DEBENZOTRIAZOLYLATION OF α-BENZOTRIAZOLYL KETONES WITH SAMARIUM DIIODIDE

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Abstract- Removal of the benzotriazolyl moiety of α-benzotriazolyl ketones by samarium diiodide at room temperature to give the corresponding ketones in good yields is described.

INTRODUCTION

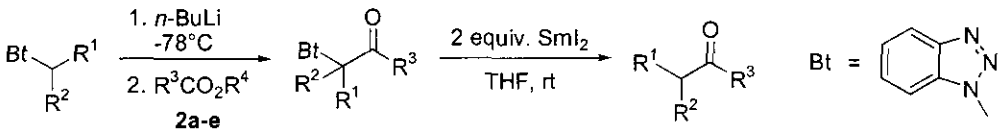
The benzotriazolyl group is a useful synthetic auxillary for organic synthesis whose chemistry has been extensively studied and recently reviewed.[1] In particular, α-benzotriazolyl ketones are readily available compounds that can be prepared in a number of ways: (i) from the corresponding α-bromo ketones and sodium benzotriazolate;[2a,b] (ii) from α-chloro ketones and benzotriazole;[3a,b] (iii) by the reaction between lithiated 1-methylbenzotriazole[4] or 1-(arylmethyl)benzotriazoles[5] and esters; (iv) treating lithiated 1-trimethylsilylmethylbenzotriazole[6] or (benzotriazol-1-yl)methanes[7] with acid chlorides.

The utility of α-benzotriazolyl ketones has already been demonstrated by our group for the preparation of a wide variety of organic compounds including α-alkyl- and α-aryl-substituted ketones,[2a] α-nonsubstituted ketones,[6] 2-phenylquinoxaline and 1,3,6-triphenyl-6-phenylazo-1,4,5,6-tetrahydro-pyridazine derivatives,[8] pyrid-2-ones and indolopyridones,[3b] alkynes,[5] and 3,5-diaryl substituted phenols.[2b]

We have now found that the reaction of α-benzotriazolyl ketones with two equivalents of samarium diiodide at room temperature results in the removal of the benzotriazolyl moiety to give the corresponding ketones in good yields. This procedure constitutes an alternative method for the preparation of some types of ketones.

RESULTS AND DISCUSSION

Lithiation of *N*-substituted benzotriazolyl derivatives (**1a-j**) followed by reaction with esters (**2a-e**) gave α-benzotriazolyl ketones (**3a-l**) which could be isolated in high yields. A similar procedure has previously been used to prepare 2-ethoxy-2-cyclopentenones[9] and alkynes.[5] The α-benzotriazolyl ketones (**3a-l**) were generally used without isolation in the debenzotriazolylation reaction with samarium diiodide to give ketones (**4a-l**) in good yields (Scheme 1, Table 1).



1a-i **3a-l** **4a-l**

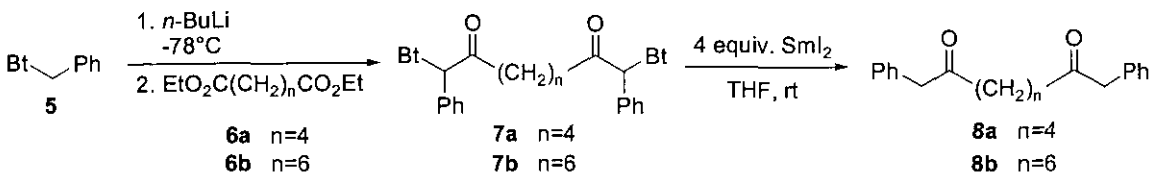
1	R^1	R^2
a	Ph	H
b	*PhCH=CH*	H
c	5-methylthien-2-yl	H
d	2,4-dimethoxyphenyl	H
e	*N*-methylindol-3-yl	H
f	pyrrol-1-yl	H
g	indol-1-yl	H
h	Ph	Et
i	Ph	Bu

2	R^3
a	Ph
b	*Tol*
c	C_7H_{15}
d	thien-2-yl
e	$(CH_2)_{15}Me$

3, 4	R^1	R^2	R^3
a	Ph	H	Ph
b	*Ph*	*H*	*Tol*
c	Ph	H	C_7H_{15}
d	PhCH=CH	H	Ph
e	5-methylthien-2-yl	H	thien-2-yl
f	2,4-dimethoxyphenyl	H	Tol
g	*N*-methylindol-3-yl	H	Tol
h	pyrrol-1-yl	H	Ph
i	indol-1-yl	H	Tol
j	pyrrol-1-yl	H	$(CH_2)_{15}Me$
k	Ph	Et	Ph
l	Ph	Bu	Ph

Scheme 1

Use of diesters (**6a-b**) and two equivalents of lithiated benzylbenzotriazole (**5**) similarly lead to bis-α-benzotriazolyl ketones (**7a-b**) which successfully underwent bis-debenzotriazolylation with samarium diiodide to give diketones (**8a-b**) (Scheme 2, Table 1).



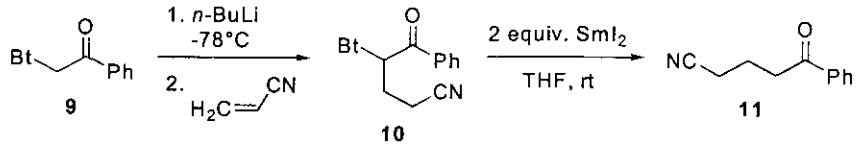
Scheme 2

Table 1. Ketones (**4a-l**, **8a-b**, **11**) Prepared *via* Samarium Diiodide Debenzotriazolylation of α-Benzotriazolyl Ketones and bis- α-Benzotriazolyl Ketones.

Compound	Molecular Formula	Elemental Analysis Found (Calculated) C	H	N	mp, °C (lit. mp, °C)	Yield %[a]
4a	$C_{14}H_{12}O$				53-54 (58)[10]	85
4b	$C_{15}H_{14}O$				106-107 (108-110)[11]	80
4c	$C_{15}H_{22}O$				oil[12]	82
4d	$C_{16}H_{14}O$				84-86 (91.5-92)[13]	83
4e	$C_{11}H_{10}OS_2$	59.81 (59.43)	4.47 (4.53)		55-56	70
4f	$C_{17}H_{18}O_3$	75.88 (75.53)	6.98 (6.71)		65-66	78
4g	$C_{18}H_{17}NO$	82.07 (82.10)	6.62 (6.51)	5.43 (5.32)	108-109	55
4h	$C_{12}H_{11}NO$				120-122 (120-125)[14]	61
4i	$C_{17}H_{15}NO$	81.76 (81.90)	6.37 (6.17)	5.70 (5.62)	147-148	64
4j	$C_{22}H_{39}NO$	79.33 (79.22)	11.80 (11.78)	4.20 (4.20)	67-69	72
4k	$C_{16}H_{16}O$				52-53 (52)[15]	81
4l	$C_{18}H_{20}O$				71-72 (73-74)[16]	82
8a	$C_{20}H_{22}O_2$				67-68 (64-67)[17]	70
8b	$C_{22}H_{26}O_2$	81.99 (81.95)	7.97 (8.13)		56-57	73
11	$C_{11}H_{11}NO$				oil[18]	76

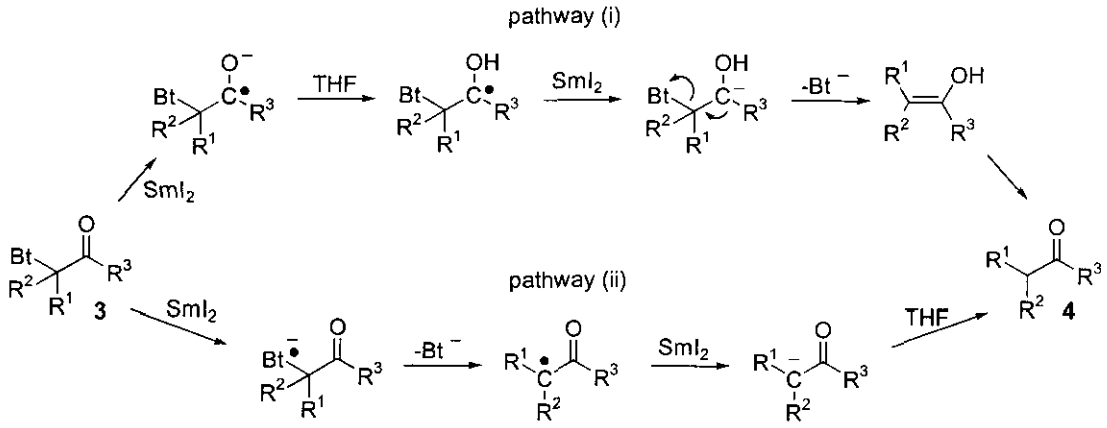
[a] Isolated yield based on α-benzotriazolyl ketone (**3**, **7**, **10**).

By a procedure similar to one reported earlier by our group,[3b] lithiation of benzotriazole derivative (**9**) and treatment with acrylonitrile lead to α-benzotriazolyl ketone (**10**) which was treated directly with samarium diiodide to give ketone (**11**) in good yield (Scheme 3, Table 1).



Scheme 3

Two possible mechanisms for the samarium diiodide induced debenzotriazolylation reaction are shown in Scheme 5. They are based on mechanisms proposed by Molander and Hahn for the reduction of α-heterosubstituted ketones.[19]

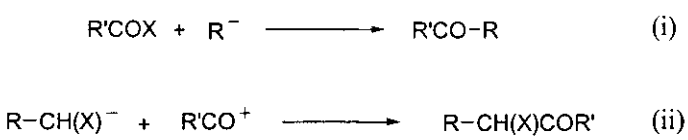


Scheme 4

Pathway (i) involves a single electron transfer (SET) from samarium diiodide to the ketone to generate a ketyl which abstracts a proton from the solvent. Further reduction by the second equivalent of samarium diiodide gives a carbanion, causing β-elimination. The enol tautomerises to give the observed ketone. Alternatively, pathway (ii) involves SET directly to the benzotriazolyl moiety and cleavage of the C-N bond. Reduction of the resultant carbon radical and abstraction of a proton from the solvent, either directly or *via* the enol, gives the desired ketone.

The most usual method for the preparation of ketones is treatment of carboxylic acid derivatives with organometallic reagents in a family of reactions all of the general type depicted in Scheme 5 (i).[20] Our method is of the type depicted in Scheme 5 (ii). Addition is aided by an activating group (X) which can

then be removed easily. In our case the activating group is benzotriazole. Previously sulfones,[21a] sulfoxides,[21a,b] and phosphonates[22a,b] have been used as the temporary activating group.



Scheme 5

The method of Corey and Chaykovsky[21a,b] using sulfoxides has been limited to the preparation of methyl ketones. The use of phosphonates[22a,b] as the temporary activating group requires the use of lithium aluminum hydride for removal. Our method therefore offers an alternative way to prepare some types of ketones.

CONCLUSION

The benzotriazolyl moiety was removed from α-benzotriazolyl ketones by treatment with samarium diiodide at room temperature to give the corresponding ketones in good yields.

EXPERIMENTAL

General. Melting points were determined on a hot stage apparatus and are uncorrected. NMR spectra were obtained in chloroform-*d* and chemical shift values are reported as δ downfield from tetramethylsilane as an internal standard for ^{1}H (300 MHz) and solvent for ^{13}C (75 MHz).
THF was distilled under nitrogen immediately prior to use from a solution containing sodium/benzophenone. Column chromatography was carried out on MCB silica gel (230-400 mesh). Other chemicals were used as obtained from commercial sources.

General Procedure for α-Benzotriazolyl Ketone Preparation. To a stirred solution of the *N*-substituted benzotriazole (**1a-j, 5, 9**) (1 mmol) in THF (22 mL) under nitrogen was added *n*-butyllithium (10 mmol) at -78°C followed by the corresponding ester (**2a-e**), diester (**6a-b**), or acrylonitrile (10 mmol) in THF (10 mL). The mixture was stirred for 12 h and allowed to warm to rt. The mixture was quenched with water, extracted with ethyl acetate and dried over anhydrous $MgSO_4$. Removal of the solvent *in vacuo* gave α-benzotriazolyl ketones (**4a-l, 8a-b, 11**) which were used directly in the debenzotriazolylation reaction.

General Procedure for Debenzotriazolylation with SmI_2. The α-benzotriazolyl ketones (**3a-l, 7a-b, 10**) (1 mmol) in THF (2 mL) were added by syringe to a solution of SmI_2 (2 mmol) in THF (22 mL), prepared from samarium (0.32 g, 2.1 mmol) and iodine (0.5 g, 2 mmol), under an atmosphere of argon. The mixture was stirred at rt until the dark blue solution turned yellow. Saturated NH_4Cl solution (10 mL) was added and the mixture was extracted with ether (2 x 20 mL). The combined organic extracts were washed with saturated $Na_2S_2O_3$ solution (20 mL), water (2 x 20 mL), and dried over anhydrous Na_2SO_4. The solvent was removed *in vacuo* and the residue purified by column chromotography (hexane/ethyl acetate 10:1) to give compounds (**4a-l, 8a-b, 11**).

1,2-Diphenylethanone[10] (**4a**): ^{1}H-NMR δ: 4.28 (s, 2H), 7.22-7.35 (m, 5H), 7.42-7.47 (t, J = 7.4 Hz, 2H), 7.53-7.57 (t, J = 7.3 Hz, 1H), 7.99 (d, J = 7.1 Hz, 2H); ^{13}C-NMR δ: 45.5, 126.9, 128.6 (2C), 129.4 (2C), 133.1, 134.5, 136.6, 197.6.

1-(4-Methylphenyl)-2-phenylethanone[11] (**4b**): ^{1}H-NMR δ: 2.40 (s, 3H), 4.26 (s, 2H), 7.22-7.34 (m, 7H), 7.92 (d, J = 8.2 Hz, 2H); ^{13}C-NMR δ: 21.6, 45.4, 111.2, 126.8, 128.6, 128.8, 129.3, 129.5, 134.8, 144.0, 197.3.

1-Phenylnonan-2-one[12] (**4c**): ^{1}H-NMR δ: 0.86 (t, J = 7.0 Hz, 3H), 1.22-1.27 (m, 8H), 1.52-1.56 (m, 2H), 2.43 (t, J = 7.3 Hz, 2H), 3.67 (s, 2H), 7.19-7.35 (m, 5H); ^{13}C-NMR δ: 14.0, 22.5, 23.7, 29.0 (2C), 31.6, 42.0, 50.1, 126.9, 128.6, 129.4, 134.4, 208.5.

(*E*)-1,4-Diphenyl-3-buten-1-one[13] (**4d**): ^{1}H-NMR δ: 3.91 (d, J = 5.8 Hz, 2H), 6.44-6.58 (m, 2H), 7.19-7.60 (m, 8H), 7.99 (d, J = 7.2 Hz, 2H); ^{13}C-NMR δ: 42.7, 122.6, 126.3, 127.5, 128.3, 128.5, 128.7, 128.9, 133.2, 133.6, 137.0, 198.2.

1-(2-Thienyl)-2-(5-methyl-2-thienyl)ethanone (**4e**): ^{1}H-NMR δ: 2.42 (s, 3H), 4.29 (s, 2H), 6.59 (d, J = 2.5 Hz, 1H), 6.72 (d, J = 3.2 Hz, 1H), 7.12 (t, J = 4.4 Hz, 1H), 7.64 (d, J = 4.7 Hz, 1H), 7.78 (d, J = 3.9 Hz, 1H); ^{13}C-NMR δ: 16.9, 42.1, 126.6, 128.3, 129.8, 134.3, 134.5, 135.8, 141.3, 144.8, 190.6.

2-(2,5-Dimethoxyphenyl)-1-(4-methylphenyl)ethanone (**4f**): ^{1}H-NMR δ: 2.40 (s, 3H), 3.76 (s, 3H), 3.79 (s, 3H), 4.17 (s, 2H), 6.43-6.47 (m, 2H), 7.06 (d, J = 7.9 Hz, 1H), 7.23 (d, J = 8.3 Hz, 2H), 7.93 (d, J = 8.0 Hz, 2H); ^{13}C-NMR δ: 21.6, 39.1, 55.3, 55.4, 98.7, 104.3, 116.2, 128.5, 129.1, 131.2, 134.5, 143.5, 158.1, 160.0, 197.9.

2-(1-Methylindol-3-yl)-1-(4-methylphenyl)ethanone (**4g**): ^{1}H-NMR δ: 2.39 (s, 3H), 3.73 (s, 3H), 4.36 (s, 2H), 6.98 (s, 1H), 7.10-7.30 (m, 5H), 7.61 (d, J = 7.9 Hz, 1H), 7.95 (d, J = 8.0 Hz, 2H); ^{13}C-NMR δ: 21.6, 32.7, 35.3, 107.5, 109.3, 118.5, 118.9, 119.1, 121.7, 127.8, 128.7, 129.2, 134.2, 136.9, 143.7, 193.1.

α-Pyrrol-1-ylacetophenone[14] (**4h**): ^{1}H-NMR δ: 5.30 (s, 2H), 6.25 (s, 2H), 6.66 (s, 2H), 7.50 (t, J = 7.4 Hz, 2H), 7.62 (t, J = 7.4 Hz, 2H), 7.95 (d, J = 7.4 Hz, 2H); ^{13}C-NMR δ: 55.4, 109.0, 121.9, 128.0, 128.9, 133.9, 135.5, 193.8.

2-Indol-1-yl-1-(4-methylphenyl)ethanone (**4i**): ^{1}H-NMR δ: 2.43 (s, 3H), 5.47 (s, 2H), 6.60 (d, J = 3.0 Hz, 1H), 7.10-7.32 (m, 6H), 7.65 (d, J = 7.6 Hz, 1H), 7.90 (d, J = 8.0 Hz, 2H); ^{13}C-NMR δ: 21.7, 52.2, 102.4, 109.0, 119.7, 121.2, 121.9, 128.1, 128.6, 129.6, 132.3, 136.7, 145.0, 151.8, 192.7.

1-Pyrrol-1-yloctadecan-2-one (**4j**): ^{1}H-NMR δ: 0.88 (t, J = 5.1 Hz, 3H), 1.24 (m, 26H), 1.54 (br s, 2H), 2.31 (t, J = 7.4 Hz, 2H), 4.60 (s, 2H), 6.22 (s, 2H), 6.60 (s, 2H); ^{13}C-NMR δ: 14.0, 22.6, 23.3, 29.0, 29.2, 29.3, 29.4, 29.5 (2C), 29.6 (2C), 31.9, 38.8, 58.5, 109.2, 121.6, 206.0.

1,2-Diphenylbutan-1-one[15] (**4k**): ^{1}H-NMR δ: 0.90 (t, J = 7.3 Hz, 3H), 1.80-1.91 (m, 1H), 2.11-2.25 (m, 1H), 4.44 (t, J = 7.2 Hz, 1H), 7.14-7.45 (m, 8H), 7.96 (d, J = 8.2 Hz, 2H); ^{13}C-NMR δ: 12.2, 27.1, 55.4, 126.9, 128.2, 128.4, 128.5, 128.7, 132.7, 137.0, 139.6, 200.0.

1,2-Diphenylhexan-1-one[16] (**4l**): ^{1}H-NMR δ: 0.86 (t, J = 7.7 Hz, 3H), 1.17-1.38 (m, 4H), 1.79-1.86 (m, 1H), 2.13-2.22 (m, 1H), 4.54 (t, J = 7.4 Hz, 1H),7.16-7.49 (m, 8H), 7.96 (d, J = 6.1 Hz, 2H); ^{13}C-NMR δ: 13.9, 22.7, 29.9, 33.8, 53.6, 126.9, 128.2, 128.5, 128.6, 128.8, 132.7, 137.0, 139.8, 200.1.

1,8-Diphenyloctan-2,9-dione[17] (**8a**): ^{1}H-NMR δ: 1.47 (br s, 4H), 2.40 (br s, 4H), 3.64 (s, 4H), 7.16-7.31 (m, 10H); ^{13}C-NMR δ: 22.9, 41.5, 50.1, 126.9, 128.7, 129.3, 134.2, 207.9.

1,10-Diphenyldecan-2,9-dione (**8b**): ^{1}H-NMR δ: 1.17 (m, 4H), 1.49 (m, 4H), 2.40 (t, J = 7.2 Hz, 4H), 3.66 (s, 4H), 7.18-7.34 (m, 10H); ^{13}C-NMR δ: 23.4, 28.7, 41.8, 50.1, 126.9, 128.7, 129.3, 134.3, 208.4.

4-Cyano-1-phenylbutan-1-one[18] (**11**): ^{1}H-NMR δ: 2.07-2.16 (quintet, J = 6.9 Hz, 2H), 2.52 (t, J = 7.0 Hz, 2H), 3.18 (t, J = 6.7 Hz, 2H), 7.45-7.61 (m, 3H), 7.96 (d, J = 8.2 Hz, 2H); ^{13}C-NMR δ: 16.6, 19.7, 36.3, 119.3, 127.9, 128.7, 133.4, 136.4, 198.1.

REFERENCES

1. A. R. Katritzky, X. Lan, J. Z. Yang, O. V. Denisko, *Chem. Rev.*, 1998, **98**, 409
2. (a) A. R. Katritzky, L. Wrobel, G. P. Savage, and M. Deyrup-Drewniak, *Aust. J. Chem.*, 1990, **43**, 133; (b) A. R. Katritzky, S. A. Belyakov, S. A. Henderson, and P. J. Steel, *J. Org. Chem.*, 1997, **62**, 8215.
3. (a) A. R. Katritzky, and J. Wu, *Synthesis,* 1994, 597; (b) A. R. Katritzky, and I. V. Shcherbakova, *J. Heterocycl. Chem.*, 1996, **33**, 2031.
4. A. R. Katritzky, J. Wu, W. Kuzmierkiewicz, and S. Rachwal, *Liebigs Ann. Chem.*, 1994, 1.
5. A. R. Katritzky, J. Wang, N. Karodia, and J. Li, *J. Org. Chem.*, 1997, **62**, 4142.
6. A. R. Katritzky, and J. N. Lam, *Heteroatom Chem.*, 1990, **1**, 21.
7. A. R. Katritzky, H. Wu, and L. Xie, *Tetrahedron Lett.*, 1997, **38**, 903.
8. A. R. Katritzky, J. Wu, L. Wrobel, S. Rachwal, and P. J. Steel, *Acta Chem. Scand.*, 1993, **47**, 167.
9. A. R. Katritzky, G. Zhang, and J. Jiang, *J. Org. Chem.*, 1995, **60**, 7605.
10. A. Dehnel, J. P. Finet, and G. Lavielle, *Synthesis,* 1977, 474.
11. M. S. Newman, and R. Gaertner, *J. Am. Chem. Soc.*, 1950, **72**, 264.
12. J. E. Baldwin, R. M. Adlington, J. C. Bottaro, J. N. Kolhe, M. W. D. Perry, and A. U. Jain, *Tetrahedron,* 1986, **42**, 4223.
13. S.-I. Inaba, and R. D. Rieke, *J. Org. Chem.*, 1985, **50**, 1373.
14. M. Artico, F. Corelli, S. Massa, and G. Stefancich, *Synthesis,* 1983, 931.
15. H. Fiesselmann, and J. Ribka, *Chem. Ber.*, 1956, **89**, 27.
16. G. D. Reddy, and V. Ramamurthy, *J. Org. Chem.*, 1987, **52**, 5521.
17. A. M. van Leusen, R. Oosterwijk, E. van Echten, and D. van Leusen, *Recl. Trav. Chim. Pays-Bas,* 1985, **104**, 50.
18. R. D. Rieke, R. M. Wehmeyer, T.-C. Wu, and G. W. Ebert, *Tetrahedron,* 1989, **45**, 443.
19. G. A. Molander, G. Hahn, *J. Org. Chem.* 1986, **51**, 1135
20. E. Muller, 'Methoden der Organischen Chemie (Houben-Weyl),' Vol. 7/2a, Geory Thieme, Stuttgart, 1973, p. 548.
21. (a) E. J. Corey, and M. Chaykovsky, *J. Am. Chem. Soc.*, 1964, **86**, 1639; (b) E. J. Corey, and M. Chaykovsky, *J. Am. Chem. Soc.*, 1965, **87**, 1345.
22. (a) J. E. Hong, W. S. Shin, W. B. Jang, and D. Y. Oh, *J. Org. Chem.*, 1996, **61**, 2199; (b) S. Y. Lee, J. E. Hong, W. B. Jang, and D. Y. Oh, *Tetrahedron Lett.*, 1997, **38**, 4567.

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