[Ir$_4$(CO)$_{12}$]-Catalyzed Coupling Reaction of Imidazoles with Aldehydes in the Presence of a Hydrosilane to Give 2-Substituted Imidazoles**

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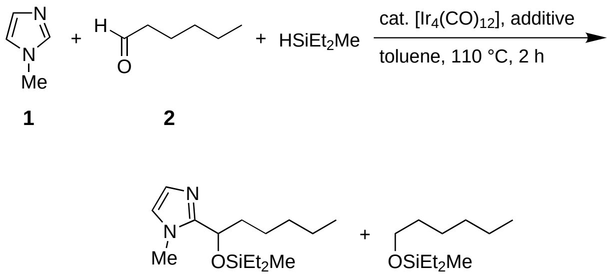
Imidazole rings are components of a number of natural products and biologically active molecules. As a result, the development of methods for the alkylation of imidazole carbons is an important subject in organic synthesis.[1] Generally, C2 of an imidazole ring can be alkylated by lithiation with strong bases at low temperature followed by treatment with electrophiles.[1, 2] 1-Alkyl-2-trimethylsilylimidazoles react with electrophiles to give 2-substituted imidazoles in good yields, although a stoichiometric amount of *n*-butyllithium is required to prepare the 2-silylimidazoles.[3] Thermal condensations with aldehydes[4] or isocyanates[5] have also been reported, but yields in the aldehyde reaction are dependent on the structure of substrates. Imidazolium ylides, which are generated by the reaction of 1-alkylimidazoles with acid halides in the presence of amines, have been proposed as the reactive intermediate in the pathway to 2-acylimidazoles.[6] Quite recently, Hlasta reported that imidazolium ylides react with various electrophiles.[7] It is known that transition-metal-catalyzed reactions are useful synthetic tools for selective C–C-bond formation.[8] Cross-coupling reactions catalyzed by palladium complexes[9] or copper salts[10] were applied to introduce substituents at C2 of imidazoles. We have found that [Ru$_3$(CO)$_{12}$] is an efficient catalyst for direct carbonylation at a C–H bond in imidazole derivatives.[11] Bergman, Ellman, and Tan demonstrated intramolecular cyclization of N-*ω*-alkenyl benzimidazole, which was proceeded by a RhCl(PPh$_3$)$_3$-catalyzed C–H/olefin coupling reaction.[12] We report herein a unique new reaction for the derivatization of imidazoles. The new reaction enables direct coupling of 1-methylimidazole with aldehydes when [Ir$_4$(CO)$_{12}$] is used as the catalyst with a hydrosilane as a co-reactant.

The reaction of 1-methylimidazole (**1**; 1 mmol) with hexanal (**2**; 1 mmol) and diethylmethylsilane (2 mmol) in the presence of [Ir$_4$(CO)$_{12}$] (0.02 mmol) in toluene at 110 °C for 2 h gave 2-[1-(diethylmethylsiloxy)hexyl]-1-methyl-1*H*-imidazole (**3**) in 35% and the hydrosilylation product of hexanal **4** in 17% (Scheme 1). No reaction occurred in the absence of diethylmethylsilane. It occurred to us that the addition of a hydrogen acceptor to the reaction system would improve the yield of **3**, since two hydrogen atoms (2-H of **1** and the hydrogen atom of H-SiR$_3$) were not found in the product on the formation of **3**. Among the hydrogen acceptors examined, it was found that diethyl acetylenedicarboxylate (DMAD) was the additive of choice; curiously, no hydrogenation products such as dimethyl fumarate or dimethyl succinate were detected. This result indicates that DMAD plays a role, not as a hydrogen acceptor, but rather as a ligand,[13] although the details of the mechanism are not clear at present. Other transition-metal complexes including [Fe$_3$(CO)$_{12}$], [Ru$_3$(CO)$_{12}$], [Os$_3$(CO)$_{12}$], [Co$_2$(CO)$_8$], [Rh$_4$(CO)$_{12}$], [IrH(CO)(PPh$_3$)$_3$], [{IrCl(cod)}$_2$] (cod = cycloocta-1,5-diene), [H$_2$IrCl$_6$], and [Ir(cod)]BF$_4$, had no catalytic activity.



additive	3	4
none	35 %	17 %
DMAD	94 %	6 %

Scheme 1. [Ir$_4$(CO)$_{12}$]-catalyzed reaction of 1-methylimidazole (**1**) with hexanal (**2**) with and without added DMAD.

The results of these reactions with some aldehydes are summarized in Table 1. All reactions were completed within 4 h and the products were isolated in good yields by bulb-to-bulb distillation. The reaction of pivaldehyde (**7**) required a higher reaction temperature to obtain **8** in good yield (Table 1, entry 3). Acetal (**11**) and ester (**13**) groups were also compatible in the present reaction (Table 1, entries 4, 5). The reaction of benzaldehyde (**15**) gave **16** in 76% yield as well as the silylated dimerization product, 1,2-bis(diethylmethylsiloxy)-1,2-diphenylethane, in 8% yield (Table 1, entry 7).[14] Although the reaction of acetophenone resulted in the formation of the corresponding enol silyl ether, trifluoroacetophenone (**17**) afforded **18** (Table 1, entry 8) in 32% yield.

The reaction of *N*-propylisocyanate (**19**) with 1-methylimidazole and hydrosilane gave **20**, which might be formed by hydrolysis of the desired product during the work-up (Scheme 2). The reaction of 1-methylbenzimidazole (**21**) with hexanal required the further addition of DMAD and a longer reaction time (19 h) to give **22** (Scheme 3). Other heterocyclic compounds such as thiazole, oxazole, 1,2,4-triazole, and pyrimidine were also examined, but only hydrosilylation products of aldehydes were obtained in all cases.

A possible reaction mechanism is shown in Scheme 4. The addition of Ir–SiR$_3$ to the aldehyde, followed by carboiridation of the C–N double bond of the imidazole[15] gives amidoiridium intermediate **A**. Successive *β*-hydride elimination of **A** gives the product and the Ir–H species. A very similar dehydrometallation reaction of iridium amide com-

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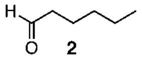
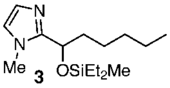
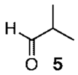
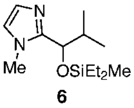
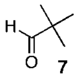
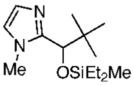
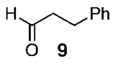
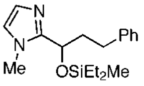
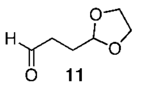
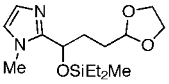
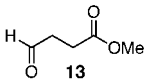
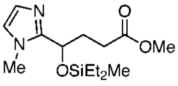
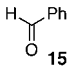
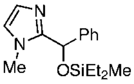
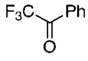
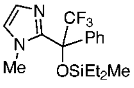
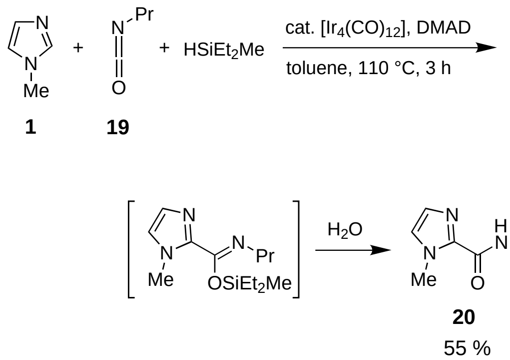
Table 1. $[Ir_4(CO)_{12}]$-catalyzed coupling reaction of **1** with carbonyl compound in the presence of diethylmethylsilane.[a]

Entry	Carbonyl Compounds	Product	t [h]	Yield [%][b]
1	 **2**	 **3**	2	92
2	 **5**	 **6**	3	91
3	 **7**	 **8**	4	76[c]
4	 **9**	 **10**	1	72
5	 **11**	 **12**	1	62
6	 **13**	 **14**	1	87
7	 **15**	 **16**	2	76[d]
8	 **17**	 **18**	3	32

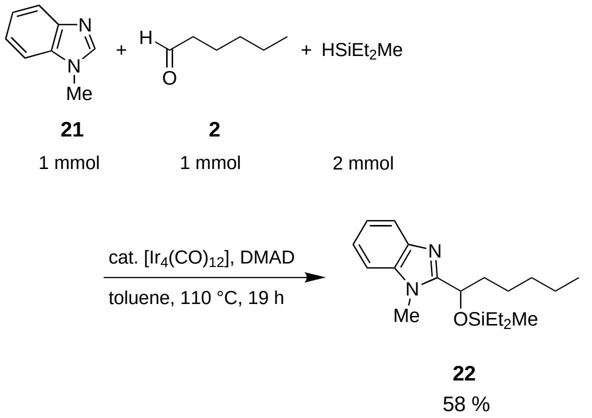
[a] Reaction conditions: 1-methylimidazole (1 mmol), carbonyl compound (1 mmol), diethylmethylsilame (2 mmol), $[Ir_4(CO)_{12}]$ (0.02 mmol), DMAD (0.16 mmol), in toluene (5 mL) at 110 °C, unless otherwise noted. [b] Yields of isolated products. [c] $T = 135$ °C. [d] 1,2-Bis(diethylmethylsiloxy)-1,2-diphenylethane was also obtained in 8% yield.



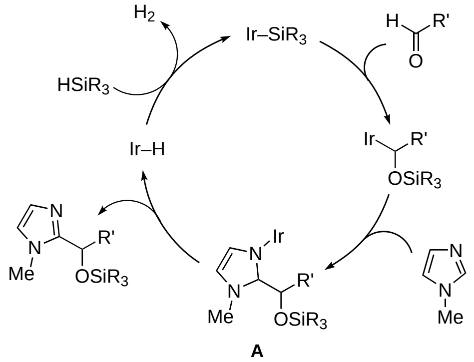
Scheme 2. $[Ir_4(CO)_{12}]$-catalyzed reaction of 1-methylimidazole (**1**) with N-propylisocyanate (**19**), with DMAD additive, to form **20**.

plexes has been observed directly.[16] The regeneration of the initial catalyst species might take place by the reaction of the Ir–H species with H–SiR$_3$ to give Ir–SiR$_3$ and H$_2$.[17]

In summary, $[Ir_4(CO)_{12}]$ catalyzes the coupling reaction of imidazoles with aldehydes in the presence of a hydrosilane to give 2-alkyl imidazoles. Detailed mechanistic studies are currently underway in our laboratories.[18]



Scheme 3. $[Ir_4(CO)_{12}]$-catalyzed reaction of 1-methylbenzimidazole (**21**) with hexanal (**2**), with DMAD additive, to give **22.**



Scheme 4. Possible reaction mechanism.

Experimental Section

3: $[Ir_4(CO)_{12}]$ (22 mg, 0.02 mmol), 1-methylimidazole (82 mg, 1 mmol), hexanal (100 mg, 1 mmol), diethylmethylsilane (204 mg, 2 mmol), DMAD (23 mg, 0.16 mmol), and toluene (5 mL) were mixed in a 10-mL flame-dried flask. The reaction mixture was heated at reflux for 2 h. After cooling to room temperature, the volatile components were removed in vacuo. Compound **3** was isolated by bulb-to-bulb distillation under reduced pressure. ^{1}H NMR (270 Hz, CDCl$_3$, TMS): $\delta = -0.05$ (s, 3H; CH$_3$Si), 0.51 (q, ^3J(H,H) = 7.8 Hz, 4H; SiCH$_2$), 0.83 (t, ^3J(H,H) = 7.8 Hz, 3H; SiCH$_2$CH_3), 0.86 (t, ^3J(H,H) = 7.8 Hz, 6H; SiCH$_2$CH$_3$, CH$_3$), 1.27–1.50 (c, 6H; CH_2CH_2CH_2), 1.80 (m, 2H; CHCH_2), 3.74 (s, 3H; NCH$_3$), 4.88 (dd, ^3J(H,H) = 6.2, 1.6 Hz, 1H; CH), 6.75 (d, ^3J(H,H) = 1.1 Hz, 1H; =CH), 6.88 ppm (d, ^3J(H,H) = 1.1 Hz, 1H; =CH); ^{13}C NMR (68 Hz, CDCl$_3$, TMS): $\delta = -4.89$ (SiCH$_3$), 6.22 (SiCH$_2$), 6.33 (SiCH$_2$), 6.51 (SiCH$_2$CH$_3$), 6.54 (SiCH$_2$CH$_3$), 13.95 (CH$_3$), 22.50 (CH$_2$), 25.52 (CH$_2$), 31.48 (CH$_2$), 33.25 (NCH$_3$), 36.89 (CH$_2$), 70.51 (CH), 121.64 (=CH), 126.72 (=CH), 148.97 ppm (NCN); MS (70 eV): m/z (%): 282 ([M^+], 8), 253 ([$M^+ - $Et], 100); elemental analysis (%) calcd for $C_{15}H_{30}N_2OSi$: C 63.78, H 10.70, N 9.92; found: C 63.53, H 10.96, N 10.19.

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$[\text{Lewis Acid}]^+[\text{Co(CO)}_4]^-$ Complexes: A Versatile Class of Catalysts for Carbonylative Ring Expansion of Epoxides and Aziridines**

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Introduction of carbonyl functional groups by using transition-metal-catalyzed carbon monoxide (CO) insertion is a synthetically useful transformation.[1–3] Application of this methodology, in conjunction with readily available epoxide and aziridine substrates provides facile access to β-lactones[4] and β-lactams,[5, 6] useful precursors for organic synthesis as well as for the synthesis of polymers such as poly(3-hydroxyalkanoates)[7] and poly(β-peptides).[8, 9] Few catalysts are known to perform ring-expansive CO insertion into epoxides to give β-lactones.[10, 11, 12d] Likewise, a limited number of reagents[13] and catalysts[12, 14, 15] are known to carbonylate aziridines to yield β-lactams. Recently, regioselective epoxide and aziridine carbonylation was achieved using a catalyst system consisting of a mixture of [PPN][Co(CO)$_4$] and $BF_3 \cdot Et_2O$ ($PPN = Ph_3P{=}N{=}PPh_3$).[12d] However, most of these catalysts require long reaction times, high temperatures, high catalyst loading, and/or external additives. There is continuing motivation for developing fast, single-component catalysts; ideally a single catalyst would efficiently carbonylate both epoxides and aziridines. Herein, we report a well-defined $[Cp_2Ti(thf)_2][Co(CO)_4]$ catalyst (**1**; $Cp = C_5H_5$),[16] readily synthesized from commercially available $[Cp_2Ti(CO)_2]$ and $[Co_2(CO)_8]$, is efficient for carbonylation of both epoxide and aziridine substrates. During the course of this work we discovered that the discrete catalyst $[(salph)Al(thf)_2][Co(CO)_4]$ (**2**),[11, 17] is also active for regioselective aziridine carbonylation (Scheme 1).

The $[Co(CO)_4]^-$ ion is the putative active species for CO insertion reactions that use $[Co_2(CO)_8]$ as the catalyst.[1, 11, 12a] Based on this postulate, a variety of [cation][Co(CO)$_4$] complexes[18] were previously screened[11] for CO insertion into propylene oxide. Complexes **1** and **2** are efficient catalysts for the carbonylation of a variety of *both* epoxides and aziridines.

Catalyst **1** (5 mol %) regioselectively carbonylates a variety of epoxides under mild conditions and in high yields. Propylene oxide is converted into β-butyrolactone in 95 % yield in 4 h at 60 °C; the carbonylation is highly regioselective producing exclusively the 4-methyloxetan-2-one isomer (Table 1, entry 1). Carbonylation of propylene oxide was not observed with other potential catalysts[18, 19]under a variety of

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