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Synthesis of 1,3-Diarylacetones from *N*-(Arylacetyl)benzotriazoles via Arylketene Intermediates

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ABSTRACT

Several 1-acylbenzotriazoles were synthesized and treated with sodium hydride to afford symmetrical ketones via the dimerization of intermediate ketenes followed by hydrolysis and the loss of carbon dioxide.

INTRODUCTION

Ketenes are important organic intermediates [1,2], usually prepared by the dehalogenation of *α*-chloroacyl chlorides or the dehydrohalogenation of acyl chlorides [1–4]. Benzotriazole is a good leaving group and used extensively as a novel synthetic auxiliary [5,6]. For example, 1-formylbenzotriazole is an excellent formulating reagent [7]. Generally, *N*-acylbenzotriazoles are more stable than acid chlorides and easier to handle. Accordingly, we believed that *N*-acylbenzotriazoles could be good precursors of ketenes, and we now report the novel preparation of symmetrical ketones via ketene intermediates derived from *N*-acylbenzotriazoles.

Dedicated to Professor Louis D. Quin on the occasion of his retirement from the University of Massachusetts at Amherst.

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RESULTS AND DISCUSSION

N-(Arylacetyl)benzotriazoles **1a–h** were synthesized in good yields (Table 1; all except **1a** are novel) from acids by treating acyl chlorides prepared in situ with benzotriazole in the presence of triethylamine [8].

N-(Arylacetyl)benzotriazoles **1a,c,e,f,g** on treatment with sodium hydride in tetrahydrofuran (THF) followed by hydrolysis with water gave the symmetrical ketones **2a,c,e–g** in good yields (Scheme 1). Evidently, the ketones **2** are formed by the intermediate ketenes [9] dimerizing to **3** (or possibly the corresponding *β*-lactone), followed by addition of water and loss of carbon dioxide [10].

N-(Diphenylacetyl)benzotriazole (**1b**) and *N*-(1-phenylbutanoyl)benzotriazole (**1h**) were treated under the same conditions, and only the corresponding acid was obtained. Under these conditions, **1d** formed no identified product.

The formation of symmetrical ketones from carboxylic acids and their derivatives is well documented in the literature. The pyrolysis of alkaline earth salts of acids at 340°C [11] and the coupling of acid chlorides in the presence of $Fe_2(CO)_4$ or $Ni(CO)_4$ gives symmetrical ketones in fair to good yields [12].

In conclusion, *N*-(arylacetyl)benzotriazoles were synthesized and treated with sodium hydride to give symmetrical ketones in good yields.

EXPERIMENTAL

Melting points were determined on a Bristoline hot-stage microscope and are uncorrected. ^{1}H NMR

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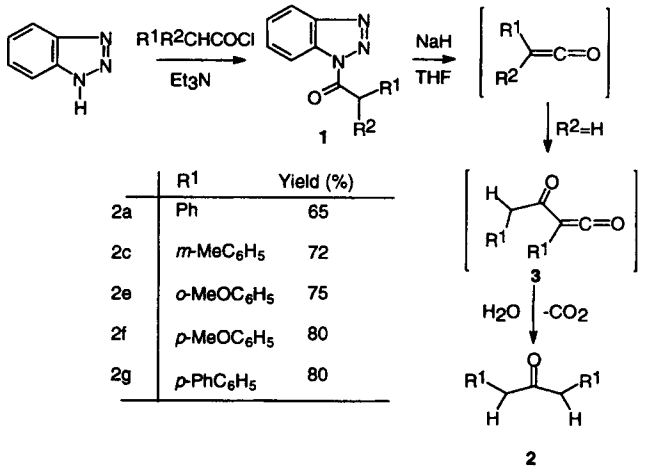
TABLE 1 Synthesis of *N*-Acylbenzotriazole 1

Cpd	R^1	R^2	Yield (%)	Mp(°C)	MF	CHN Found (required) C	H	N
1a	Ph	H	80	66–67	$C_{14}H_{11}N_3O$			
1b	Ph	Ph	80	70–71 [8] 106–107	$C_{20}H_{15}N_3O$	76.31 (76.66	4.97 4.85	13.41 13.41)
1c	*m*-MeC_6H_5	H	70	92–93	$C_{15}H_{13}N_3O$	71.64 (71.70	5.33 5.21	16.81 16.72)
1d	*o*-$NO_2C_6H_5$	H	67	153–154	$C_{14}H_{10}N_4O_3$	59.81 (59.57	3.49 3.57	19.85 19.85)
1e	*p*-$MeOC_6H_5$	H	60	90–91	$C_{15}H_{13}N_3O_2$	67.67 (67.41	4.96 4.90	15.97 15.72)
1f	*o*-$MeOC_6H_5$	H	75	113–114	$C_{15}H_{13}N_3O_2$	67.64 (67.41	5.03 4.90	15.81 15.72)
1g	*p*-PhC_6H_5	H	80	129–130	$C_{20}H_{15}N_3O$	76.57 (76.66	4.94 4.82	13.14 13.41)
1h	Ph	C_2H_5	80	56–57	$C_{16}H_{15}N_3O$	72.83 (72.53	5.76 5.70	15.75 15.54)

spectra were recorded on a Varian VXR-300 spectrometer with tetramethylsilane (TMS) as an internal reference. ^{13}C NMR spectra were recorded at 75 MHz on the same instrument using the solvent peak ($CDCl_3$, δ = 77.0) as a reference. Microanalyses were carried out using a Carlo Erba 1106 elemental analyzer.

General Procedure for Preparation of N-(Arylacetyl)benzotriazole (1a–1h)

To a solution of acid (20 mmol) in dry benzene (100 mL), $SOCl_2$ (25 mmol) was added slowly at room temperature. Then the mixture was refluxed for 1 hour, and the solvent and excess $SOCl_2$ were removed by an evaporator. The residue was dissolved in methylene chloride (100 mL), followed by addition of benzotriazole (20 mmol) and triethylamine (4 mL) at room temperature. The formed mixture was then refluxed for 2–3 hours. After cooling to room temperature, the mixture was washed with 2 M NaOH aqueous solution (2 × 30 mL) and extracted with methylene chloride (2 × 50 mL). The combined organic layer was dried over anhydrous sodium sulfate. After removal of the solvent, the residue was applied on a column, and pure acylbenzotriazoles were obtained.



	R^1	Yield (%)
2a	Ph	65
2c	*m*-MeC_6H_5	72
2e	*o*-$MeOC_6H_5$	75
2f	*p*-$MeOC_6H_5$	80
2g	*p*-PhC_6H_5	80

SCHEME 1

N-(Phenylacetyl)benzotriazole **1a**. ^1H NMR ($CDCl_3$): δ 8.27–8.28 (m, 1H), 8.10–8.13 (m, 1H), 7.61–7.66 (m, 1 H), 7.46–7.52 (m, 3H), 7.30–7.40 (m, 3H), 4.73 (s, 2H); ^{13}C NMR ($CDCl_3$): δ 170.2, 146.3, 132.5, 131.2, 130.5, 129.8, 128.8, 127.6, 126.2, 120.2, 114.6, 42.0.

N,N-(Diphenylacetyl)benzotriazole **1b**. ^1H NMR ($CDCl_3$): δ 8.31–8.37 (m, 1H), 8.06–8.15 (m, 1H), 7.62–7.70 (m, 1H), 7.44–7.54 (m, 4H), 7.23–7.39 (m, 7H), 6.82 (s, 2H); ^{13}C NMR ($CDCl_3$): δ 171.2, 146.4, 137.5, 131.3, 130.5, 129.0, 128.8, 127.7, 126.3, 120.2, 114.6, 55.8.

N-[(m-Methylphenyl)acetyl]benzotriazole **1c**. ^1H NMR ($CDCl_3$): δ 8.25–8.30 (m, 1H), 8.11–8.16 (m, 1H), 7.62–7.69 (m, 1H), 7.49–7.53 (m, 1H), 7.27–7.31 (m, 3H), 7.10–7.16 (m, 1H), 4.70 (s, 2H), 2.37 (s, 3H); ^{13}C NMR ($CDCl_3$): δ 170.4, 146.3, 138.5, 132.4, 131.3, 130.5, 130.4, 128.7, 128.4, 126.8, 126.2, 120.2, 114.5, 41.9, 21.3.

N-[(o-Nitrophenyl)acetyl]benzotriazole **1d**. ^1H

NMR ($CDCl_3$): δ 8.10–8.30 (m, 3H), 7.48–7.75 (m, 5H), 5.19 (s, 2H); ^{13}C NMR ($CDCl_3$): δ 168.7, 146.2, 134.0, 133.8, 131.1, 130.6, 129.9, 128.5, 126.3, 125.6, 120.2, 114.3, 41.4.

N-[(p-Methoxyphenyl)acetyl]benzotriazole **1e**. ^1H NMR ($CDCl_3$): δ 8.22–8.30 (m, 1H), 8.10–8.16 (m, 1H), 7.61–7.69 (m, 1H), 7.48–7.56 (m, 1H), 6.90 (d, 2H, J = 7.5 Hz), 7.39 (d, 2H, J = 7.5 Hz), 4.68 (s, 2H), 3.80 (s, 3H); ^{13}C NMR ($CDCl_3$): δ 170.6, 159.2, 145.3, 131.3, 130.9, 130.4, 126.9, 124.5, 120.7, 114.5, 55.3, 41.2.

N-[(o-Methoxyphenyl)acetyl]benzotriazole **1f**. ^1H NMR ($CDCl_3$): δ 8.28–8.32 (m, 1H), 8.12–8.18 (m, 1H), 7.62–7.68 (m, 1H), 7.50–7.55 (m, 1H), 7.31–7.39 (m, 2H), 6.92–7.04 (m, 2H), 4.77 (s, 2H), 3.79 (s, 3H); ^{13}C NMR ($CDCl_3$): δ 170.3, 157.7, 146.2, 131.4, 131.3, 130.3, 129.2, 126.0, 121.9, 120.7, 120.1, 114.5, 110.7, 55.5, 37.1.

N-[(p-Phenylphenyl)acetyl]benzotriazole **1g**. ^1H NMR ($CDCl_3$): δ 8.28–8.31 (m, 1H), 8.13–8.16 (m, 1H), 7.33–7.69 (m, 11H), 4.79 (s, 2H); ^{13}C NMR ($CDCl_3$): δ 170.2, 146.4, 140.6, 140.7, 131.5, 131.3, 130.5, 130.2, 128.8, 127.6, 127.4, 127.1, 126.3, 120.2, 114.5, 41.7.

N-(Phenylbutoyl)benzotriazole **1h**. ^1H NMR ($CDCl_3$): δ 8.28–8.32 (m, 1H), 8.06–8.12 (m, 1H), 7.59–7.66 (m, 1H), 7.44–7.52 (m, 3H), 7.20–7.38 (m, 3H), 5.20 (t, 1H, J = 7.5 Hz), 2.32–2.44 (m, 1H), 2.04–2.16 (m, 1H), 1.00 (t, 3H, J = 7.5 Hz); ^{13}C NMR ($CDCl_3$): δ 173.1, 146.0, 137.8, 130.3, 128.8, 128.6, 127.6, 126.1, 120.1, 114.6, 111.2, 52.4, 26.7, 12.1.

General Procedure for Synthesis of Symmetrical Ketones 2

To a solution of sodium hydride (excess, 200 mg) in THF (100 mL), *N*-(arylacetyl)benzotriazole (6 mmol) in THF (20 mL) was added slowly at room temperature. The formed mixture was stirred for 2 hours. The reaction was then quenched with water and extracted with ethyl acetate (2 × 100 mL). The combined organic layer was dried over sodium sulfate. After solvent removal on an evaporator, the residue was purified on a column, and the symmetrical ketone was obtained.

1,3-Diphenylacetone **2a** Mp 34°C (mp 34.8°C, Ref. [13]); ^1H NMR ($CDCl_3$): δ 7.11–7.32 (m, 10H), 3.69 (s, 4H); ^{13}C NMR ($CDCl_3$): δ 205.4, 133.9, 129.4, 128.6, 126.9, 48.9.

1,3-Di(3-Methylphenyl)acetone **2c**. Oil (bp 204°C/16 mmHg, Ref [14]); ^1H NMR ($CDCl_3$): δ 6.95–7.24 (m, 8H), 3.67 (s, 4H), 2.28 (s, 6H); ^{13}C NMR ($CDCl_3$): δ 205.9, 138.2, 133.9, 130.2, 128.5, 127.7, 126.5, 49.0, 29.7.

1,3-Di(4-Methoxyphenyl)acetone **2e**. Mp 85–86°C (mp 84–86°C, Ref. [15]); ^1H NMR ($CDCl_3$): δ 7.06, 6.86 (AB, 8H, J = 8.5 Hz), 3.79 (s, 6H), 3.65 (s, 4H); ^{13}C NMR ($CDCl_3$): δ 206.4, 158.7, 130.5, 126.1, 114.1, 55.2, 48.0.

1,3-Di(2-Methoxyphenyl)acetone **2f**. Oil [16]; ^1H NMR ($CDCl_3$): δ 7.23–7.25 (m, 2H), 7.07–7.10 (m, 2H), 6.84–6.92 (m, 4H), 3.77 (s, 6H), 3.71 (s, 4H); ^{13}C NMR ($CDCl_3$): δ 206.3, 157.4, 131.2, 128.3, 123.8, 120.5, 110.4, 55.3, 43.8.

1,3-Di(4-Phenylphenyl)acetone **2g**. Mp 161–163°C (mp 162°C, Ref. [17]); ^1H NMR ($CDCl_3$): δ 7.22–7.59 (m, 18H), 3.79 (s, 4H); ^{13}C NMR ($CDCl_3$): δ 205.5, 140.7, 140.1, 133.0, 129.9, 128.8, 127.6, 127.4, 127.2, 127.0, 48.8.

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