallenes into acetylenes.[10]



Scheme 13.

The ring expansion from **9c** to **14** could take place by a heterocyclic opening/closing mechanism, probably initiated by the action of the silylcuprate reagent as a base to give a diazatriene, which undergoes an electrocyclic closure (Scheme 14).

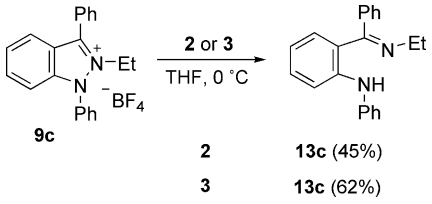


Scheme 14.

When treatment of **9c** with either silylcuprate **2** or **3** was carried out at 0 °C, only the reductive heterocycle opening took place, providing the same β-enaminoimine **13c** that had resulted from the treatment of **9c** with lithium dimethylcuprate (Scheme 15).

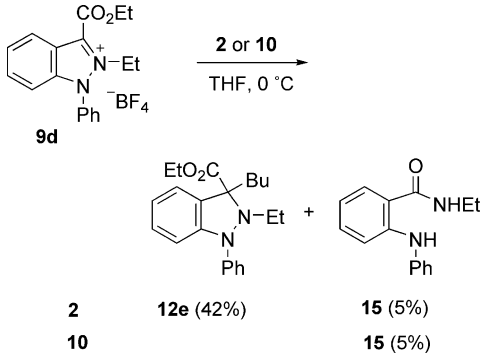
The same result was obtained with the bis(silyl)cuprates **10** and **11**.

Finally, we studied the reactivity of the 3-(ethoxycarbonyl)indazolium tetrafluoroborate **9d** toward the higher-order silylcuprates **2** and **10** (Scheme 16). Surprisingly, when **9d** was treated with the mixed carbosilylcuprate **2**, this transferred the butyl group instead of the dimethylphenylsilyl group. We obtained the 3-butylindazoline **12e** together



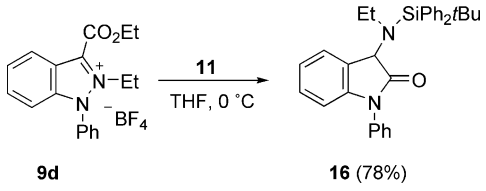
Scheme 15.

with minor amounts of the β-enaminoamide **15** resulting from the initial reaction of the silylcuprate with the ester group.[11] Undoubtedly, the use of bis(dimethylphenylsilyl) cuprate **10** prevents the alkylation of the ring but it did not enhance the reactivity. Only minor amounts (5%) of the enaminoamide **15** were obtained.



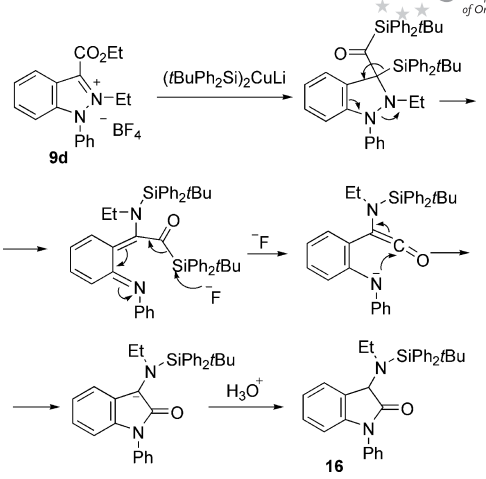
Scheme 16.

In contrast, the bis(*tert*-butyldiphenylsilyl)cuprate **11** was shown to be especially reactive towards this salt **9d**, leading to the *N*-silylated ethylamino-*N*-phenyloxindole **16** with a good yield (Scheme 17).



Scheme 17.

This result could be tentatively explained in terms of the simultaneous addition of the silylcuprate at C-3 and the ester group, to give a silylindazoline containing an acylsilane moiety, which is opened with concomitant silyl rearrangement from carbon to nitrogen. The acylsilane unit of this intermediate is attacked by the fluoride ion present in the reaction medium, affording a ketene, which experiences a 5-*endo*-*dig* intramolecular nucleophilic addition, yielding **16** in the final hydrolysis (Scheme 18).



Scheme 18.

Conclusions

We have studied a reaction without precedent in carbon chemistry. We have for the first time synthesized versatile *N*-silyl-β-enaminoimines through the opening of pyrazolium salts with lithium silylcuprates. The isolation of these compounds takes advantage of the stabilizing effect of the *N*-silyl framework. In addition to their applications as powerful silylating agents, silylamines are used in organic synthesis in several ways. In the first of these, silicon is essentially a protecting group, where its presence in place of hydrogen enables us to carry out reactions, at the nitrogen atom or elsewhere in the molecule, which would otherwise be thwarted. Moreover, a silylated amine is a reactive nitrogen nucleophile toward a wide variety of electrophiles (halogens, alkyl or acyl halides, ketenes, isocyanates, anhydrides etc.), due to the fact that a relatively weak Si–N bond is replaced by the much stronger Si–O or Si–X bond.

Furthermore, the application of this methodology to indazolium salts has allowed us to synthesize 3-silylindazolines and other interesting new products such as the *N*-silylated oxindole **16**, precursor for the synthesis of differently substituted and functionalized 3-aminooxindoles with potential biological activity.[12] Oxindoles, appropriately substituted at both nitrogen and C-3, are precursors in the synthesis of biologically active alkaloids,[13] and some of the compounds derived from the oxindole moiety are among the most active dopamine receptor agonists.[14] Functionalized indolin-2-ones have also turned out to be key synthons in the synthesis of antiinflammatory agents.[15]

Experimental Section

General: THF was distilled from sodium benzophenone ketyl in a recycling still. Dichloromethane was distilled from P_2O_5. Copper(I) cyanide was dried in vacuo over P_2O_5. All chromatographic and workup solvents were distilled prior to use. The 2-methylpyrazolium or -indazolium iodides were prepared by heating of the corresponding pyrazoles or indazoles with methyl iodide in a pressure tube, whereas 2-ethylpyrazolium tetrafluoroborates were prepared by treatment of the corresponding pyrazoles and indazoles with

triethyloxonium fluoroborate in dry dichloromethane at room temperature for several hours (12–20 h). All pyrazolium and indazolium salts were recrystallized from acetone/ether. Lithium bis(dimethylphenylsilyl)cuprate[9,16] (**10**) and bis(*tert*-butyldiphenylsilyl)-cuprate[10,17] (**11**) were prepared as described previously, and the mixed silylcuprate reagents **2** and **3** in the same way, through mixing of one equivalent of the corresponding silyllithium, one equivalent of butyllithium and one equivalent of copper(I) cyanide.[4] All reactions involving organometallic reagents were carried out under an atmosphere of nitrogen. ^{1}H and ^{13}C NMR spectra were recorded at 300 and 75 MHz, respectively, in $CDCl_3$ as an internal standard. Carbon multiplicities were assigned by DEPT experiments. Reactions were monitored by TLC on precoated silica gel 60 plates (nano-SIL-20, Macherey–Nagel). Flash chromatography was performed on silica gel 60 (230–400 mesh, M–N).

General Procedure for the Reactions of Pyrazolium and Indazolium Salts with Lithium Silylcuprate Reagents: A THF solution of the lithium silylcuprate reagent **2**, **3**, **10** or **11** (3 mmol) was added at 0 °C or –78 °C under an atmosphere of N_2 to a stirred solution of the pyrazolium or indazolium salt (3 mmol) in dry THF (2 mL). The reaction mixture was stirred at this temperature until TLC indicated that the reaction was complete. When the reaction was carried out at 0 °C, the mixture was quenched with aqueous NH_4Cl, and with methanol in the reactions at –78 °C. The organic layer was extracted with Et_2O and dried with $MgSO_4$, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography to give the following products.

Enamine 4a: Yield: 463 mg (48%); oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.40 (s, 6 H), 1.89 (s, 3 H), 2.03 (s, 3 H), 2.97 (s, 3 H), 4.74 (s, 1 H), 6.87 (dd, J = 1.2, 8.3 Hz, 2 H), 7.05 (tt, J = 1.2, 7.1 Hz, 1 H), 7.33 (dd, J = 7.1, 8.3 Hz, 2 H), 7.35–7.50 (m, 3 H), 7.60 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = –4.04, 19.11, 20.90, 29.43, 93.63, 121.92, 127.59, 128.30, 128.49, 132.87, 133.72, 139.65, 151.75, 156.81, 166.36 ppm. IR (film): $\tilde{\nu}$ = 3100, 1580, 1250, 1100 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 322 (2) $[M]^+$, 187 (21), 135 (100), 93 (40), 77 (78). $C_{20}H_{26}N_2Si$ (322.19): calcd. C 74.48, H 8.13, N 8.69; found C 74.77, H 7.95, N 8.36.

Enamine 4b: Yield: 840 mg (73%); oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.35 (s, 6 H), 2.07 (s, 3 H), 3.06 (s, 3 H), 4.91 (s, 1 H), 6.68 (dd, J = 1.2, 8.3 Hz, 2 H), 6.83 (tt, J = 1.2, 7.1 Hz, 1 H), 7.08 (dd, J = 7.1, 8.3 Hz, 2 H), 7.36–7.42 (m, 3 H), 7.56 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = –4.08, 19.46, 30.44, 95.44, 121.46, 127.59, 127.69, 127.87, 128.17, 128.42, 129.22, 129.62, 132.97, 139.71, 139.97, 150.42, 159.49, 166.55 ppm. IR (film): $\tilde{\nu}$ = 3120, 1585, 1250, 1100 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 384 (3) $[M]^+$, 249 (19), 193 (100), 135 (11), 77 (45). $C_{25}H_{28}N_2Si$ (384.20): calcd. C 78.07, H 7.34, N 7.28; found C 77.87, H 7.51, N 7.06.

Enamine 4c: Yield: 1.01 g (76%); oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.33 (s, 6 H), 2.96 (s, 3 H), 5.03 (s, 1 H), 6.75 (dd, J = 1.2, 8.3 Hz, 2 H), 6.86 (tt, J = 1.2, 7.1 Hz, 1 H), 7.13 (dd, J = 7.1, 8.3 Hz, 2 H), 7.18–7.48 (m, 15 H), 7.56 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = –4.00, 32.12, 97.54, 118.83, 121.71, 122.57, 125.12, 125.68, 127.61, 127.90, 128.14, 128.32, 128.75, 129.16, 133.71, 136.76 138.77, 139.47, 150.16, 167.88, 166.55 ppm. IR (film): $\tilde{\nu}$ = 3115, 1580, 1250, 1100 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 446 (1) $[M]^+$, 431 (11), 369 (23), 311 (98), 296 (26), 220 (100), 180 (12), 135 (7), 118 (14), 77 (73). $C_{30}H_{30}N_2Si$ (446.22): calcd. C 80.67, H 6.77, N 6.27; found C 80.88, H 6.54, N 6. 46.

Enamine 4d: Yield: 616 mg (75%); oil. Tautomer A (43%): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.09 (t, J = 7.2 Hz, 3 H), 1.41 (t, J = 7.1 Hz, 3 H), 2.01 (s, 3 H), 2.37 (s, 3 H), 3.06 (m, 2 H), 4.36 (q, J = 7.1 Hz, 2 H), 6.78 (d, J = 7.8 Hz, 2 H), 7.00 (t, J = 7.3 Hz, 1 H), 7.23 (dd, J = 7.8, 7.3 Hz, 2 H), 8.91 (br. s, 1 H) ppm. Tautomer B (57%): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.24 (t, J = 7.0 Hz, 3 H), 1.35 (t, J = 7.1 Hz, 3 H), 1.70 (s, 3 H), 2.55 (s, 3 H), 3.51 (q, J = 7.0 Hz, 2 H), 4.22 (q, J = 7.1 Hz, 2 H), 6.82 (d, J = 7.7 Hz, 2 H), 7.07 (t, J = 7.6 Hz, 1 H), 7.27 (dd, J = 7.7, 7.6 Hz, 2 H), 9.42 (br. s, 1 H) ppm. IR (film): $\tilde{\nu}$ = 1723, 1585, 730, 690 cm^{-1}. $C_{16}H_{22}N_2O_2$ (274.17): calcd. C 70.04, H 8.08, N 10.21; found C 69.83, H 8.32, N 9.91.

2-Ethyl-5-ethoxycarbonyl-3-methyl-1-phenyl-3-pyrazoline (8): Yield: 553 mg (71%); oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.11 (t, J = 7.0 Hz, 3 H), 1.36 (t, J = 7.1 Hz, 3 H), 1.89 (s, 3 H), 3.16 (q, J = 7.0 Hz, 2 H), 4.31 (q, J = 7.1 Hz, 2 H), 4.74 (d, J = 2.4 Hz, 1 H), 4.84 (d, J = 2.4 Hz, 1 H), 6.97 (t, J = 7.4 Hz, 1 H), 7.10 (d, J = 7.9 Hz, 2 H), 7.28 (dd, J = 7.4, 7.9 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 10.08, 12.70, 14.28, 46.59, 61.15, 73.28, 98.88, 114.73, 120.33, 127.83, 145.14, 152.46, 172.22 ppm. IR (film): $\tilde{\nu}$ = 1735, 1595, 1500, 825 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 260 (3) $[M]^+$, 245 (42), 231 (4), 215 (30), 187 (51), 77 (100). $C_{15}H_{20}N_2O_2$ (260.15): calcd. C 69.20, H 7.74, N 10.76; found C 69.45, H 7.91, N 10.52.

3-*tert*-Butyldiphenylsilyl-1,2-dimethylindazoline (12a): Yield: 625 mg (54%) from **3** and 868 mg (75%) from **11**; oil. R_f = 0.43 (hexane/CH_2Cl_2, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.22 (s, 9 H), 2.40 (s, 3 H), 2.56 (s, 3 H), 4.38 (s, 1 H), 6.38 (d, J = 7.9 Hz, 1 H), 6.57 (m, 2 H), 6.95 (m, 1 H), 7.19–7.60 (m, 10 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.22, 28.62, 41.30, 48.08, 62.21, 110.19, 120.16, 122.72, 126.71, 127.22, 127.27, 127.62, 129.11, 130.69 132.75, 134.95, 136.75, 136.87, 150.24 ppm. IR (film): $\tilde{\nu}$ = 1598, 1490, 1106 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 329 (100) [M – *t*Bu]$^+$, 309 (15), 224 (22), 146 (31), 77 (40), 57 (53). $C_{25}H_{30}N_2Si$ (386.22): calcd. C 77.67, H 7.82, N 7.25; found C 77.37, H 7.95, N 7.04.

3-Dimethylphenylsilyl-1-ethyl-2-phenylindazoline (12b): Yield: 343 mg (32%) from **2** and 590 mg (55%) from **10**; oil. R_f = 0.49 (hexane/CH_2Cl_2, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.42 (s, 3 H), 0.46 (s, 3 H), 1.24 (t, J = 7.2 Hz, 3 H), 2.85 (dq, J = 14.2, 7.2 Hz, 1 H), 3.12 (dq, J = 14.2, 7.2 Hz, 1 H), 4.61 (s, 1 H), 6.74 (d, J = 7.5 Hz, 1 H), 6.86 (m, 2 H), 7.10–7.64 (m, 11 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = –3.97, 14.22, 45.03, 53.27, 112.37, 112.75, 116.25, 120.98, 123.87, 127.65, 128.37, 129.21, 132.94, 132.45, 133.80, 139.74, 149.64, 155.25 ppm. IR (film): $\tilde{\nu}$ = 3015, 1590, 1486, 1250, 1100 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 343 (16) [M – Me]$^+$, 281 (5), 223 (100), 194 (19), 135 (31), 77 (14). $C_{23}H_{26}N_2Si$ (358.19): calcd. C 77.05, H 7.31, N 7.81; found C 77.32, H 7.49, N 7.67.

3-*tert*-Butyldiphenylsilyl-1-ethyl-2-phenylindazoline (12c): Yield: 582 mg (42%) from **3** and 887 mg (64%) from **11**; oil. R_f = 0.50 (hexane/CH_2Cl_2, 1:2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.02 (t, J = 7.2 Hz, 3 H), 1.33 (s, 9 H), 2.25 (dq, J = 14.1, 7.2 Hz, 1 H), 2.51 (dq, J = 14.1, 7.2 Hz, 1 H), 5.28 (s, 1 H), 6.61 (m, 2 H), 6.94 (m, 2 H), 7.14–7.54 (m, 15 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.03, 19.01, 28.45, 50.93, 63.27, 111.95, 117.23, 121.02, 121.15, 122.22, 126.46, 127.17, 127.79, 128.69, 129.36, 132.45, 133.89, 134.77, 135.66, 137.01, 137.08, 150.02, 157.18 ppm. IR (film): $\tilde{\nu}$ = 3018, 1596, 1486, 1105 cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 405 (100) [M – *t*Bu]$^+$, 300 (18), 222 (11), 105 (15), 77 (20), 57 (54). $C_{31}H_{34}N_2Si$ (462.25): calcd. C 80.47, H 7.41, N 6.05; found C 80.25, H 7.56, N 5.91.

3-Dimethylphenylsilyl-2-ethyl-1,3-diphenylindazoline (12d): Yield: 585 mg (45%) from **2**; oil. R_f = 0.43 (hexane/CH_2Cl_2, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.23 (s, 3 H), 0.25 (s, 3 H), 1.11 (t, J = 7.1 Hz, 3 H), 3.05 (m, 2 H), 6.90 (t, J = 7.4 Hz, 1 H), 7.05 (m,

3 H), 7.18 (dd, J = 7.6, 8.0 Hz, 1 H), 7.21–7.68 (m, 14 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = –4.87, 12.13, 52.19, 71.25, 112.05, 121.60, 122.72, 124.11, 127.21, 127.48, 127.90, 128.38, 128.90, 129.41, 132.31, 133.68, 139.22, 143.17, 145.38, 147.55 ppm. IR (film): $\tilde{\nu}$ = 3015, 1590, 1486, 1250, 1100 cm^{-1}. MS (EI, 70 eV): m/z (%) = 419 (11) $[M - Me]^+$, 300 (17), 299 (35), 222 (41), 135 (22), 77 (100). $C_{29}H_{30}N_2Si$ (434.22): calcd. C 80.14, H 6.96, N 6.45; found C 80.36, H 7.14, N 6.63.

Ethyl 3-Butyl-2-ethyl-1-phenylindazoline-3-carboxylate (12e): Yield: 443 mg (42%) from **2**; oil. R_f = 0.48 (hexane/CH_2Cl_2, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.82 (t, J = 7.1 Hz, 3 H), 1.16 (t, J = 7.0 Hz, 3 H), 1.19 (t, J = 7.0 Hz, 3 H), 1.20–1.34 (m, 4 H), 1.79 (dt, J = 13.6, 4.7 Hz, 1 H), 2.04 (dt, J = 13.6, 4.7 Hz, 1 H), 2.81 (m, 2 H), 4.15 (q, J = 7.1 Hz, 2 H), 6.96 (t, J = 7.3 Hz, 1 H), 7.04 (t, J = 7.4 Hz, 1 H), 7.15 (d, J = 7.7 Hz, 1 H), 7.27 (dd, J = 7.3, 7.7 Hz, 2 H), 7.30 (dd, J = 7.4, 7.7 Hz, 1 H), 7.37 (d, J = 7.4 Hz, 1 H), 7.47 (d, J = 7.7 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.49, 13.83, 13.91, 22.76, 26.25, 36.54, 47.20, 61.16, 78.16, 116.16, 116.63, 12151, 122.35, 125.33, 127.87, 128.57, 133.87, 145.12, 148.77, 171.09 ppm. IR (film): $\tilde{\nu}$ = 3015, 1735, 1590, 1486, 750, 685 cm^{-1}. MS (EI, 70 eV): m/z (%) = 352 (5) $[M]^+$, 307 (36), 279 (55), 218 (11), 250 (22), 77 (100). $C_{22}H_{28}N_2O_2$ (352.22): calcd. C 74.97, H 8.01, N 7.95; found C 75.22, H 7.94, N 8.11.

***N*-[2-(Methylamino)benzylidene]methylamine (13a):** Yield: 159 mg (36%); oil. R_f = 0.79 (hexane/CH_2Cl_2, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.05 (d, J = 5.1 Hz, 3 H), 3.27 (s, 3 H), 6.40–7.40 (m, 4 H), 8.11 (s, 1 H), 9.00 (br. s, 1 H) ppm. IR (film): $\tilde{\nu}$ = 3015, 1590, 1495, 830 cm^{-1}. $C_9H_{12}N_2$ (148.10): calcd. C 72.94, H 8.16, N 18.90; found C 73.20, H 8.29, N 19.16.

***N*-[2-(Ethylamino)benzylidene]phenylamine (13b):** Yield: 235 mg (35%) from **2** and 282 mg (42%) from **3**; oil. R_f = 0.68 (hexane/CH_2Cl_2, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.28 (t, J = 7.1 Hz, 3 H), 3.35 (dq, J = 5.1, 7.1 Hz, 2 H), 6.57–7.72 (m, 9 H), 8.57 (s, 1 H), 9.19 (br. s, 1 H) ppm. IR (film): $\tilde{\nu}$ = 3015, 1590, 1495, 830, 750, 680 cm^{-1}. $C_{15}H_{16}N_2$ (224.13): calcd. C 80.32, H 7.19, N 12.49; found C 80.51, H 6.92, N 12.66.

***N*-[2-(Phenylamino)phenylbenzyliden]ethylamine (13c):** Yield: 405 mg (45%) from **2** and 558 mg (62%) from **3**; oil. R_f = 0.46 (hexane/AcOEt, 10:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.28 (t, J = 7.2 Hz, 3 H), 3.30 (q, J = 7.2 Hz, 2 H), 6.57 (t, J = 7.2 Hz, 1 H), 6.86 (dd, J = 7.3, 7.8 Hz, 1 H), 7.01–7.54 (m, 12 H), 12.34 (br. s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 16.66, 47.60, 113.77, 116.38, 120.96, 122.06, 127.43, 128.09, 128.47, 129.26, 130.24, 132.00, 133.46, 137.01, 141.94, 146.05, 171.27 ppm. IR (film): $\tilde{\nu}$ = 3010, 1600, 1490, 830, 745, 690 cm^{-1}. $C_{21}H_{20}N_2$ (300.16): calcd. C 83.96, H 6.71, N 9.33; found C 84.28, H 6.51, N 9.69.

2-Methyl-1,4-diphenyl-1,2-dihydroquinazoline (14): Yield: 277 mg (31%) from **2** and 196 mg (22%) from **3**; oil. R_f = 0.40 (hexane/AcOEt, 2:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.47 (d, J = 6.2 Hz, 3 H), 5.79 (q, J = 6.2 Hz, 1 H), 6.80 (t, J = 7.3 Hz, 1 H), 7.06 (d, J = 8.1 Hz, 2 H), 7.14 (dd, J = 7.3, 8.1 Hz, 2 H), 7.27–7.64 (m, 9 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.31, 71.91, 117.64, 118.77, 119.86, 122.65, 123.71, 128.08, 128.39, 128.58, 129.15, 129.35, 132.05, 138.02, 143.21, 144.70, 163.30 ppm. IR (film): $\tilde{\nu}$ = 3018, 1664, 1607, 1494, 762, 690 cm^{-1}. $C_{21}H_{18}N_2$ (298.15): calcd. C 84.53, H 6.08, N 9.39; found C 84.77, H 6.21, N 9.47.

***N*-Ethyl-2-(phenylamino)benzamide (15):** Yield: 36 mg (5%) from **2** and **10**; m.p. 74–75 °C (cyclohexane). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.25 (t, J = 7.3 Hz, 3 H), 3.48 (dq, J = 5.4, 7.3 Hz, 2 H), 6.21 (br. s, 1 H), 6.76 (t, J = 8.0 Hz, 1 H), 7.01 (dd, J = 7.1, 7.6 Hz, 1 H), 7.18–7.43 (m, 7 H), 9.32 (s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.78, 34.69, 115.40, 117.91, 118.69, 120.47, 122.20, 127.42, 129.21, 131.95, 141.54, 145.15, 169.44 ppm. IR ($CHCl_3$): $\tilde{\nu}$ = 3300 (br.), 3015, 1630, 1590, 1500, 740, 690 cm^{-1}. $C_{15}H_{16}N_2O$ (240.13): calcd. C 74.97, H 6.71, N 11.66; found C 74.72, H 6.63, N 11.85.

3-[*N*-(*tert*-Butyldiphenylsilyl)-*N*-ethylamino]-1-phenylindolin-2-one (16): Yield: 1.14 g (78%); oil. R_f = 0.34 (hexane/CH_2Cl_2, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.91 (t, J = 7.0 Hz, 3 H), 1.33 (s, 9 H),3.10 (m, 2 H), 5.00 (s, 1 H), 6.82 (d, J = 7.7 Hz, 1 H), 7.13 (t, J = 7.2 Hz, 1 H), 7.23 (t, J = 7.7 Hz, 1 H), 7.39–7.57 (m, 13 H), 7.97 (m, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 16.44, 20.08, 29.18, 41.90, 60.83, 109.52, 122.74, 124.97, 126.41, 127.71, 127.90, 128.33, 129.30, 129.38, 129.60, 134.65, 134.80, 135.04, 135.58, 136.38, 136.57, 143.22, 177.75 ppm. IR (film): $\tilde{\nu}$ = 1723, 1611, 1595, 1501, 1105 cm^{-1}. $C_{32}H_{34}N_2OSi$ (490.24): calcd. C 78.32, H 6.98, N 5.71; found C 78.54, H 7.15, N 5.52.

Hydrolysis of *N*-Silyl-β-enaminoimines. General Procedure: A solution of the *N*-silyl-β-enaminoimine **4a**–**c** (1 mmol) in an ethanol/water mixture (1.5:1, 8 mL) was stirred at reflux for 1 h 30 min. The ethanol was then evaporated under reduced pressure, and the reaction mixture was extracted with diethyl ether. The organic layer was dried ($MgSO_4$) and concentrated. The residue was purified by flash chromatography on silica gel with CH_2Cl_2 as eluent to give the following β-aminoenones.

(*Z*)-4-(Phenylamino)pent-3-en-2-one (6a): Yield: 166 mg (95%); oil. R_f = 0.57 (CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.98 (s, 3 H), 2.09 (s, 3 H), 5.18 (s, 1 H), 7.09 (d, J = 8.7 Hz, 2 H), 7.17 (t, J = 7.4 Hz, 1 H), 7.32 (dd, J = 8.7, 7.4 Hz, 2 H), 9.49 (br. s, 1 H) ppm. IR (film): $\tilde{\nu}$ = 3240, 1620, 1595, 1501, 752, 680 cm^{-1}. $C_{11}H_{13}NO$ (175.10): calcd. C 75.40, H 7.48, N 7.99; found C 75.64, H 7.31, N 7.85.

(*Z*)-4-Phenyl-4-(phenylamino)but-3-en-2-one (6b): Yield: 225 mg (95%); oil. R_f = 0.55 (CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.21 (s, 3 H), 5.40 (s, 1 H), 6.74 (d, J = 7.8 Hz, 2 H), 6.96 (t, J = 7.4 Hz, 1 H), 7.11 (dd, J = 7.8, 7.4 Hz, 2 H), 7.33 (m, 5 H), 9.69 (br. s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 29.81, 100.47, 123.09, 123.89, 127.73, 128.32, 128.67, 129.28, 135.47, 139.80, 159.62, 197.42 ppm. IR (film): $\tilde{\nu}$ = 3280, 1610, 1590, 1500, 740, 685 cm^{-1}. $C_{16}H_{15}NO$ (237.12): calcd. C 80.98, H 6.37, N 5.90; found C 81.18, H 6.45, N 6.15.

(*Z*)-1,3-Diphenyl-3-(phenylamino)prop-2-en-1-one (6c): Yield: 290 mg (97%); oil. R_f = 0.32 (CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.70 (s, 1 H), 6.65 (d, J = 7.8 Hz, 2 H), 7.06 (t, J = 7.4 Hz, 1 H), 7.15 (dd, J = 7.8, 7.4 Hz, 2 H), 7.43 (m, 8 H), 7.90 (m, 2 H), 11.33 (br. s, 1 H) ppm. IR (film): $\tilde{\nu}$ = 3300, 1615, 1580, 1500, 745, 695 cm^{-1}. $C_{21}H_{17}NO$ (299.13): calcd. C 84.25, H 5.72, N 4.68; found C 84.41, H 5.65, N 4.82.

Reaction between *N*-Silyl-β-enaminoimine 4b and Hydroxylamine Hydrochloride. Regioselective Synthesis of 3-Methyl-5-phenylisoxazole (7): Hydroxylamine hydrochloride (1.12 mmol) and Na_2CO_3 (0.46 mmol) were added to a solution of **4b** (1 mmol) in an ethanol/water mixture (1:1, 10 mL). The mixture was heated at reflux for 3 h and then extracted with diethyl ether. The ethereal layer was dried ($MgSO_4$), the solvent was removed and the residue was recrystallized from ethanol to give **7**. Yield: 133 mg (84%). M.p. 67–68 °C (ref.[18] 65 °C).

Acknowledgments

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