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Substitution of Acyl for Acetyl with *N*-Acylbenzotriazoles Catalyzed by Samarium Triiodide

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Abstract: Catalyzed by samarium triiodide (SmI_3), substitution of acyl with *N*-acylbenzotriazoles for acetyl in acetoacetic esters and acetylacetone proceeds smoothly under neutral conditions in open air, affording the corresponding β-keto esters and β-diketones in good yields.

Keywords: *N*-acylbenzotriazoles, β-diketones, β-ketoesters, SmI_3

β-Keto esters and β-diketones are very important intermediates in organic synthesis, and their new reactions and applications continue to be an area of interest.[1]

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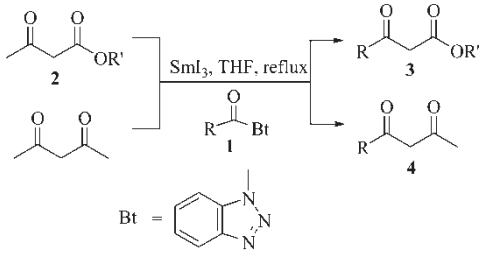
Among numerous methods developed for the syntheses of β-keto esters and β-diketones,[2,3] acyl exchange of the acetyl in acetoacetic ester or acetylacetone with acyl halides in the presence of either a base[4a–d] or a metal salt[4e–g] remains one frequently employed method. Despite being practical in many cases, acyl halides as highly active acylating agents can favor O-acylation of the enol form of ethyl acetoacetate or acetylacetone instead of C-acylation.[5] Moreover, acylation with acyl chlorides generally suffers from sensitivity to moisture and difficulty in handling.

Alternatively, esters,[6a] nitriles,[6b] and anhydrides[6c] may serve as less active acylating agents, but usually harsh conditions and tedious procedures are required. Very recently, it was reported *N*-acylbenzotriazoles were able to undergo C-acylation of ethyl acetoacetate and acetonyl acetone with the acetyl being cleaved spontaneously. The reaction offered a novel method for the preparation of β-keto esters and β-diketones[7] in that *N*-acylbenzotriazoles—a kind of mild and stable crystalline acylating agents[8]—were introduced. Nevertheless, the method is subject to certain disadvantages such as using strong alkaline (NaH) conditions and requiring inert atmospheric protection. Herein we report that under neutral conditions and in open air, the substitution of acyl for acetyl with *N*-acylbenzotriazoles can be realized with SmI_3 as a catalyst to afford the expected β-keto esters and β-diketones with good efficiency (Scheme 1 and Table 1).

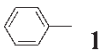
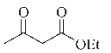
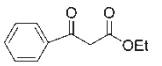
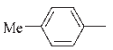
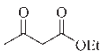
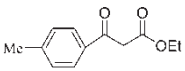
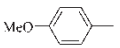
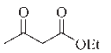
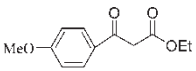
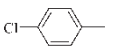
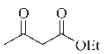
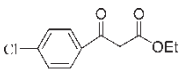
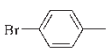
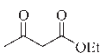
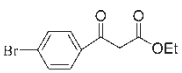
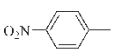
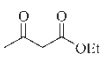
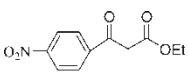
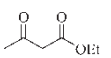
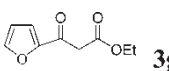
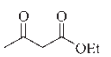
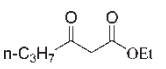
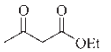
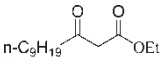
The appropriate amount of SmI_3 was found to be 20 mol% of the substrate. THF other than CH_3CN[4e] was chosen as the solvent, which was based on the fact that *N*-acylbenzotriazoles, unlike acyl chlorides, would not induce the ring opening of THF in the presence of SmI_3. Finally, the acyl exchange was carried out in refluxing THF with 0.2 equiv. of SmI_3.

As shown in Table 1, this method is especially efficient for the synthesis of β-aroyl substituted acetoacetic esters (Table 1, entries 1–7, 10). The substitution of aroyl for acetyl (naphthoyl is an exception, Table 1, entry 11) could proceed to a complete stage within 2 h, which is in contrast to the recently reported acyl exchange reaction where 14[7] or more than 30[4g] h were required. The acyl substitution with aliphatic *N*-acylbenzotriazoles proceeded smoothly under the same conditions, though relatively low



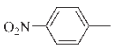
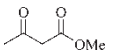
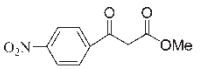
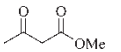
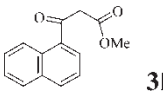
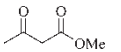
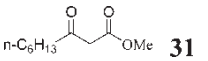
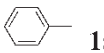
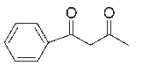
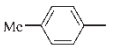
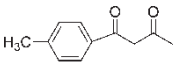
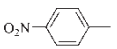
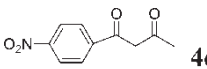
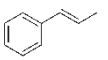
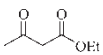
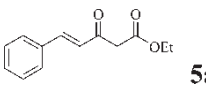
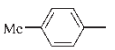
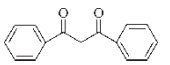
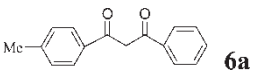
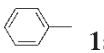
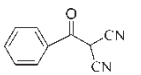
Scheme 1.

Table 1. SmI_3-catalyzed substitution of acyl for acetyl with *N*-acylbenzotriazoles

Entry	R	Substrates **2**	Products **3**	Time (h)	Yields (%)[a]
1	 **1a**		 **3a**	1.5	75
2	 **1b**		 **3b**	1.5	73
3	 **1c**		 **3c**	1.5	76
4	 **1d**		 **3d**	1	80
5	 **1e**		 **3e**	1	82
6	 **1f**		 **3f**	1	87
7	 **1g**		 **3g**	2	78
8	n-C_3H_7- **1h**		 **3h**	20	70
9	n-C_9H_{19}- **1i**		 **3i**	20	72

(*continued*)

Table 1. Continued

Entry	R	Substrates **2**	Products **3**	Time (h)	Yields (%)[a]
10	 **1f**		 **3j**	1	80
11	 **1j**		 **3k**	20	70
12	n-C_6H_{13}- **1k**		 **31**	20	71
13	 **1a**		 **4a**	10	78
14	 **1b**		 **4b**	12	70
15	 **1f**		 **4c**	10	82
16	 **1l**		 **5a**	20	No reaction
17	 **1b**		 **6a**	16	No reaction
18	 **1a**		 **7a**	16	No reaction

[a]Yields of pure isolated products.

reactivity was observed. Time as long as 20 h was taken for the reaction to afford comparable yields (Table 1, entries 8, 9, 12). ^{1}H NMR spectra show that the β-keto esters **3a**–**3l** exist in $CDCl_3$ solution with their keto forms predominant.

The analogous substitution for acetyl in acetylacetone with *N*-acylbenzotriazoles also proved successful with 10 h or longer reaction time required (Table 1, entries 13–15). Unlike β-keto esters, the enol forms of β-diketone **4a**–**4c** predominate in the $CDCl_3$ solution.

Further investigation was carried out with an attempt to find wider application of the reaction, with discouraging results. For example, unsaturated *N*-acylbenzotriazole **11** was used with the intention to prepare compound **5a** (Table 1, entry 16). The reaction did not occur at all, indicating the remarkable influence of the C═C bond existing therein. The reaction between *N*-acylbenzotriazole **1b** and dibenzoyl methane was also examined to elucidate the possibility of substitution of one aroyl for the other. However, no reaction occurred even after 16 h (Table 1, entry 17). The acylation of other active methylene compounds such as malonitrile with *N*-acylbenzotriazole under the SmI_3-catalyzed conditions failed too (Table 1, entry 18).

In conclusion, the scope and limitation of the acyl substitution with *N*-acylbenzotriazoles catalyzed by SmI_3 were explored. Substitutions of acyl for acetyl in ethyl acetoacetate, methyl acetoacetate, and acetylacetone with *N*-acylbenzotriazoles were found to proceed smoothly under neutral conditions without the necessity of inert gas protection. The operational simplicity and good efficiency makes the reaction practical for the preparation of β-keto esters and β-diketones.

EXPERIMENTAL

Tetrahydrofuran was distilled from sodium benzophenone immediately prior to use. Melting points are uncorrected. ^{1}H NMR (400-MHz) spectra were recorded on a Bruker AV400 NMR instrument as $CDCl_3$ solutions using TMS as internal standard. Chemical shifts (δ) are reported in parts per million (ppm), and coupling constants (J) are given in Hertz. IR spectra were recorded in film or using KBr disks with a Nexus 670 FTIR spectrometer.

General Procedure for the Preparation of β-Ketoesters

Anhydrous THF (10 mL) and I_2 (0.076 g, 0.3 mmol) were added to samarium powder (0.03 g, 0.2 mmol) in a flask. The mixture was stirred at room temperature for 1 h. To the SmI_3–THF suspension thus prepared, acetoacetic ester (1 mmol) and *N*-acylbenzotriazole (1 mmol) were added. The reaction mixture was refluxed until the disappearance of *N*-acylbenzotriazole (the time taken is indicated in Table 1). Then the reaction was quenched with

dilute hydrochloric acid (0.1 mol/L, 3 mL) and extracted with diethyl ether (3 × 30 mL). The combined extracts were washed with saturated solution of $Na_2S_2O_3$ and brine and were dried over anhydrous Na_2SO_4. Removal of the solvent under reduced pressure afforded the crude product, which was purified by preparative thin-layer chromatography (TLC) on silica gel (eluent: ethyl acetate/cyclohexane 1:6) to give β-ketoesters **3**.

Data

Compound 3a: oil.[7] ν_{max}(film)/cm^{-1}: 3063, 2983, 2938, 1740, 1687, 1624. Keto tautomer: ^{1}H NMR ($CDCl_3$) 7.95–7.92 (m, 2H), 7.48–7.40 (m, 3H), 4.23 (q, $J = 8.0$ Hz, 2H), 3.99 (s, 2H), 1.25 (t, $J = 8.0$ Hz, 3H).

Compound 3b: oil.[7] ν_{max}(film)/cm^{-1}: 2956, 2854, 1742, 1683, 1624. Keto tautomer: ^{1}H NMR ($CDCl_3$) 7.85 (d, $J = 7.8$ Hz, 2H), 7.28 (d, $J = 7.8$ Hz, 2H), 4.21 (q, $J = 7.1$ Hz, 2H), 3.97 (s, 2H), 2.42 (s, 3H), 1.26 (t, $J = 7.1$ Hz, 3H).

Compound 3c: oil.[4g] ν_{max}(film)/cm^{-1}: 2983, 2938, 2842, 1739, 1678. Keto tautomer: ^{1}H NMR ($CDCl_3$) 7.92 (d, $J = 6.8$ Hz, 2H), 6.94 (d, $J = 6.8$ Hz, 2H), 4.20 (q, $J = 8.0$ Hz, 2H), 3.95 (s, 2H), 3.85 (s, 3H), 1.26 (t, $J = 8.0$ Hz, 3H).

Compound 3d: oil.[7] ν_{max}(film)/cm^{-1}: 2928, 2851, 1746, 1691. Keto tautomer: ^{1}H NMR ($CDCl_3$) 7.89 (d, $J = 8.7$ Hz, 2H), 7.45 (d, $J = 8.7$ Hz, 2H), 4.22 (q, $J = 8.0$ Hz, 2H), 3.98 (s, 2H), 1.25 (t, $J = 8.0$ Hz, 3H).

Compound 3e: oil.[4g] ν_{max}(film)/cm^{-1}: 3091, 3062, 2920, 2851, 1744, 1687. Keto tautomer: ^{1}H NMR ($CDCl_3$): 7.82 (d, $J = 8.4$ Hz, 2H), 7.65 (d, $J = 8.4$ Hz, 2H), 4.22 (q, $J = 8.0$ Hz, 2H), 3.98 (2H, s), 1.25 (t, $J = 8.0$ Hz, 3H).

Compound 3f: yellow plates, mp 71–73°C (lit.[9] 73°C). ν_{max}(KBr)/cm^{-1}: 3114, 3083, 2994, 2909, 1735, 1643, 1619. Keto tautomer: ^{1}H NMR ($CDCl_3$) 8.34 (m, 2H), 8.28 (m, 2H), 4.23 (q, $J = 8.0$ Hz, 2H), 4.04 (s, 2H), 1.26 (t, $J = 8.0$ Hz, 3H).

Compound 3g: oil.[7] ν_{max}(film)/cm^{-1}: 3137, 2923, 1740, 1677. Keto tautomer: ^{1}H NMR ($CDCl_3$): 7.63 (d, $J = 1.6$ Hz, 1H), 7.28–7.29 (1H, m), 6.57–6.59 (1H, m), 4.21 (2H, q, $J = 7.2$ Hz), 3.86 (2H, s), 1.26 (3H, t, $J = 7.2$ Hz).

Compound 3h: oil.[9] ν_{max}(film)/cm^{-1}: 2965, 2938, 2877, 1742, 1717, 1647, 1624. Keto tautomer: ^{1}H NMR ($CDCl_3$) 4.19 (q, $J = 8.0$ Hz, 2H), 3.44 (s, 2H),

2.53 (t, $J = 8.0$ Hz, 2H), 1.65 (m, 2H), 1.28 (t, $J = 8.0$ Hz, 3H), 0.92, (t, $J = 8.0$ Hz, 3H).

Compound 3i: oil.[10a] ν_{max}(film)/cm^{-1}: 2927, 2856, 1743, 1716, 1650, 1624. Keto tautomer: ^{1}H NMR ($CDCl_3$) 4.19 (q, $J = 8.0$ Hz, 2H), 3.44 (s, 2H), 2.54, (t, $J = 8.0$ Hz, 2H), 1.59, (m. 2H), 1.28 (m, 15H), 0.88 (m, 3H).

Compound 3j: yellow plates, mp 105–106°C (lit.[10b] 104–105°C). ν_{max}(KBr)/cm^{-1} 3111, 3054, 2963, 2916, 2851, 1746, 1662, 1631. Keto tautomer: ^{1}H NMR ($CDCl_3$) 8.33 (m, 2H), 8.27 (m, 2H), 4.07 (s, 2H), 3.80 (s, 3H).

Compound 3k: white solid, mp 60–62°C (lit.[10c] 60–61°C). ν_{max}(KBr)/cm^{-1}: 2963, 2870, 1756, 1685. Keto tautomer: ^{1}H NMR ($CDCl_3$) 8.35–7.22 (m, 7H), 4.15 (s, 2H), 3.80 (s, 3H).

Compound 3l: oil.[1a] ν_{max}(film)/cm^{-1}: 2930, 2832, 1755, 1716, 1654, 1623. Keto tautomer: ^{1}H NMR ($CDCl_3$) 3.73 (s, 3H), 3.46 (s, 2H), 2.54 (t, 2H, $J = 7.2$ Hz), 1.58–1.61 (m, 2H), 1.27–1.31 (m, 6H), 0.88 (t, 3H, $J = 7.0$ Hz).

Compound 4a: solid, mp 50–52°C (lit.[7] 52–53°C). ν_{max}(KBr)/cm^{-1}: 3447, 2924, 2848, 1721, 1605. Enol tautomer: ^{1}H NMR ($CDCl_3$) 16.17 (br s, 1H), 7.88 (m, 2H), 7.45–7.53 (m, 3H), 6.19 (s, 1H), 2.21 (s, 3H).

Compound 4b: oil.[11] ν_{max}(film)/cm^{-1}: 3427, 2923, 2858, 1716, 1612. Enol tautomer: ^{1}H NMR ($CDCl_3$) 16.26 (br s, 1H), 7.77 (d, $J = 8.0$ Hz, 2H), 7.23 (d, $J = 8.0$ Hz, 2H), 6.14 (s, 1H), 2.39 (s, 3H), 2.17 (s, 3H).

Compound 4c: yellow plates, mp 108–110°C (lit.[6c] 111°C). ν_{max}(KBr)/cm^{-1}: 3423, 3110, 3073, 1627. Enol tautomer: ^{1}H NMR ($CDCl_3$) 15.90 (br s, 1H), 8.29 (m, 2H), 8.02 (m, 1H), 6.24 (s, 1H), 2.26 (s, 3H).

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