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Novel Synthesis of α-Benzotriazolyl-substituted Ketones†

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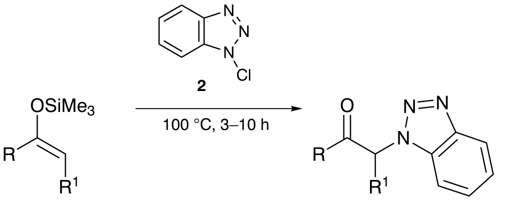
Silyl enol ethers react with 1-chlorobenzotriazole to provide a new general method for the preparation of α-benzotriazolyl-substituted ketones.

α-Benzotriazolyl-substituted ketones are versatile intermediates in the synthesis of a variety of organic compounds, including substituted acetylenes,[1] 3,5-diarylphenols[2] and alkyl aryl ketones;[3] these ketones were also used to prepare 2-arylquinoxalines, 1,4,5,6-tetrahydropyridazines,[4] 5-(amino-substituted)pyrid-2-ones and indolopyrid-2-ones.[5] α-Benzotriazolyl-substituted ketones possess enhanced reactivity based on the increased acidity of the bridge proton(s) which is(are) activated by the neighbouring benzotriazole moiety and carbonyl group. Some of their reactions (*e.g.* of their hydrazones with metalloorganic compounds, *etc.*[6]) can not be performed using their structural analogues, α-halo ketones, because of the high lability of the C–Hal bond.

Ketones bearing a benzotriazole moiety in an α-position were previously prepared by (i) reactions of α-halo ketones with benzotriazole or its sodium salt in refluxing aprotic solvents,[4–7] (ii) acylation of *N*-(trimethylsilylmethyl)benzotriazole with acid chlorides[3] and (iii) reactions of α-lithiated-1-methylbenzotriazoles with aromatic or aliphatic esters.[1] These methods were mostly applied to the preparation of aryl benzotriazolylmethyl ketones.

We now report that reactions of 1-chloromethylbenzotriazole with ketone silyl enol ethers represent a general method for the preparation of aliphatic, alicyclic and aromatic ketones substituted at the α-carbon atom by a benzotriazole moiety.



1 3

1,3	R	R^1	1,3	R	R^1
a	Ph	H	**g**	2-pyridyl	H
b	C_6H_4Me-4	H	**h**	Bu^t	H
c	C_6H_4OMe-4	H	**i**	Pr^n	H
d	C_6H_4Br-4	H	**j**	1-adamantyl	H
e	Ph	Me	**k**	2-($CH_2C_6H_4$)	
f	Ph	Ph	**l**	2-($CH_2CH_2C_6H_4$)	

Scheme 1

Table 1 Preparation of α-benzotriazole-substituted ketones **3a–l**

Ketone **3**	Reaction time (*t*/h)	Yield (%)	mp, (τ/°C) (lit. mp, (τ/°C)	Molecular formula	Found (calcd.) (%) C	H	N
a	3	59	111–113 (112–113[6])	$C_{14}H_{16}N_3O$			
b	3	54	129–131 (130–131[1])	$C_{15}H_{13}N_3O$			
c	4	56	141–143	$C_{15}H_{13}N_3O_2$	(67.39)	(4.91)	15.64 (15.73)
d	4	58	157–159	$C_{14}H_{10}BrN_3O$	53.27 (53.33)	3.11 (3.20)	13.24 (13.34)
e	4	62	97–99	$C_{15}H_{13}N_3O$	(71.68)	(5.22)	16.61 (16.73)
f	5	65	158–159 (161–163[7])	$C_{20}H_{15}N_3O$			
g	8	51	138–139	$C_{13}H_{10}N_4O$	(65.54)	(4.23)	23.28 (23.52)
h	6	38	101–103	$C_{12}H_{15}N_3O$	66.12 (66.34)	6.73 (6.96)	19.05 (19.34)
i	5	42	100–102	$C_{11}H_{13}N_3O$	(64.99)	(6.45)	20.34 (20.68)
j	6	52	157–159	$C_{18}H_{21}N_3O$	(73.19)	(7.17)	14.16 (14.23)
k	6	56	126–128	$C_{15}H_{11}N_3O$	71.86 (72.26)	4.42 (4.45)	16.75 (16.87)
l	10	54	142–144	$C_{16}H_{13}N_3O$	[a]		

[a]Found: *m/z*, 263.1058. $C_{16}H_{13}N_3O$ requires M_r 263.1058.

The silyl enol ethers used were prepared by known reactions of the corresponding ketones with trimethylsilyl chloride in the presence of lithium diisopropylamide (LDA)

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(**1a**–**e**)[8] or LDA–NaI for (**1f**–**j**).[9] Indanone (**1k**) and tetralone (**1l**) silyl enol ethers were synthesized in a DMF–triethylamine mixture.[10] All ethers were purified by distillation except **1h** which was used without purification.

Heating neat mixtures of a ketone silyl enol ether **1a**–**l** and 1-chlorobenzotriazole (**2**) at 100 °C (Scheme 1) gave the corresponding α-benzotriazolyl-substituted ketones **3a**–**l**. These compounds were isolated by column chromatography in moderate yields (38–65%) and characterized by NMR (^{1}H, ^{13}C) and elemental analysis or HRMS (Table 1). Our new methodology enables the preparation of ketones of types **3 g**,**k**,**l**, which previously known methods [see above, (i)–(iii)] do not allow.

Experimental

General Procedure for the Preparation of α-Benzotriazolyl-substituted Ketones **3a**–**l**.—A mixture of the corresponding silyl enol ether **1a**–**l** (2 mmol) and 1-chlorobenzotriazole **2** (0.36 g, 2.4 mmol) was stirred at 100 °C for the time specified in Table 1. Chloroform (60 ml) was added, and the mixture was washed with NaOH solution (5%, 3 × 30 ml). The organic layer was separated and dried over $MgSO_4$. The solvent was removed *in vacuo*, and the remaining oil was subjected to column chromatography (silica gel; eluent, $CHCl_3$) to give the pure product **3a**–**l**.

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