Cobalt-catalyzed intermolecular C–H amination with bromamine-T as nitrene source†

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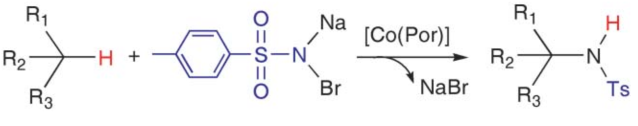
Cobalt, supported by porphyrin ligands, is capable of catalyzing intermolecular nitrene insertion of sp^3 C–H bonds with bromamine-T as the nitrene source, forming the desired tosyl-protected amines with NaBr as the by-product.

Nitrogen-containing molecules are abundant in nature and their importance in biology and medicine has been widely documented. Among modern amination methods,[1] metal-catalyzed nitrene insertion provides an attractive strategy for direct transformation of ubiquitous C–H bonds to value-added amine functionalities through the use of appropriate nitrene sources.[2] The reagent PhI=NTs and related iminoiodane derivatives have been widely used as primary nitrene sources,[2,3] resulting in significant advances in amination of C–H bonds.[4] In view of some limitations associated with the use of the hypervalent iodine reagents, including their instability and the generation of ArI as a by-product, considerable efforts have been made to develop alternative nitrene sources for catalytic C–H amination. One such remarkably successful effort has been the approach of *in situ* iminoiodane generation from amides using terminal oxidants such as the combination of sulfamates with PhI(OAc)$_2$ or sulfonamides with PhI=O.[3,5] In addition, efforts have been devoted to employ other potential nitrene sources that obviate the need of terminal oxidants for the catalytic amination process, including chloramine-T,[4g,6] bromamine-T,[7] tosyloxycarbamates,[8] and azides.[9] Using these nitrene sources, complexes of manganese, iron, ruthenium, rhodium, and copper supported by various ligands have been identified to catalyze C–H amination reactions, with dirhodium tetracarboxylates being the most widely used catalysts.[2–5] In the light of various remaining challenges in intermolecular C–H amination,[2–5] it is desirable to search for new catalytic systems based on other metal ions in combination with alternative nitrene sources. To this end, silver[10]- and cobalt[11]-based systems were recently reported to aminate C–H bonds with PhI=NNs and aryl azides, respectively.

Attracted by their practical attributes as alternative nitrene sources, we recently initiated a research project on the development of catalytic nitrene transfer processes using bromamine-T and azides. In connection with our studies on catalytic carbene transfer reactions by cobalt porphyrins [Co(Por)],[12,13] we documented new Co-based catalytic systems that can catalyze aziridination of alkenes with diphenylphosphoryl azide (DPPA)[14] and bromamine-T.[15] The Co(Por)/bromamine-T system, which proved to be superior to the Fe(Por)Cl/bromamine-T system,[16] can be effectively operated under mild conditions with alkenes as the limiting reagent, generating NaBr as the by-product, and is generally suitable for a wide range of alkene substrates. While the desired aziridines were formed in high yields for most of the substrates, low aziridination yields were obtained from certain substrates containing activated C–H bonds, such as 1,2-dihydronaphthalene.[15] At that time, without being able to obtain concrete experimental data, we presumed a competitive amination reaction to be the cause of low yields. Since then, we have carried out a thorough study on the possibility of catalytic C–H amination by Co(Por) with bromamine-T as the nitrene source (Scheme 1). Herein, we wish to report our findings.

Using indan as a model substrate, we systematically evaluated its catalytic C–H nitrene insertion with bromamine-T under different conditions by cobalt complexes of porphyrin ligands possessing varied electronic and steric environments (Fig. 1). Selected results are summarized in Table 1. While most of the tested cobalt complexes exhibited poor catalytic activity toward C–H amination, the cobalt complex of electron-deficient porphyrin Co(TPFPP) was found to aminate one of the benzylic C–H bonds of indan effectively to form the desired product **2a** in 66% yield at room temperature (Table 1, entries 9–13). Further experiments indicated the use of electron-deficient as well as more sterically demanding porphyrin TDClPP could further improve the Co-catalyzed amination reaction, producing **2a** in 75% yield (Table 1, entry 3). This reaction was performed with a **1a** : bromamine-T ratio of 10 : 1 since the use of other reactant ratios appeared to give lower yields of **2a** (Table 1, entries 1–3). Among the solvents examined, CH_3CN proved to be the best for the catalytic process (Table 1, entries 3–7). Although the employment of lower catalyst loading could result in the formation of the desired amination product (Table 1, entry 8), 5 mol% of Co(TDClPP) was needed for an effective transformation (Table 1, entry 3).

Under the optimized catalytic conditions derived from the above experiments for the amination of indan, the Co(TDClPP)/bromamine-T catalytic systems could also be applied to aminate other substrates at room temperature (Table 2). While the isolated



Scheme 1 Cobalt-catalyzed C–H amination with bromamine-T.

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† Electronic supplementary information (ESI) available: Full experimental procedures for the synthesis of compounds **2a–f**, their characterization data and ^{1}H NMR spectra. See DOI: 10.1039/b710677g

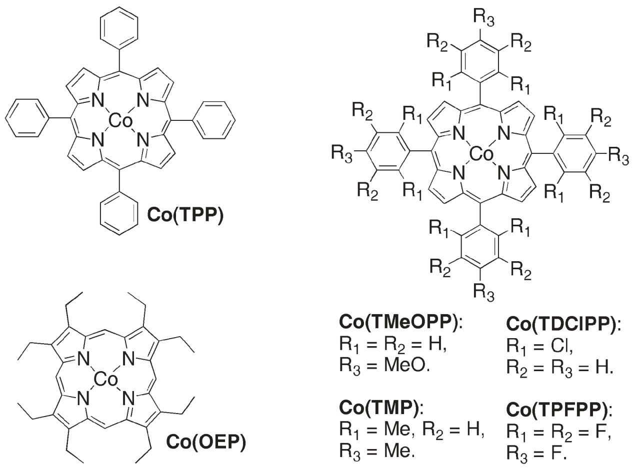
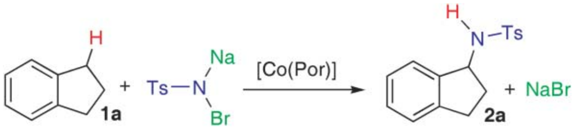


Fig. 1 Structures of cobalt(II) complexes of porphyrins.

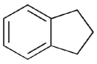
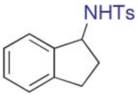
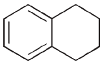
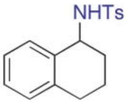
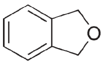
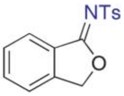
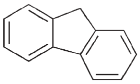
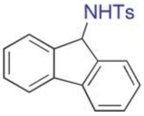
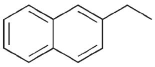
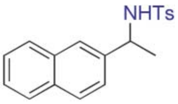
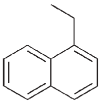
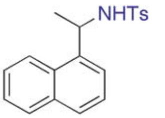
Table 1 Intermolecular C–H amination of indan with bromamine-T by cobalt(II) porphyrins[a]



Entry	S : BT[b]	[Co(Por)][c]	mol (%)	Solvent	Time/h	Yield (%)[d]
1	1 : 1	Co(TDClPP)	5	CH_3CN	19	43
2	1 : 5	Co(TDClPP)	5	CH_3CN	17	30
3	10 : 1	Co(TDClPP)	5	CH_3CN	18	75
4	10 : 1	Co(TDClPP)	5	THF	20	15
5	10 : 1	Co(TDClPP)	5	$CH_3C_6H_5$	18	14
6	10 : 1	Co(TDClPP)	5	ClC_6H_5	20	12
7	10 : 1	Co(TDClPP)	5	CH_2Cl_2	18	<2
8	10 : 1	Co(TDClPP)	2	CH_3CN	20	15
9	10 : 1	Co(TPP)	5	CH_3CN	19	<2
10	10 : 1	Co(TMP)	5	CH_3CN	18	<2
11	10 : 1	Co(TPFPP)	5	CH_3CN	18	66
12	10 : 1	Co(OEP)	5	CH_3CN	18	7
13	10 : 1	Co(TMeOPP)	5	CH_3CN	20	23

[a] Reactions were carried out at room temperature under N_2 with bromamine-T in the presence of 5 Å molecular sieves at a concentration of 2.0 mmol substrate/3–5 mL solvent. [b] The mole ratio of indan substrate to bromamine-T. [c] See Fig. 1 for structures. [d] Yields represent GC yields using tridecane as an internal standard.

Table 2 Co(TDClPP)-catalyzed intermolecular C–H amination reactions with bromamine-T[a]

Entry	Substrate	Product	Yield (%)[b]
1	**1a** 	**2a** 	73
2	**1b** 	**2b** 	66
3	**1c** 	**2c** 	50
4	**1d** 	**2d** 	14
5	**1e** 	**2e** 	34
6	**1f** 	**2f** 	33

[a] Reactions were carried out at room temperature in CH_3CN under N_2 with bromamine-T as the limiting reagent (substrate/bromamine-T = 10 : 1) using 5 mol% Co(TDClPP) in the presence of 5 Å molecular sieves at a concentration of 2.0 mmol substrate/3–5 mL CH_3CN. [b] Yields represent isolated yields in >95% purity as determined by ^1H NMR.

yield of **2a** was 73% (Table 2, entry 1), the corresponding amination product **2b** from 1,2,3,4-tetrahydronaphthalene (**1b**) was isolated in 66% yield (Table 2, entry 2). In both of the cases, high chemoselectivity toward benzylic C–H bonds was observed. The benzylic C–H bond of the cyclic ether **1c** seemed to be similarly aminated with bromamine-T. The reaction, however, didn't afford the corresponding amine product. Instead, the corresponding imine product **2c** was isolated in 50% yield (Table 2, entry 3), presumably formed from the initial amine *via* a secondary reaction.[17] Although fluorene **1d** contains more activated benzylic C–H bonds, its catalytic amination reaction by Co(TDClPP) gave the C–H insertion product **2d** in a much lower yield (Table 2, entry 4). Steric hindrance is likely responsible for the adverse outcome. When substrates that contain both secondary benzylic and primary C–H bonds such as 1- and 2-ethylnaphthalene (**1e** and **1f**) were used, the corresponding amination products of the benzylic C–H bonds **2e** and **2f** were produced as the major products, albeit in lower yields (Table 2, entries 5–6), affirming the high chemoselectivity towards benzylic C–H bonds.

In summary, we have demonstrated the capability of cobalt porphyrins in catalyzing intermolecular nitrene insertion of sp^3 C–H bonds with bromamine-T at room temperature. In addition to mild conditions, the cobalt-based catalytic system enjoys the use of bromamine-T as the nitrene source since it produces innocent NaBr as the by-product. Furthermore, the current Co(TDClPP)/bromamine-T catalytic intermolecular amination system has high chemoselectivity towards benzylic C–H bonds. Efforts are underway to design and synthesize new porphyrin ligands to further improve the scope and efficacy of the Co-catalyzed intermolecular C–H amination system.

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17 A similar secondary reaction was reported previously in ref. 11. The presence of the electron-rich oxygen heteroatom presumably activated the initial amine product toward the formation of the corresponding imine **2c**. Attempts at arresting the reaction for the amine formation were unsuccessful, indicating a fast secondary reaction.