Oxygen stoichiometry changes were performed between 650 and 730 °C by switching P_{O_2} between $0.0012 \leftrightarrow 0.005 \leftrightarrow 0.02 \leftrightarrow 0.08$ bar (achieved with O_2/Ar mixtures; flow rate 100 mL min^{-1}). The set-up for the in situ optical spectroscopy is described in detail in ref. [15]. The integral Fe^{4+} concentration was monitored continuously by measuring the absorption at 595 nm with a UV/Vis spectrometer (Perkin – Elmer Lambda 2). A narrow bandpass filter was placed between the sample and the detector to block thermal radiation.

For the irradiation experiments, a 200 W Hg high pressure arc lamp (LOT Oriel) was used, whose spectral output was restricted to 280 – 420 nm by means of UG5 and WG280 filters (Schott). The bandgap of $SrTiO_3$ at 700 °C is 2.7 eV,[15] which corresponds to the absorption of light of 460 nm. The total irradiation intensity was 250 mW cm^{-2} in front of the quartz rod, that acted as light guide to irradiate one of the large faces of the sample, and was attenuated for some experiments by neutral density filters. The UV irradiation was interrupted for ≈30 s at appropriate intervals to permit the 595 nm extinction measurements to be made. The effect of sub-bandgap irradiation of 515 – 700 nm with a total intensity of 190 mW cm^{-2} was also investigated.

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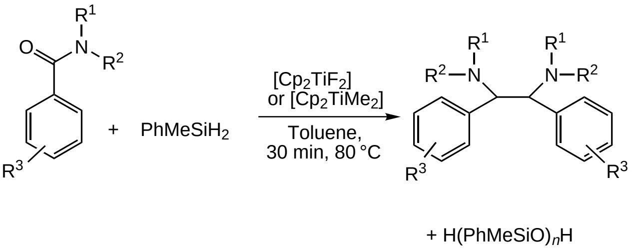
Titanocene-Catalyzed Coupling of Amides in the Presence of Organosilanes To Form Vicinal Diamines[**]

Kumaravel Selvakumar and John F. Harrod[*]

Vicinal diamines occur widely in natural products and have many applications in medicinal chemistry and organic synthesis.[1] Despite the existence of many synthetic approaches, there is still a pressing need for better and more general methods based on simple and inexpensive starting materials. We report herein a novel reduction – deoxygenation coupling of amides catalyzed by $[Cp_2TiX_2]$ (Cp = η^5-cyclopentadienyl; X = Me or F) in the presence of a stoichiometric amount of an organosilane. To the best of our knowledge, such a reaction has not been reported previously, although the literature extensively covers the titanium-mediated coupling of carbonyl[1, 2] and imine[1, 3] compounds in the presence of strong reducing agents.[2] The intramolecular coupling of 1,2-acylamido compounds to form indoles and pyrroles has also been extensively studied.[4]

Both dimethyltitanocene and difluorotitanocene have been used as catalysts for a variety of hydrosilylation reactions.[5–7] We attempted to use these catalysts to effect the hydrosilylation of some amides with $PhMeSiH_2$ and found that the main reaction product in the case of *N*,*N*-dimethylbenzamide was the vicinal diamine, 1,2-dimethylamino-1,2-diphenylethane [Eq. (1)].



(1)

The effects of a number of chemical and physical variables on the outcome of the reaction are summarized in Tables 1 – 3. At 80 °C, the reactions of *N*,*N*-dialkylbenzamides and some other related aromatic amides proceed smoothly to give good to excellent yields of the substituted ethylenediamine products (Table 1). Different substituents can be tolerated, as shown in the reactions of 4-chloro-, 4-methoxy-, and 4-trifluoromethylbenzamide. There is no significant difference in the results obtained with the difluoro- and dimethyltitanocene precatalysts. None of the reactions shows significant stereoselectivity.

Reactions at room temperature show an interesting decline in chemoselectivity relative to those carried out at higher temperature (Table 2). Certain substitution patterns also

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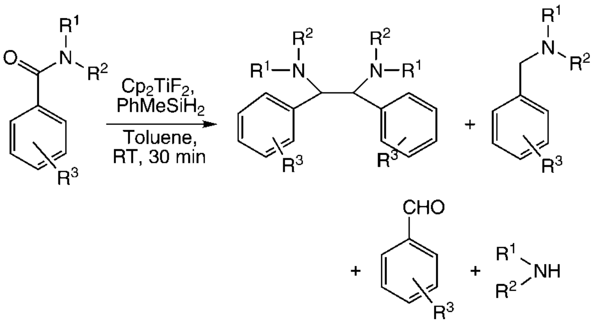
Table 1. Results for the titanocene-catalyzed reductive coupling of amides at 80 °C.

R^1	R^2	R^3	Method[a]	*meso*:*rac*[b]	Yield[c]
Me	Me	H	A	52:48	84
			B	52:48	80
Et	Et	H	A	52:48	92
			B	53:47	88
Et	Et	4-Cl	A	53:47	93
			B	53:47	90
Et	Et	4-OMe	B	56:44	94
Me	Ph	H	A	50:50[e]	77[d]
Et	Et	4-CF_3	A	53:47	96
Et	Et	4-Me	A	62:38	91
N,*N*-diethyl-2-naphthamide			A	54:46	83[f]
N,*N*-diethylnicotinamide			A	57:43	27[g]

[a] See Experimental Section: A = Cp_2TiF_2, B = Cp_2TiMe_2. [b] Ratios of isomers are calculated after isolation, or by ^1H NMR spectroscopic analysis. [c] Yields are given for isolated compounds. [d] *N*-Methyl-*N*-benzylaniline is one of the products (8%). [e] Isomers were not separated. [f] *N*,*N*-Diethyl-2-naphthylamine is formed as a side product (9%). [g] 3-(*N*,*N*-Diethylaminomethyl)pyridine is also formed as a side product (25%).

favor the formation of a tertiary benzylamine (carbonyl reduction) and a benzaldehyde (N–C bond hydrogenolysis) product as well as the ethylenediamine coupling product ([Eq. (2)], Table 2). The formation of the tertiary benzylamine product is analogous to the reactions of amides with silanes catalyzed by rhodium complexes in which the tertiary amine is the only reported product.[8] We have also shown that $[Cp_2TiX_2]$ complexes catalyze silane reduction of *N*,*N*-dialkylacetamides to the tertiary amine, with no coupling product, and the results will be reported elsewhere.



(2)

Table 2. Results for the $[Cp_2TiF_2]$-catalyzed reductive coupling of amides at 20 °C.

R^1	R^2	R^3	Ratio of products [%] diamines (*meso*:*rac*)	amine	aldehyde
Me	Me	H	81.3 (54:46)	2.0	16.7
Et	Et	H	97.7 (60:40)	–	2.3
Et	Et	4-Cl	44.8 (53:47)	29.9	25.3
Et	Et	4-OMe	100 (53:47)	–	–
Me	Ph	H	14.7 (55:45)	44.2	41.1
Et	Et	4-CF_3	55.9 (53:47)	20.6	23.5
Et	Et	4-Me	100 (50:50)	–	–
N,*N*-diethyl-2-naphthamide			51.2 (48:52)	39.6	9.2
N,*N*-diethylnicotinamide			43.5 (56:44)	34.1	22.4

In the cases in which the benzaldehyde product is observed, an equivalent amount of the secondary amine is also produced (Table 2). The stoichiometric reaction of $Ti(OiPr)_4$ and Ph_2SiH_2 with acetamides has been reported previously as a method for the transformation of acetamides into aldehydes.[9]

Several hydrosilanes were studied as reducing agents (Table 3). In general there is no significant difference in the stereoselectivity, but some variation in chemoselectivity is apparent. In particular, the use of *n*-hexylsilane results in more carbonyl reduction (benzylamine) and more C–N bond cleavage than $PhMeSiH_2$ or $PhSiH_3$. On the other hand, the hydrosiloxanes D_4^H and PMHS show greatly increased C–N bond cleavage at room temperature. In contrast to other titanocene-catalyzed hydrosilylations, in which the polymerization of $PhSiH_3$ to polyphenylsilane by dehydrocoupling competes with the hydrosilylation reaction, and results in the inefficient use of the Si–H, no concomitant polymerization of $PhSiH_3$ was detected in the amide reactions. The behavior of $PhSiH_3$ and $PhMeSiH_2$ is essentially identical.

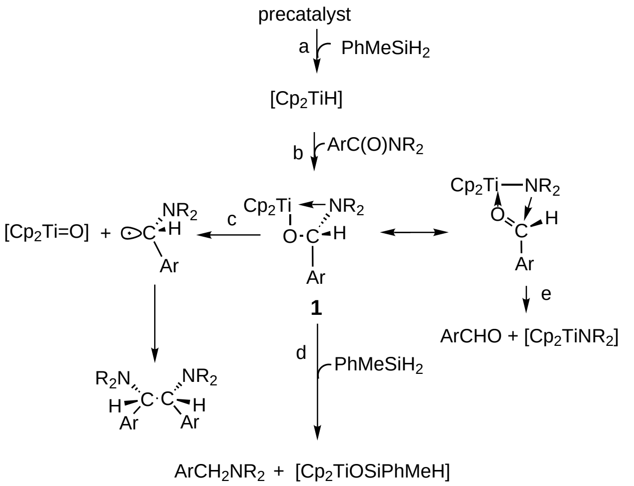
Table 3. Results for the reductive coupling reactions of *N*,*N*-dimethylbenzamide using various silanes.

T [°C]	Silane[a]	Ratio of products [%][b] diamines (*meso*:*rac*)	benzylamine	aldehyde	Yield [%][c]
20	$PhSiH_3$	92(54:46)	8	–	86
80	$PhSiH_3$	100(57:43)	–	–	83
20	*n*-$HexSiH_3$	51(55:45)	30	19	66
80	*n*-$HexSiH_3$	85(56:44)	15	–	90
20	D_4^H[d]	43(52:48)	9	48	40
80	D_4^H[d]	92(55:45)	8	–	81[e]
20	PMHS[f]	59(56:44)	1	40	37
80	PMHS[f]	no reaction			

[a] D_4^H = 2,4,6,8-Tetramethylcyclotetrasiloxane. PMHS = Polymethylhydrosiloxane. [b] By integration of ^1H NMR peaks. [c] Yields are for isolated amine products separated by HCl extraction. [d] One equivalent of D_4^H was used. [e] The solution gels at the end of the reaction. [f] 300 mg of PMHS was used.

So far, the simple titanocene catalysts have only shown high activity and specificity for the deoxygenative coupling of tertiary aromatic amides. We continue to seek similar catalysts of broader and greater activity, as well as greater stereoselectivity.

On the basis of presently available evidence it is difficult to assign mechanisms to these reactions with any degree of confidence. Scheme 1 shows a cycle which provides a reasonable explanation for many of their features. In this scheme, it is assumed that the primary catalyst is $[Cp_2TiH]$, a species frequently cited in the mechanisms of titanocene-catalyzed reactions of silanes.[7] The amide carbonyl group is expected to undergo insertion into the Ti–H bond, with the oxygen atom attacking the oxophilic Ti, as proposed for other hydrosilylations of carbonyl compounds.[10–12] The resulting α-aminoalkoxy product **1** could undergo several different reactions. First, in pathway c it is presumed to undergo homolysis of the C–O bond, followed by subsequent coupling of two benzylamine radicals to form the 1,2-diaminoethane product. We are unaware of any precedent for this homolysis reaction, but it is expected to be a high activation-energy process that would be favored under the high temperatures of the experimental conditions. A consequence of the radical



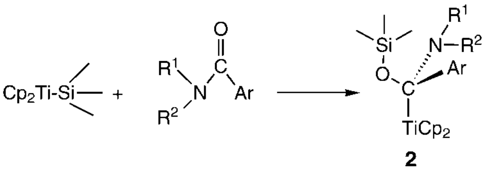
Scheme 1. A $[Cp_2TiH]$-mediated reaction sequence for the reduction, deoxygenation, and coupling of amides in the presence of $PhMeSiH_2$. See text for details.

coupling mechanism in this reaction is that the structure of the catalyst complex has no influence over its stereochemical outcome.

In pathway d a σ-bond metathesis between the C–O bond and Si–H cleaves off the benzylamine product, with the concomitant formation of a siloxytitanium complex. Another possible mechanism for the formation of the benzylamine is the abstraction of an H atom from Si–H by the aminotolyl radical. In this case, the ratio of ethylenediamine to benzylamine products is simply a reflection of the competitive rates of the recombination and hydrogen-abstraction rates of the aminotolyl radicals. Some of the variations in chemoselectivity evident in Table 3 may be a result of the different rates of H-atom abstraction from the different silanes.

Finally, in step **e** an intramolecular metathesis, which is initiated by attack of the basic amine nitrogen, leads to the formation of a covalent Ti–N bond and the displacement of the aryl aldehyde. In these reactions, the aldehyde appears directly in the reaction and does not seem to be derived from an enamine intermediate (see ref. [8]). The titanium complexes produced as coproducts in pathways c, d, and e are all expected to regenerate the titanocene hydride catalyst by reaction with $PhMeSiH_2$.

A plausible set of alternative reactions could involve the addition of a silyl titanocene catalyst to the carbonyl group [Eq. (3)]. It is well established that both Ti–H and Ti–Si species are formed by the reactions of hydrosilanes with $[Cp_2TiX_2]$ complexes,[7] and that hydrosilylation can be initiated either by the addition of M–H or M–Si to a multiple bond.[13] The direction of insertion shown in Equation 3 is chosen on the basis of the known greater oxophilicity of Si than that of Cp_2Ti. The presence of a Ti–C bond would facilitate the production of a C-based radical because of the relatively weak Ti–C bond. Further speculation concerning the possible reactions of **2** will be deferred until more is known about the chemistry of such species.



2

(3)

Experimental Section

The reactions with $[Cp_2TiF_2]$ were carried out at both 20 °C and 80 °C (Method A, Table 1). The reactions with $[Cp_2TiMe_2]$ were carried out only at 80 °C (Method B, Table 1), by using the same procedure as with the fluoride. Typical procedures are as follows:

80 °C: *N,N*-Dimethylbenzamide (149 mg, 1 mmol), $[Cp_2TiF_2]$ (21 mg, 0.1 mmol), and $MePhSiH_2$ (0.28 mL, 2 mmol) were mixed in toluene (1 mL) at room temperature and then stirred on a preheated 80 °C oil bath for 1 h. On cooling the green solution to room temperature, *meso-N,N,N',N'*-tetramethyl-1,2-diphenylethylenediamine precipitated as a crystalline solid. Diethyl ether (5 mL) was added to the mother liquor, and the solution was extracted with aqueous HCl (1M, 3 × 2 mL). The aqueous extract was neutralized with KOH (3M) and extracted with diethyl ether. *rac-N,N,N',N'*-Tetramethyl-1,2-diphenylethylenediamine was separated from the residual *meso* isomer by column chromatography.

20 °C: $[Cp_2TiF_2]$ (21 mg, 0.1 mmol) and $MePhSiH_2$ (40 μL, 3 mmol) in toluene (0.5 mL) were heated at 70 °C for 10 min to effect activation (reduction) of the precatalyst. The green solution was cooled to room temperature, and further aliquots of $MePhSiH_2$ (0.28 mL, 2 mmol) and *N,N*-dimethylbenzamide (149 mg, 1 mmol) dissolved in toluene (0.5 mL) were added. The reaction was monitored by thin-layer chromatography, and the ratios of the products were calculated from their ^1H NMR spectra. The identities of the products were confirmed by comparing their properties to those in the literature.[14]

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