Reductive cross-coupling between *N*-acylbenzimidazoles and diarylketones promoted by Sm/$TiCl_4$

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The reductive cross-coupling reaction between *N*-acylbenzimidazoles and diarylketones promoted by Sm/$TiCl_4$ was performed in refluxing THF under a nitrogen atmosphere, to give 1,2,2-triaryl ethanones in moderate to good yields.

Keywords: *N*-acylbenzimidazole, diarylketone, cross-coupling, low-valent titanium

Reductive couplings are amongst the most valuable methods for making carbon–carbon bonds.[1]

Although reductive self-coupling and cross-coupling reactions between a number of functional groups have been studied, the reductive cross-coupling between ketones and *N*-acylbenzimimdazoles or *N*-acylimidazoles is less well known. *N*-Acylbenzimidazoles are known as a class of acylating agents, where the benzimidazole anion acts as a leaving group. The reports that such acylating agents as acylchlorides,[2] acylcyanides[3] and acylbenzotriazoles[4] with Cl^-, CN^- and benzotriazole as their respective leaving groups, undergo coupling reactions when subject to a reducing agent led us to investigate the effect of regular reducing agents on *N*-acylbenzimidazoles for application in organic synthesis.

Very recently, the electroreductive cross-coupling between aromatic ketones and *N*-acylimidazoles in the presence of chlorotrimethylsilane was reported to give α-trimethylsiloxy ketones and esters, indicating that the acylimidazoles could undergo other reductive coupling reaction.[5] Herein we report the reductive coupling of aromatic ketones and *N*-acylbenzimidazoles promoted by Sm/$TiCl_4$ in THF (Scheme 1).

When the popular reductive coupling reagent SmI_2 was used, it was found that the self-coupling between either *N*-acylbenzimidazoles or *N*-acylimidazoles failed to occur, and no 1,2-diketones or 2-hydroxylketones could be detected by TLC. On the other hand, the failure of self-coupling may indicate a satisfactory cross-coupling reaction.

Diaryl ketones were used as a cross-coupling substrates, and under the SmI_2 conditions, product **3** was obtained but only in poor yields. Another frequently used reductive coupling reagent is the low-valent titanium system.[6] This was then introduced, and to our delight, 1,1,2-triaryl substituted ethanones were obtained in satisfactory yields as listed in Table 1 by using Sm/$TiCl_4$ in THF under reflux conditions.

Good synthetic generality was observed since the R substituent, could be either an electron-donating or an electron-withdrawing group, on the aromatic rings of substrate **1**. These did not have a significant effect on the reductive coupling reaction. The R^1 and R^2 of the aromatic ketones **2** did not have much effect either.

Table 1 The cross-coupling of *N*-acyllbenzimidazoles and diarylketones by Sm/$TiCl_4$ system

Entry	R	R^1	R^2	Product	Yield/%[a]
1	H	H	H	**3a**	70
2	H	CH_3	CH_3	**3b**	76
3	H	Cl	Cl	**3c**	71
4	H	OCH_3	OCH_3	**3d**	76
5	H	H	Ph	**3e**	58
6	CH_3	H	H	**3f**	75
7	CH_3	CH_3	CH_3	**3g**	78
8	CH_3	Cl	Cl	**3h**	77
9	CH_3	OCH_3	OCH_3	**3i**	76
10	Cl	H	H	**3j**	72
11	Cl	CH_3	CH_3	**3k**	71
12	OCH_3	H	H	**3l**	74
13	H[b]	H	H	**3a**	68

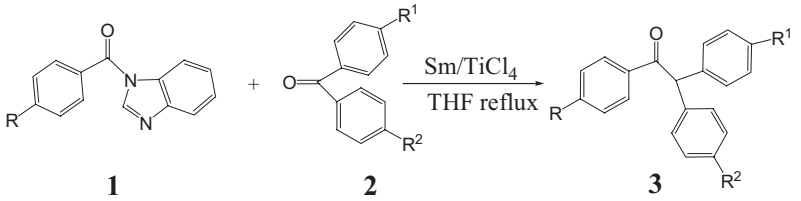
[a] Yields were isolated yields and based on *N*-acylbenzimidazoles.
[b] A is *N*-acylimidazole.

The reductive coupling between *N*-acylimidazoles and diarylketones (entry 13) underwent smoothly as well under the same conditions and 1,2,2-triphenylethanone was formed in comparable yields. It showed that both benzimidazole and imidazole could act as good leaving group under the reducing conditions.

Due to the ready availability of the starting materials, and the moderate to good yields of the products, the reaction described here may provide a useful addition to the known methods for the preparation of 1,2,2-triarylethanones.

Experimental

Melting points are uncorrected. IR spectra were recorded using KBr disks with a NEXUS 670 FTIR spectrometer with absorption in cm^{-1}. ^1H NMR and ^{13}C NMR spectra were determined in a Bruker AC–400 spectrometer as $CDCl_3$ solutions. *J* values are in Hertz. Chemical shifts are expressed in ppm downfield from internal TMS. Elemental analyses was carried out on a EA 1110 instrument. Metallic samarium and diarylketones were purchased from commercial sources, without further purification before use. Substrates **1a–1l** were synthesised according to literature.[9] THF was distilled from sodium/benzophenone under nitrogen immediately prior to use. All reaction were carried out under a nitrogen atmosphere.



Scheme 1

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Typical procedure for the synthesis of compounds **3**: Samarium powder (0.33 g, 2.2 mmol) and $TiCl_4$ (0.22 ml) in dry THF (20 ml) was refluxed under nitrogen atmosphere, for 2 h to obtain a black slurry. After being cooled to room temperature, a solution of *N*-acylimidaxole (0.225 g, 1 mmol) and diarylketone (0.182 g, 1 mmol) dissolved in THF (5 ml) was added. The resulting mixture was heated to reflux for 24 h and then cooled to room temperature. Dilute hydrochloric acid (5%, 10 ml) was added and the resulting mixture extracted with ethyl acetate (3 × 15 ml). The combined organic layer was washed with brine, dried over anhydrous sodium sulfate, and concentrated under reduced pressure. The residue was separated by preparative TLC on silica gel with ethyl acetate and cyclohexane (1: 5, V/V) as eluent to afford product **3**.

1,2,2-Triphenylethanone **(3a)**: White crystals, m.p. 135–136°C (lit[7] 134–136°C). IR (KBr): ν_{max}(cm^{-1}) 3084, 3060, 3027, 2919, 1680, 1595, 1493. δ_H($CDCl_3$): 8.00 (2H, d, *J* = 8.0 Hz), 7.48–7.52 (1H, m), 7.38–7.42 (2H, m), 7.17–7.34 (10H, m), 6.04 (1H, s).

1-Phenyl-2,2-di-p-tolylethanone **(3b)**: White crystals, m.p. 55–57°C (lit[8] 57–58°C). IR (KBr): ν_{max}(cm^{-1}) υ_{max}(film)/cm^{-1}: 3064, 3002, 2954, 2934, 2835, 1687, 1509, 1463. δ_H($CDCl_3$): 7.99 (2H, d, *J* = 8.0 Hz), 7.47–7.49 (1H, m), 7.37–7.41 (2H, m), 7.15 (4H, d, *J* = 8.0 Hz), 7.12 (4H, d, *J* = 8.0 Hz), 5.96 (1H, s), 2.30 (6H, s).

2,2-Bis-(4-chlorophenyl)-1-phenylethanone **(3c)**: White crystals, m.p. 90–92°C (lit[9] 90–91°C). ν_{max}(KBr)/cm^{-1}: 3087, 3067, 3028, 2925,1686, 1596, 1491. δ_H($CDCl_3$): 7.96 (2H, d, *J* = 6.4 Hz), 7.48–7.50 (1H, m), 7.38–7.40 (2H, m), 7.26 (4H, d, *J* = 7.2 Hz), 7.16 (4H, d, *J* = 7.2 Hz), 5.98 (1H, s). ^{13}C NMR (100 MHz, $CDCl_3$): 197.5, 137.3, 136.3, 133.5, 133.4, 130.5, 129.1, 129.0, 128.9, 57.9.

2,2-Bis-(4-methoxyphenyl)-1-phenylethanone **(3d)**: Viscous yellow oil (lit[10]). ν_{max}(KBr)/cm^{-1}: 3057, 2955, 2835, 1683, 1608, 1510, 1463. δ_H($CDCl_3$): 8.00 (2H, d, *J* = 7.6 Hz), 7.44–7.46 (1H, m), 7.35–7.38 (2H, m), 7.18 (4H, d, *J* = 8.4 Hz), 6.85 (4H, d, *J* = 8.4 Hz), 5.95 (1H, s), 3.72 (6H, s). ^{13}C NMR (100 MHz, $CDCl_3$): 198.8, 158.7, 136.9, 133.0, 131.6, 130.1, 129.0, 128.7, 114.2, 57.8, 55.3.

Biphenyl-4-yl-1,2-diphenylethanone **(3e)**: White crystals, m.p. 145–148°C (lit[11] 146–149°C). ν_{max}(KBr)/cm^{-1}: 3083, 3062, 3027, 2924, 2847, 1682, 1596, 1488. δ_H($CDCl_3$): 8.03 (2H, d, *J* = 7.2 Hz), 7.54–7.56 (4H, m), 7.41–7.44 (4H, m), 7.33–7.36 (8H, m), 7.13–7.16 (1H, m), 6.08 (1H, s). ^{13}C NMR (100 MHz, $CDCl_3$): 199.8, 142.3, 141.6, 140.6, 139.8, 138.4, 134.7, 131.1, 130.7, 130.6, 130.4, 130.3, 130.2, 129.0, 128.9, 128.8, 128.7.

2,2-Diphenyl-1-p-tolylethanone **(3f)**: White crystals, m.p. 97–98°C (lit[7] 98–99°C). ν_{max}(KBr)/cm^{-1}: 3083, 3061, 3029, 2923, 2848, 1675, 1604, 1495. δ_H($CDCl_3$): 7.91 (2H, d, *J* = 8.2 Hz), 7.21–7.34 (10H, m), 7.20 (2H, d, *J* = 8.2 Hz), 6.03 (1H, s), 2.37 (3H, s).

1,2,2-Tri-p-tolylethanone **(3g)**: White crystals m.p. 89–90°C (lit[12] 88°C). ν_{max}(KBr)/cm^{-1}: 3025, 2923, 2858, 1684, 1607, 1513.. δ_H($CDCl_3$): 7.89 (2H, d, *J* = 8.0 Hz), 7.06–7.15 (10H, m), 5.94 (1H, s), 2.27 (3H, s), 2.24 (6H, s). ^{13}C NMR (100 MHz, $CDCl_3$): 198.2, 143.9, 136.7, 134.6, 129.6, 129.4, 129.3, 129.2, 58.7, 21.7, 21.2.

2,2-Bis-(4-chloro-phenyl)-1-p-tolylethanone **(3h)**: M.p. 119–121°C. ν_{max}(KBr)/cm^{-1}: 3088, 3031, 2925, 2853, 1685, 1606, 1491. δ_H($CDCl_3$): 7.87 (2H, d, *J* = 8.0 Hz), 7.23 (4H, d, *J* = 8.0 Hz), 7.14–7.16 (6H, m), 5.96 (1H, s), 2.30 (3H, s). ^{13}C NMR (100 MHz, $CDCl_3$): 197.1, 144.5, 137.5, 133.9, 133.3, 130.5, 129.6, 129.2, 129.0, 57.7, 21.7. Anal. Calcd. for $C_{21}H_{16}Cl_2O$: C, 71.00; H, 4.54. Found C, 70.79; H, 4.60.

2,2-Bis-(4-methoxy-phenyl)-1-p-tolylethanone **(3i)**: White crystals, m.p. 72–74°C (lit[12] 74°C). ν_{max}(KBr)/cm^{-1}: 3057, 2925, 2847, 1678, 1606, 1510. δ_H($CDCl_3$): 7.89 (2H, d, *J* = 8.0 Hz), 7.18 (2H, d, *J* = 8.0 Hz), 7.16 (2H, d, *J* = 8.3 Hz), 6.83 (2H, d, *J* = 8.3 Hz), 5.91 (1H, s), 3.74 (6H, s), 2.35 (3H, s). ^{13}C NMR (100 MHz, $CDCl_3$): 198.4, 158.6, 143.8, 132.6, 131.8, 130.2, 129.3, 129.1, 114.1, 57.6, 55.2, 21.7.

1-(4-Chloro-phenyl)-2,2-diphenylethanone **(3j)**: White crystals, m.p. 110–112°C (lit[4b] 110–112°C). ν_{max}(KBr)/cm^{-1}: 3083, 3062, 3024, 2923, 2847, 1678, 1588, 1494. δ_H($CDCl_3$): 7.93 (2H, d, *J* = 8.4 Hz), 7.24–7.38 (12H, m), 5.96 (1H, s). ^{13}C NMR (100 MHz, $CDCl_3$): 197.0, 139.5, 138.8, 138.7, 135.1, 130.4, 129.1, 129.0, 128.9, 128.8, 128.5, 128.1, 127.3, 59.6.

1-(4-Chloro-phenyl)-2,2-di-p-tolylethanone **(3k)**: White crystals, m.p. 113–116°C (lit[12] 116°C). ν_{max}(KBr)/cm^{-1}: 3093, 3057, 3027, 2918, 2852, 1685, 1585, 1471. δ_H($CDCl_3$): 7.92 (2H, d, *J* = 8.8 Hz), 7.35 (2H, d, *J* = 8.8 Hz), 7.12 (8H, s), 5.88 (1H, s), 2.31 (6H, s). ^{13}C NMR (100 MHz, $CDCl_3$): 197.3, 139.3, 136.9, 135.9, 135.2, 130.4, 129.5, 128.9, 128.8, 58.9, 21.1.

1-(4-Methoxy-phenyl)-2,2-diphenylethanone **(3l)**: White crystals, m.p. 127–129°C (lit[4b] 126–128°C). ν_{max}(KBr)/cm^{-1}: 3085, 3059, 3028, 2935, 2842, 1675, 1596, 1494. δ_H($CDCl_3$): 7.99 (2H, d, *J* = 8.0 Hz), 7.24–7.33 (10H, m), 6.88 (2H, d, *J* = 8.0 Hz), 6.00 (1H, s), 3.82 (3H, s). ^{13}C NMR (100 MHz, $CDCl_3$): 196.7, 163.4, 139.4, 131.3, 129.2, 129.1, 128.7, 127.1, 113.8, 59.1, 55.5.

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