



SmI₂-mediated synthesis of 2,4-diarylpyrroles from phenacyl azides

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Abstract—A novel reduction of phenacyl azides induced by SmI₂ was investigated and 2,4-diarylpyrroles were prepared in moderate to good yields under mild conditions. © 2002 Elsevier Science Ltd. All rights reserved.

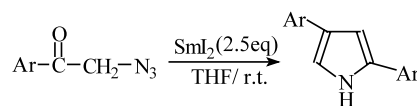
The synthesis of pyrroles is an important area of heterocyclic chemistry due primarily to the fact that many pyrroles are subunits of natural products, pharmaceutical agents and polymers.¹ A wide variety of chemistry has been used for the preparation of pyrroles,² but most of the available methods lead to pyrroles which are substituted at various positions with functional groups and thus require further synthetic operations to afford simple alkyl or aryl substituted pyrroles. In particular, synthetic routes to simple 2,4-diaryl substituted pyrroles are limited³ and convenient procedures for preparing 2,4-diarylpyrroles with substituents on the aryl rings are even more rare.^{3c}

Kagan's reagent, samarium(II) iodide⁴ is an exceptional reagent for promoting reductive reactions, and the chemistry of this reagent has been well documented in several reviews.⁵ The reactivity of SmI₂ towards various nitrogen-containing organic compounds⁶ including nitro compounds, imines, oximes, hydrazones and azo compounds has already been examined and it has been reported that SmI₂ can efficiently promote the reduction of alkyl, aryl and aroyl azides to give the corresponding primary amines and amides.⁷ However, to our knowledge, there are no literature precedents for the reduction of phenacyl azides by this reagent.⁸ In this report, we describe, for the first time, the efficient reduction of phenacyl azides upon treatment with SmI₂ to afford 2,4-diarylpyrroles in moderate to good yields. The results are summarized in Table 1.

We found that SmI₂ can efficiently promote the reduction of phenacyl azides at room temperature. This reductive process is completed within a few minutes and affords 2,4-diarylpyrroles in fair yields. In addition, both phenacyl azides bearing electron-donating groups (4-Me and 4-OMe, entries 2 and 3, Table 1) and phenacyl azides bearing electron-withdrawing groups (4-Br and 4-Cl, entries 4 and 5, Table 1) underwent smooth reduction under the same conditions. The absence of observable substituent effect suggests that this method may afford a general method for the preparation of 2,4-diarylpyrroles bearing various substituents on the aryl rings.

Although the detailed mechanism of the above reaction has not been clarified, a plausible mechanism (shown in

Table 1. Reduction of phenacyl azides mediated by SmI₂

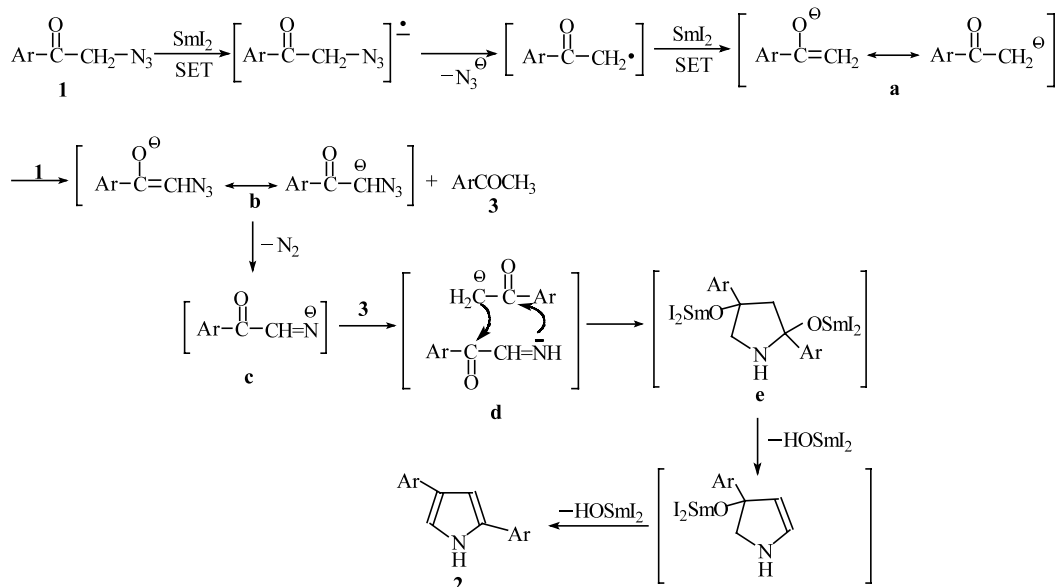


Entry	Ar	Reaction time (min)	Yield (%) ^a
1	C ₆ H ₅	5	72
2	4-CH ₃ C ₆ H ₄	5	70
3	4-CH ₃ OC ₆ H ₄	5	65
4	4-BrC ₆ H ₄	5	76
5	4-ClC ₆ H ₄	5	75
6	2-Naphthyl	10	56

^a Isolated yields based on phenacyl azides.

Keywords: samarium(II) iodide; pyrroles; phenacyl azides; reduction.

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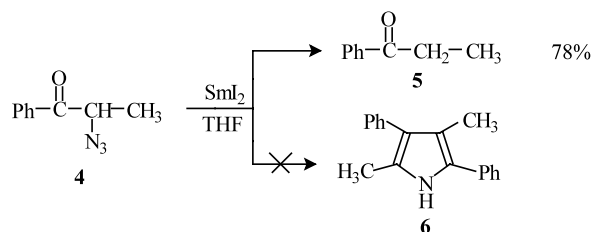


Scheme 1.

Scheme 1) for the formation of 2,4-diarylpyrroles is proposed based on the literature. In a first step, the cleavage of the C–N₃ bond takes place through two SET (single electron transfer) processes with SmI₂ donating two electrons sequentially and leads to the corresponding enolate (**a**).⁹ By abstracting a proton from another substrate molecule, (**a**) is transformed into a new enolate (**b**) and the aryl methyl ketone (**3**).⁸ Then enolate (**b**) loses a N₂ molecule to be transformed into anion (**c**). As a strong base, anion (**c**) can abstract a proton from acetophenone (**3**) to afford the phenyl glyoxal imino intermediate (**d**) and enolate (**a**). Reaction of the phenyl glyoxal imino intermediate (**d**) and enolate (**a**) followed by the loss of two HOSmI₂ fragments from the resulting intermediate (**e**) gives the 2,4-diarylpyrrole (**2**) as the final product.

Another possible mechanism for the formation of 2,4-diarylpyrroles may involve the concurrent formation and reaction of enolate (**a**) and intermediate (**d**). While enolate (**a**) may be formed through the cleavage of the C–N₃ bond mediated by SmI₂, the formation of intermediate (**d**) probably involves a one-electron transfer process from SmI₂ to the azido group to give an aminyl radical,^{7c} which could then be transformed into intermediate (**d**) upon receipt of another electron from SmI₂.

In addition, the reduction of 2-azidopropiophenone (**4**) was also investigated (as shown in Scheme 2). On



Scheme 2.

treatment with SmI₂, 2-azidopropiophenone (**4**) was transformed into propiophenone (**5**) rather than the expected 2,4-diphenyl-3,5-dimethylpyrrole (**6**).

In conclusion, with high yields, mild and neutral conditions as well as easily accessible starting materials,¹⁰ the present work may provide a useful method for the preparation of 2,4-diarylpyrroles.¹¹ Further studies to clarify the mechanism of this process and to develop other new uses of SmI₂ are now in progress in our laboratory.

Acknowledgements

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 - Phenacyl azides were conveniently prepared from phenacyl bromides and sodium azide according to the following literature: Boyer, H. J.; Straw, D. J. *J. Am. Chem. Soc.* **1953**, *75*, 1642.
 - Representative procedure*: A solution of phenacyl azide (1 mmol) in dry THF (3 mL) was added dropwise to a solution of SmI_2 (2.5 mmol) in THF (20 mL) at room temperature under a nitrogen atmosphere. The deep blue color of the solution changed to yellow immediately. After stirring for ca. 5 min, the reaction mixture was quenched with dilute HCl (0.1 mol/L, 3 mL) and extracted with ether (3×20 mL). The organic phase was successively washed with a saturated solution of $\text{Na}_2\text{S}_2\text{O}_3$ (10 mL), saturated brine (10 mL), and dried over anhydrous Na_2SO_4 . The solvent was removed under reduced pressure to give the crude product, which was purified by preparative TLC using ethyl acetate and cyclohexane (1:6) as eluant to yield 2,4-diphenylpyrrole (72%), mp 166–169°C (lit.^{3a} 166–170°C); IR (KBr): ν 3350 (NH) cm^{-1} ; ^1H NMR (400 MHz, DMSO): δ 6.95 (t, 1H, $J=2$ Hz), 7.10–7.19 (m, 2H), 7.30–7.39 (m, 5H), 7.61 (d, 2H, $J=7.2$ Hz), 7.68 (d, 2H, $J=7.6$ Hz), 11.3 (bs, 1H, NH); ^{13}C NMR (100 MHz, DMSO): δ 103.7, 117.1, 123.9, 124.9, 125.2, 125.5, 126.2, 129.0, 129.2, 132.7, 133.1, 136.2; MS m/z (%): 219 (M^+ , 100), 191 (13), 116 (17), 115 (21), 89 (6), 77 (5). Anal. calcd for $\text{C}_{16}\text{H}_{13}\text{N}$: C, 87.67; H, 5.98; N, 6.39. Found: C, 87.57; H, 6.08; N, 6.34.