Facile Cleavage of *N*-Arylsulfonyl Bond of *N*-Arylsulfonyl-imidazolidinone with Magnesium in Methanol

Upender K Nadir* and R. Vijaya Krishna

Department of chemistry, Indian Institute of Technology Delhi, Hauz Khas,
New Delhi-110016, India. E-mail: ukn@chemistry.iitd.ac.in, FAX: +91-11-26581102

Received March 2, 2004

Cleavage of *N*-arylsulfonyl bond in *N*-arylsulfonylimidazolidinones is best carried out selectively with magnesium in methanol.

J. Heterocyclic Chem., **41**, 737 (2004).

Introduction.

Sulfonyl groups are often used as protecting groups for nitrogen heteroaromatics like pyrroles, indoles, pyrazoles, imidazoles, *etc*., they are also frequently employed to activate aziridines for reaction with nucleophiles [1]. In all these cases, the *N*-sulfonyl group needs to be cleaved subsequently. However it is not always easy to remove the *N*-sulfonyl group. Even though a wide variety of synthetic methods for the cleavage of the N-S bond are available [2], the selection of the proper reagent depends on the nature of other groups present in the product and their susceptibility to the conditions chosen. In general harsh reaction conditions [3] and long reaction times need to be avoided.

In this paper, we present our efforts to find a general yet mild method for the selective desulfonylation of imidazolidinones that leaves the five-membered ring intact. Recently, excellent results in the reduction of alkyl sulfones have been achieved by using magnesium in methanol as the cleaving agent [4]. However this method has not been widely used, and only a few examples have been briefly reported [5]. In any case no example pertaining to imidazolidinones are known.

We have reported a regio- [6] and stereo-selective [7] synthesis of imidazolidinones based on the reaction of *N*-arylsulfonylaziridines with isocyanates catalyzed by sodium and lithium iodides. In order to utilize these imidazolidinones to prepare enantiomerically pure diamines and diamino-acids we required a mild method for cleavage of the *N*-arylsulfonyl bond without affecting an ester or benzyl group. Here we report development of a facile method to do this.

Results and Discussion.

Deprotection of imidazolidinones **1a-c** could be achieved using magnesium turnings (8 equiv.) in methanol at the reflux temperatures for 8 hours. The desired imidazolidinone **2a** was obtained in 78-81% yields. Under these conditions, the benzyl and methoxycarbonyl groups were unaffected as shown by conversion of **1d** to **2b** and **1e** to **2c** (Scheme 1 and Table 1).

Other reductive methods were less effective (Table 2). Thus with sodium naphthalenide [8] **1a** gave, besides the product **2a**, the ring opened product **3a** (17 %). Sodium in liquid NH_3 [9] yielded similar results. With tetrabutylammonium fluoride [10] (TBAF), **1a** was converted to **2a** in diminished yield (30%). All these methods gave a complex mixture with the ester imidazolidinone **1e**, from which no pure product could be isolated. With SmI_2 [11] no reaction occurred and the starting imidazolidinone could be recovered unchanged.

Table 1

Desulfonylation of *N*-Arylsulfonyl Imidazolidinones with Magnesium/Methanol

Entry	R_1	R_2	R_3	Mg (eq)	Time (h)	Temp	Yield [a] (%)
1	CH_3	Ph	H	8	24	rt	42(50)
2	CH_3	Ph	H	4	8	reflux	30(60)
3	CH_3	Ph	H	8	8	reflux	78
4	H	Ph	H	8	8	reflux	80
5	Cl	Ph	H	8	8	reflux	78
6	CH_3	CH_2Ph	H	8	8	reflux	81
7	CH_3	Ph	COOMe	8	6	reflux	65

Values in parentheses are recovery yield of starting compound; [a] isolated through column chromatography (silica gel, benzene/ethylacetate).

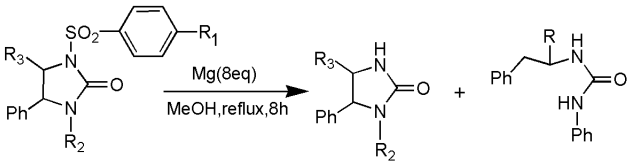
Table 2

Desulfonylation of N-Arylsulfonyl Imidazolidinones with Various Reducing Agents like Sodium Naphthalenide, Na/liquid NH_3, TBAF, and SmI_2

Entry	Reactant (3) R	Conditions	Product Yield [a] (4)	(5)
1	H	A	57	17
2	COOMe	A	[b]	
3	H	B	53	26
4	COOMe	B	[b]	
5	H	C	30	
6	COOMe	C	[b]	
7	H	D	No reaction [c]	

[a] Isolated through column chromatography(silica gel, benzene/EtOAc); [b] non analyzed complex mixture of compounds; [c] starting material was recovered. Conditions A: Na metal (5 mmole), Naphthalene (5.5 mmole), DME (5 ml), imidazolidinone (0.25 mmole) in DME (1 ml), -78 °C, 5 min; Conditions B: Na metal (10 eq), liq. NH_3, -78 °C, 45 min. Conditions C: TBAF (1eq), THF, reflux, 1.5 h. Conditions D: SmI_2 (2.5 eq), THF, rt.

Scheme 1



1a-e **2a-c** **3a**

a) R_1=CH_3, R_2=Ph, R_3=H
b) R_1=H, R_2=Ph, R_3=H
c) R_1=Cl, R_2=Ph, R_3=H
d) R_1=CH_3, R_2=CH_2Ph, R_3=H
e) R_1=CH_3, R_2=Ph, R_3=COOMe

a) R_2=Ph, R_3=H
b) R_2=CH_2Ph, R_3=H
c) R_2=Ph, R_3=COOMe

a) R=H

Conclusions.

It has been found that among the various reduction methods viz. sodium naphthalenide, sodium in liquid NH_3, TBAF, $SmI_2$and magnesium in methanol, the last one is the most convenient for cleavage of N-arylsulfonyl bond in N-arylsulfonyl imidazolidinones. Major advantages of the method are: 1) the cleavage is effected without affecting the benzyl or methoxycarbonyl group and 2) ring opening of the imidazolidinone moiety does not take place.

EXPERIMENTAL

Melting points were determined on micro melting-point apparatus and are uncorrected. TLC on aluminum backed silica plates $60F_{254}$,visualisation was accomplished with UV light. IR spectra were recorded on Nicolet 5DX FTIR instrument. Both ^1H and ^{13}C NMR ($CDCl_3$, internal standard TMS) spectra were recorded on DPX-300 Brucker instrument (300 MHz, ^1H). Chemical shifts (δ_H and δ_C) are quoted in parts per million (ppm). Low-resolution mass spectra (m/z) were recorded using a Hewlett Packard Model-5989 spectrometer with only molecular ions (M^+), and major peaks being reported with intensities quoted as percentages of the base peak. Microanalyses were performed using Perkin Elmer 240 CHN elemental analyzer.

Typical Procedure.

A mixture of imidazolidinone **1a** (0.50 g, 1.27 mmole), magnesium (0.25 g, 10.2 mmole) and methanol (30 ml) was refluxed for 8 hours. After the reaction was over, the reaction mixture was cooled and an equal volume of ethyl acetate was added. The whole was then filtered through a silica gel pad and the filtrate concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, 2:1 Benzene/ethyl acetate) to give the desired product(s). All new starting and product compounds showed satisfactory ^1H, ^{13}C NMR, IR, LRMS and elemental analysis.

1,5-Diphenylimidazolidin-2-one (**2a**).

This compound has mp 218-220 °C; ^1H NMR (300 MHz, $CDCl_3$): δ_H 3.34 (t, 1H, J=7.3 Hz, -CH_2-), 3.96 (t, 1H, J=8.8 Hz, -CH_2-), 4.9 (s, 1H, -NH-), 5.32 (dd, 1H, J=6.1, 8.8 Hz, -CHPh-), 6.96-7.39 (m, 10H, Ar); ^{13}C NMR: δ_C 46.2, 59.1, 119.5, 121.9, 125.6, 127.1, 127.6, 128.2, 138.9, 140.6, 159; ν_{max} (KBr)/cm^{-1} 1689 (C=O), 3259 (N-H); m/z 238(M^+, 100%), 181(44), 161(31), 104(28), 91(39).

Anal. Calcd. for $C_{15}H_{14}N_2O$; C, 75.69; H, 5.92; N, 11.77. Found: C, 75.64; H, 5.71; N, 11.68.

1-Benzyl-5-phenylimidazolidin-2-one (**2b**).

This compound has mp 132-134 °C; ^1H NMR (300MHz,$CDCl_3$): δ_H 3.28 (t, 1H, J=8.4 Hz, -CH_2-), 3.55 (d, 1H, J=14.89 Hz, -CH_2Ph) 3.7 (t, 1H, J=8.8 Hz, -CH_2-), 4.44 (t, 1H, J=8.37 Hz, -CHPh-), 4.8 (s, 1H, -NH-), 4.91 (d, 1H, J=14.9 Hz, -CH_2Ph), 7.11-7.39 (m, 10H, Ar); ^{13}C NMR: δ_C 45.1, 51.15, 55.6, 123.6, 124.0, 125.8, 126.8, 127.3, 127.8, 128.4, 128.6, 129.2, 129.4, 134.8, 139.8, 158.3; ν_{max} (KBr)/cm^{-1} 1678 (C=O), 3225 (N-H); m/z 253(M+2, 100%), 146, 132, 91.

Anal. Calcd. for $C_{15}H_{14}N_2O$; C, 76.26; H, 6.40; N, 11.12. Found: C, 76.14; H, 6.23; N, 11.03.

Methyl 2-Oxo-1,5-diphenylimidazolidine-2-one (**2c**).

This compound has mp 193-195 °C; ^1H NMR (300MHz, $CDCl_3$): δ_H 3.25 (s, 3H, -OCH_3), 4.76 (d, 1H, J=9.55 Hz, -$CHCOOCH_3$), 5.2 (s, 1H, -NH-), 5.57 (d, 1H, J=9.54 Hz, -CHPh-), 6.96-7.46 (m, 10H, Ar); ^{13}C NMR: δ_C 53.1, 61.4, 62.3, 119.3, 121.5, 123.6, 124.2, 125.7, 126.3, 127.5, 128.1, 129.7, 130.3, 136.5, 137.7, 150.8, 169.1; ν_{max} (KBr)/cm^{-1} 1703 (C=O), 1754 (COOMe), 3218 (N-H); m/z 297(M+1, 100%), 237(36), 194(30), 181(10), 119(15), 91(29).

Anal. Calcd. for $C_{17}H_{17}N_2O$; C, 68.98; H, 5.78; N, 9.46. Found: C, 68.95; H, 5.63; N, 9.41.

N-Phenyl-*N*'-(2-phenylethyl)urea (**3a**)

This compound has mp 144-146 °C; ^1H NMR (300MHz, $CDCl_3$): δ_H 2.81 (t, 2H, J=6.8 Hz, -CH_2CH_2-), 3.49 (q, 2H, J=6.75, 12.8 Hz, -CH_2CH_2-), 4.9 (s, 1H, -NH-), 6.48 (s, 1H, -NH-), 7.0-7.4 (m, 10H, Ar); ^1H NMR (300 MHz, $CDCl_3$, D_2O): δ_H 2.8 (t, 2H, J=6.83 Hz, -CH_2CH_2-), 3.49(t, 2H, J=6.85 Hz, -CH_2CH_2-), 7.0-7.4(m, 10H, Ar); ^{13}C NMR: δ_C 34.4, 39.1, 116.1, 119.6, 124.3, 126.6, 126.8, 127.0, 137.8, 138.7, 153.8; ν_{max} (KBr)/cm^{-1} 1646 (NHCONH), 3305 (NH), 3346 (NH); m/z 241(M+1, 30%), 240(M^+, 29%), 149(10), 136(15), 120(8), 105(12), 91(20), 93(100%).

Anal. Calcd. for $C_{15}H_{16}N_2O$; C, 75.06; H, 6.72; N, 11.67.Found: C, 74.92, H, 6.46; N, 11.53.

Acknowledgement.

R. Vijaya Krishna thanks CSIR, New Delhi for the award of fellowship.

REFERENCES AND NOTES

[1a] D. Tanner, *Angew. Chem. Int. Ed. Engl.*, **33**, 599 (1994); [b] H. M. I. Osborn, J. Sweeney, *Tetrahedron: Asymmetry*. **8**, 1693 (1997).

[2a] T. W. Greene and P. G. M. Wuts, Protective Groups in Organic Chemistry, 2nd ed.; Wiley-Interscience: New York, 1991; [b] P. J. Kocienski, Protecting Groups; Thieme; New York, 1994; [c] S. Ji, L. B. Gortler, A. Waring, A. Battisti, S. Bank, and W. D. Closson, *J. Am. Chem. Soc.* **89**, 5311 (1967); [d] W. D. Closson, S. Ji, and S. Schulenberg, *J. Am. Chem. Soc.* **92**, 650 (1970); [e] J. Rudinger, and H. Zimmermannova, *Helv. Chim. Acta* **56**, 2216 (1973); [f] G. R. Pettitand R. E. Kadunce, *J. Org. Chem.* **50**, 4566 (1962); [g] E. H. Gold and E. Babad, *J. Org. Chem.* **37**, 2208 (1972); [h] H. Knowles, A. F. Parsons, and R. M. Pettifer,

Synlett 271 (1997); [i] J. E. T. Corrie and G. J. Papageorgiou, *J. Chem. Soc., Perkin Trans*. **1** 1583 (1996); [k] I. Fleming, J. Frackenpohl, and H. Ila, *J. Chem. Soc., Perkin Trans*. **1** 1229 (1998).

[3a] S. Vangvervong and D. E. Nichols, *J. Org. Chem*. **60**, 3409(1995); [b] D. E. Yokoyama, T. Masumoto, and Y. Murakami, *J. Org. Chem*. **60**, 1486 (1995); [c] K. Okabe and M. Natume, *Tetrahedron* **36**, 7615 (1991); [d] R. J Sundberg and J. P. Laurino, *J. Org. Chem*. **49**, 249 (1984); [e] H. J. Anderson, C. E. Loader, R. X. Xu, N. L. Le, N. J. Gogan, R. McDonald, and L. G. Edwards, *Can. J. Chem*., **63**, 896 (1985).

[4] G. H. Lee, E. B. Choi, E. Lee, and C. S. Pak, *Tetrahedron Lett*., **34**, 4541 (1993).

[5a] Pak, Chwang Siek, Lim, and Dong Sung, *Synth. Commun*., **31**(14), 2209 (2001) [b] Barthelemy Nyasse, Leif Grehn, and Ulf Ragnarsson, *Chem. Commun*., 1017 (1997).

[6] U. K. Nadir and N. Basu, *Tetrahedron Lett*., **33**, 7949 (1992).

[7] U. K. Nadir and N. Basu, *Tetrahedron*, **49**, 7787 (1993).

[8] S. C. Bergmeier and P. P. Seth, *Tetrahedron Lett*., **40**, 6181 (1999).

[9a] Y. Takeda, T. Matsumoto, and F. Sato, *J. Org. Chem*.**51**, 4731 (1986); [b] J. R. Hwu, Y. S. Wein, and Y. J. Leu, *J. Org. Chem*. **61**, 1493 (1996).

[10] A. Yasuhara and T. Sakamoto, *Tetrahedron Lett*., **39**, 595 (1998).

[11] E. Vedejs and S. Lin, J. *Org. Chem*., **59**, 1602 (1994).