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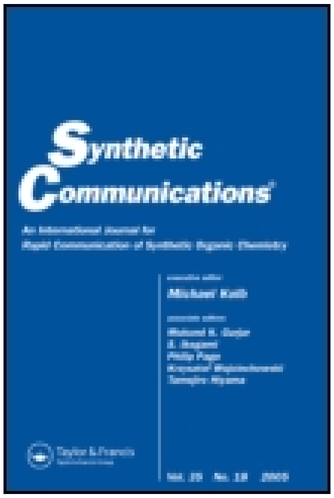

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Low-Valent Titanium Promoted Self-Coupling of N-Acylbenzotriazoles and Their Cross-Coupling with Diarylketones

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Low-Valent Titanium Promoted Self-Coupling of *N*-Acylbenzotriazoles and Their Cross-Coupling with Diarylketones

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ABSTRACT

The self-coupling reaction of *N*-acylbenzotriazoles and their cross-coupling with diarylketones promoted by $Sm/TiCl_4$ system were investigated. Self-coupling reaction could afford α-diketones or benzoins in moderate yields, while the cross-coupling reaction gave 1,2,2-triaryl ethanones in good yields.

Key Words: *N*-Acylbenzotriazole; Self-coupling; Cross-coupling; Diarylketone; 1,2,2-Triaryl ethanone; Low-valent titanium.

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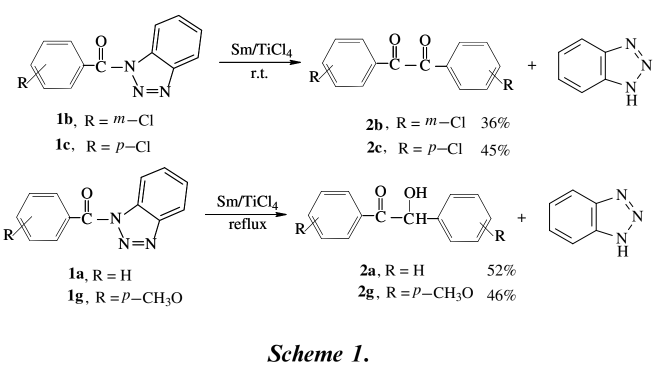
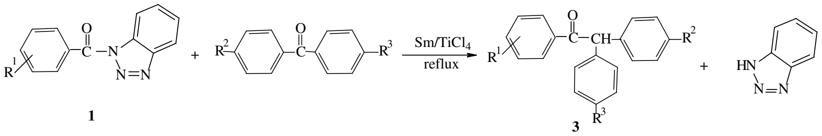
Carbon–carbon bond formation is the essence of organic synthesis and the reductive coupling of carbonyl derivatives is one of the most valuable methods for the fomation of carbon–carbon bonds.[1] Low-valent titanium has been extensively investigated as a versatile reagent in organic synthesis, especially with its exceptional ability to promote reductive coupling of many functional groups.[2] Benzotriazole is a good leaving group[3] and Li/$TiCl_3$ low-valent titanium system was reported to be an effective reagent for dehydroxybenzotriazolylation.[4] We thus deduce that the benzotriazolyl group in *N*-acylbenzotriazoles can probably be cleaved in the action of low-valent titanium, producing the corresponding acyl radicals, which may dimerize. Or, it could be expected that an active carbonyl group, when treated with low-valent titanium,[5] may attack the *N*-acylbenzotriazoles, thus cleaving the benzotriazolyl group and yielding a cross-coupling product. We now describe the results of our experiments based on the above consideration. Both the self-coupling reaction of *N*-acylbenzotriazoles and their cross-coupling reaction with diarylketones promoted by Sm/$TiCl_4$ low-valent titanium system were investigated.

Substrates **1a** and **1 g**, when subjected to the Sm/$TiCl_4$ system at room temperature for 24 h, resulted only in the recovery of the starting materials, while substrates **1b** and **1c** could afford α-diketones **2b** and **2c** in moderate yields under the same reaction conditions. When substrates **1a** and **1 g** were treated with Sm/$TiCl_4$ system under reflux conditions, the corresponding benzoins were obtained in moderate yields plus mixtures of other unidentified-products (Sch. 1).

Further investigation revealed that the cross-coupling reaction between *N*-acylbenzotriazoles and diarylketones were more successful than the self-coupling one. When *N*-acylbenzotriazoles and diarylketones were treated with Sm/$TiCl_4$ system under reflux conditions,



Scheme 1.



Scheme 2.

Table 1. The cross-coupling of *N*-acylbenzotriazoles and diarylketones promoted by Sm/TiCl$_4$ system.

Entry	R^1	R^2	R^3	Reaction time (h)	Product	Yield (%)
1	H	H	H	24[a]	**3a**	68
2	*p*-CH_3	H	H	24[a]	**3b**	80
3	*p*-Et_2N	H	H	24[a]	**3c**	82
4	*p*-$CH_3OC_6H_4$	H	H	24[a]	**3d**	57
5	H	H	Cl	24[a]	**3e**	82
6	*p*-Et_2N	H	Cl	24[a]	**3f**	86
7	*p*-$CH_3OC_6H_4$	H	Cl	24[a]	**3g**	83
8	p-$CH_3OC_6H_4$	H	CH_3	24[a]	**3h**	85
9	Cl	H	H	48[b]	**3i**	68
10	Cl	H	CH_3	48[b]	**3j**	81
11	Cl	H	Cl	48[b]	**3k**	70
12	*p*-CH_3	H	Cl	24[a]	**3l**	73

[a] The two substrates were mixed together and refluxed for the reported time.

[b] The reaction mixture was stirred at room temperature for 24 h and then refluxed for further 24 h, or else, it was found that the yield decreased greatly.

the corresponding 1,2,2-triaryl ethanones were obtained in good yields. The results are shown in Sch. 2 and Table 1.

As shown in the table, whether R^1 and R^3 are electron-donating group or electron-withdrawing group, the yields are both satisfactory.

It should be pointed that, as for aliphatic *N*-acylbenzotriazoles, the self-coupling reaction and the cross coupling reaction with diarylketones both failed to give desirable products.

In conclusion, the benzotriazole group in the *N*-acylbenzotrizoles can be cleaved efficiently when treated with Sm/TiCl$_4$ system. The self-coupling reaction of *N*-acylbenzotrizoles could afford α-diketones or α-hydroxy ketones in moderate yields depending on the reaction conditions. And their cross-coupling reaction with diarylketones could proceed smoothly to give 1,2,2-triaryl ethanones. Due to the easy availability of the starting materials, mild and neutral conditions, moderate to good yields of the products, the above study may provide a useful method in organic synthesis.

EXPERIMENTAL

Tetrahydrofuran was distilled from sodium-benzophenone ketyl immediately prior to use. All reactions were conducted under a nitrogen atomsphere. Melting points are uncorrected. ^{1}H NMR spectra were recorded on a Bruker 400 MHz instrument as $CDCl_3$ or DMSO-d_6 solutions using TMS as internal standard. Chemical shifts (δ) are reported in ppm and coupling constants J is given in Hz. Infrared spectra were recorded using KBr disks with a Bruker Vector-22 infrared spectrometer. Elemental analyses were performed on a EA-1110 instrument. Metallic samarium and all solvents were purchased from commercial sources, without further purification before use. Substrates **1a–1m** were synthesized according to reported procedure.[6]

General Procedure for the Synthesis of Compounds 2

Under nitrogen atmosphere, samarium powder (0.33 g, 2.2 mmoL) and $TiCl_4$ (0.22 mL) in dry THF (20 mL) was refluxed for 2 h to obtain black slurry, to which, after being cooled to room temperature, was added a solution of *N*-acylbenzotriazole (1 mmoL), the mixture was then stirred at room temperature or under reflux conditions till the disappearance of the starting materials (detected by TLC). Dilute hydrochloric acid (2 M, 5 mL) was added and the resulting mixture extracted with diethylether (3×20 mL). The combined organic layer was washed with brine, dried over anhydrous sodium sulphate, and concentrated under reduced pressure. The residue was separated on preparative TLC on silica gel with ethyl acetate and cyclohexane (1 : 3) as eluent to afford products **2**.

Benzoin (2a). White crystals, m.p. 132–134°C (Lit.[7] 133–135°C). δ_H: 7.91 (2H, d, $J = 8.52$ Hz), 7.50–7.54 (1H, m), 7.27–7.41 (7H, m), 5.95 (1H, s), 4.54 (1H, s). IR (KBr): ν_{max} (cm^{-1}) 3415, 3285, 3028, 3060, 3028, 2830, 1678, 1595, 1449.

1,2-Di(3-chlorophenyl)-1,2-ethanedione (2b). Yellow crystals, m.p. 116–117°C (Lit.[7] 115°C). δ_H: 7.97 (2H, s), 7.83–7.85 (2H, m), 7.64–7.66

(2H, m), 7.46–7.49 (2H, s). IR (KBr): ν_{max} (cm^{-1}) 3076, 3059, 1673, 1588, 1570, 1198.

1,2-Di(4-chlorophenyl)-1,2-ethanedione (2c). Yellow crystals, m.p. 195–197°C (Lit.[7] 199°C). δ_H: 7.91 (4H, d, $J = 8.4$ Hz), 7.50 (4H, d, $J = 8.5$ Hz). IR (KBr): ν_{max} (cm^{-1}) 3010, 1659, 1586, 1571, 1404, 1209.

4,4′-Dimethoxybenzoin (2g). White crystals, m.p. 109–112°C (Lit.[7] 110–112°C). δ_H: 7.99 (2H, d, $J = 8.8$ Hz), 7.25 (2H, d, $J = 9.5$ Hz), 6.83–6.87 (4H, m), 5.84 (1H, s), 4.49 (1H, s), 3.82 (1H, s), 3.76 (1H, s). IR (KBr): ν_{max} (cm^{-1}) 3465, 3077, 2982, 2921, 2843, 1668, 1597, 1514.

General Procedure for the Synthesis of Compounds 3

The low-valent system was prepared as above and after being cooled to room temperature, a solution of *N*-acylbenzotriazole (1 mmoL) and diarylketone (1 mmoL) dissolved in dry THF (5 mL) was added. The resulting mixture was heated to reflux for adequate time and then cooled to room temperature. Dilute hydrochloric acid (2 M, 5 mL) was added and the resulting mixture extracted with diethyl ether (3 × 20 mL). The combined organic layer was washed with brine, dried over anhydrous sodium sulphate, and concentrated under reduced pressure. The residue was separated on preparative TLC on silica gel with ethyl acetate and cyclohexane (1:3) as eluent to afford products **4**.

2,2-Diphenyl-1-phenyl ethanone (3a). White crystals, m.p. 136–138°C (Lit.[8] 138–138.5°C). δ_H: 7.99 (2H, d, $J = 8.88$ Hz), 7.24–7.33 (10H, m), 6.88 (2H, d, $J = 8.91$Hz), 6.00 (1H, s), 3.83 (3H, s). IR (KBr): ν_{max} (cm^{-1}) 3086, 3059, 3028, 2972, 2935, 2844, 1674, 1595, 1508.

2,2-Diphenyl-1-(4-methylphenyl) ethanone (3b). White crystals, m.p. 100–102°C (Lit.[9] 100–101°C). δ_H: 7.90 (2H, d, $J = 8.11$ Hz), 7.19–7.31 (12H, m), 6.02 (1H, s), 2.37 (3H, s). IR (KBr): ν_{max} (cm^{-1}) 3084, 3062, 3004, 2920, 1674, 1603, 1494.

2,2-Diphenyl-1-(4-diethylaminophenyl) ethanone (3c). White crystals, m.p. 160–161°C, δ_H: 7.93 (2H, d, $J = 8.87$ Hz), 7.20–7.32 (10H, m), 6.63 (2H, s), 5.98 (1H, s), 6.00 (1H, s), 3.39 (4H, q, $J = 7.06$ Hz), 1.17 (6H, *t*, $J = 7.03$ Hz). IR (KBr): ν_{max} (cm^{-1}) 3084, 3061, 3016, 2975, 2920, 2868, 1656, 1589, 1548, 1530. *m*/*z* (%): 344 (M^++1, 0.43), 343 (M^+, 1.10), 176 (100), 177 (13.06), 167 (4.14). Anal. calcd. $C_{25}H_{25}NO$: C, 83.93; H, 7.34; N, 4.08. Found C, 80.89; H, 7.42; N, 3.96%.

2,2-Diphenyl-1-(4-methoxyphenyl) ethanone (3d). White crystals, m.p. 126–128°C (Lit.[10] 128–130°C). δ_H: 7.99 (2H, d, $J = 8.88$ Hz), 7.24–7.33 (10H, m), 6.88 (2H, d, $J = 8.91$ Hz), 6.00 (1H, s), 3.83 (3H, s). IR (KBr): ν_{max} (cm^{-1}) 3086, 3059, 3028, 2972, 2935, 2844, 1674, 1595, 1508.

2-Phenyl-2-(4-chlorophenyl)-1-phenyl ethanone (3e). White crystals, m.p. 103–105°C (Lit.[5c] 105–106°C). δ_H: 7.97 (2H, d, $J = 8.19$ Hz), 718–7.52 (12H, m), 6.00 (1H, s). IR (KBr): ν_{max} (cm^{-1}) 3086, 3059, 3028, 2972, 2853, 1679, 1595, 1579.

2-Phenyl-2-(4-chlorophenyl)-1-(4-diethylaminophenyl) ethanone (3f). Orange crystals. m.p. 99–101°C. δ_H: 7.90 (2H, d, $J = 8.87$ Hz), 719–7.32 (9H, m), 6.62 (2H, s), 6.00 (1H, s), 3.38 (4H, q, $J = 7.07$ Hz), 1.17 (6H, t, $J = 7.08$ Hz). IR (KBr): ν_{max} (cm^{-1}) 3086, 3057, 3038, 2972, 2853, 1646, 1587, 1547, 1527. m/z (%): 378 ($M^+ + 1$, 0.32), 377 (M^+, 0.77), 201 (2.08), 203 (0.64), 177 (13.16), 176 (100). Anal. calcd. $C_{24}H_{24}ClNO$: C, 76.28; H, 6.40; N, 3.71. Found C, 76.18; H, 6.45; N, 3.61%.

2-Phenyl-2-(4-chlorophenyl)-1-(4-methoxyphenyl) ethanone (3g). White crystals, m.p. 91–94°C. δ_H: 7.96–7.98 (2H, m), 7.18–7.34 (9H, m), 6.87–6.89 (2H, m), 5.96 (1H, s), 3.83 (3H, s). IR (KBr): ν_{max} (cm^{-1}) 3016, 2952, 2838, 1671, 1594, 1574, 1509. m/z (%): 337 ($M^+ + 1$, 0.08), 320 (0.10), 201 (1.71), 165 (12.51), 135 (100). Anal. calcd. $C_{21}H_{17}ClO_2$: C, 74.89; H, 5.09; Found C, 74.80; H, 5.15%.

2-Phenyl-2-(4-methylphenyl)-1-(4-methoxyphenyl) ethanone (3h). White crystals, m.p. 107–109°C. δ_H: 7.99 (2H, d, $J = 8.87$), 7.23–7.32 (5H, m), 7.10–7.17 (4H, m), 6.87 (2H, d, $J = 8.86$), 5.96 (1H, s), 3.83 (3H, s), 2.31 (3H, s). IR (KBr): ν_{max} (cm^{-1}) 3028, 3016, 2966, 2934, 2838, 1670, 1600, 1575, 1509. m/z (%): 316 (M^+, 0.10), 181 (6.11), 165 (13.69), 135 (100). Anal. calcd. $C_{22}H_{20}O_2$: C, 83.52; H, 6.37. Found C, 83.41; H, 6.45%.

2,2-Diphenyl-1-(4-chlorophenyl) ethanone (3i). White crystals, m.p. 110–112°C (Lit.[11] 108–109°C). δ_H: 7.76–7.78 (2H, m), 7.08–7.22 (12H, m), 5.80 (1H, s). IR (KBr): ν_{max} (cm^{-1}) 3083, 3062, 3039, 3024, 3003, 1678, 1588, 1571.

2-Phenyl-2-(4-mehtylphenyl)-1-(4-chlorophenyl) ethanone (3j). Oil, δ_H: 7.91–7.93 (2H, m), 7.77–7.79 (2H, m), 7.22–7.31 (5H, m), 7.13 (4H, s), 2.30 (3H, s). IR (KBr): ν_{max} (cm^{-1}) 3085, 3059, 3027, 2921, 2838, 1686, 1587, 1511, 1398. m/z (%): 321 ($M^+ + 1$, 0.86), 320 (M^+, 0.33), 304 (0.55), 181 (100), 165 (28.66), 139 (27.64). Anal. calcd. $C_{21}H_{17}ClO$: C, 78.62; H, 5.34. Found C, 78.60; H, 5.48%.

2-Phenyl-2-(4-chlorophenyl)-1-(4-chlorophenyl) ethanone (3k). Oil, δ_H: 7.90 (2H, d, $J = 8.50$ Hz), 7.73–7.77 (2H, m), 7.43–7.49 (2H, m), 7.15–7.36 (7H, s), 5.93 (3H, s). IR (KBr): ν_{max} (cm^{-1}) 3085, 3062, 3028, 2924, 1686, 1587, 1490. m/z (%): 341 ($M^+ + 1$, 3.08), 340 (M^+, 0.55), 324 (1.27), 201 (28.12), 165 (41.86), 139 (100). Anal. calcd. $C_{20}H_{14}Cl_2O$: C, 70.40; H, 4.14. Found C, 70.45; H, 4.25%.

2-Phenyl-2-(4-chlorophenyl)-1-(4-methylphenyl) ethanone (3l). White crystals, m.p. 66–68°C, δ_H: 7.88 (2H, d, $J = 8.24$), 7.17–7.34 (11H, m), 5.98 (1H, s), 2.37 (3H, s). IR (KBr): ν_{max} (cm^{-1}) 3086, 3060, 3028, 3003, 2921, 1682, 1605, 1490. m/z (%): 321 (M^++1, 0.06), 304 (0.10), 165 (14.66), 119 (100). Anal. calcd. $C_{21}H_{17}ClO$: C, 78.62; H, 5.34. Found C, 78.59; H, 5.46%.

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