

DEPROTECTION OF *N*-SULFONYL NITROGEN-HETEROAROMATICS WITH TETRABUTYLAMMONIUM FLUORIDE

Akito Yasuhara* and Takao Sakamoto*

Faculty of Pharmaceutical Sciences, Tohoku University
Aobaku, Sendai 980-77, Japan

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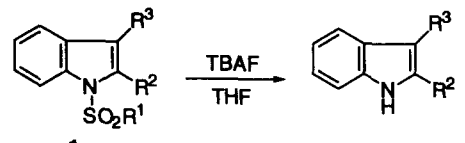
Abstract: The deprotection of *N*-methylsulfonyl, *N*-(*p*-toluenesulfonyl), and *N*-phenylsulfonyl nitrogen-heteroaromatic compounds proceeds easily in excellent yields by refluxing with tetrabutylammonium fluoride (TBAF) in THF. © 1998 Elsevier Science Ltd. All rights reserved.

Sulfonyl groups are often used as protecting groups of nitrogen containing - heteroaromatics having the so-called "indicated hydrogen", such as pyrrole, indole, pyrazole, *etc.*, because of the electron-withdrawing effect, the high stability, and the ease of formation. Although the deprotection of the sulfonyl groups have been achieved by hydrolysis with KOH (or NaOH) / MeOH¹ or by reduction,² the relatively drastic conditions (long time, strongly basic conditions) are required for these deprotective methods.

We now report a new mild and neutral deprotection method of *N*-methylsulfonyl, *N*-*p*-toluenesulfonyl, and *N*-phenylsulfonyl heteroaromatic compounds using TBAF in THF for a short time (0.5 - 3 hour).

The desulfonylation of **1a** proceeds using 1 eq. TBAF in refluxing THF.³ However, under the conditions using 0.5 eq. TBAF at reflux or 1.0 eq. TBAF at room temperature, **1a** was not completely desulfonylated.

Table 1 Desulfonylation of *N*-Sulfonylindole with TBAF



1

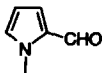
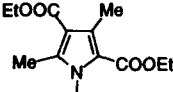
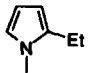
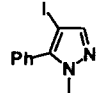
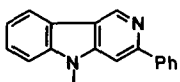
	R ¹	R ²	R ³	Time (h)	Temp	TBAF (eq.)	Yield (%)
a	Ph	Ph	H	6	reflux	0.5	38 (50)
a	Ph	Ph	H	24	rt	1	46 (45)
a	Ph	Ph	H	1.5	reflux	1	100
b	Me	H	CHO	1	reflux	1	100
c	Me	H	COMe	2	reflux	1	91
d	Me	Ph	COOMe	0.5	reflux	1	77
e	Me	Bu	H	5	reflux	1	89

Values in parentheses are recovery yield of **1**.

The desulfonylation of *N*-methylsulfonyl (**1b-d**, **2b**), *N*-*p*-toluenesulfonyl (**3**), and *N*-phenylsulfonyl nitrogen heteroaromatics (**1a**, **2a,c**, **4**) proceeds in good yields (64 - 100%)

without affecting formyl (**1b**, **2a**), acetyl (**1c**), and methoxycarbonyl (**1d**, **2b**) groups. The deprotecting reaction was found to be generally applicable to indoles (**1**), pyrroles (**2**), pyrazole (**3**), and carboline (**4**) in good yields.

Table II Desulfonylation of *N*-Sulfonyl Heteroaromatics

Ar-SO ₂ R		TBAF, THF reflux		Ar-H	
2, 3, 4					
	Ar	R	Time (h)	Yield (%)	
2a		Ph	6	90	
2b		Me	0.5	96	
2c		Ph	24	64	
3		<i>p</i> -MeC ₆ H ₄	0.5	100	
4		Ph	3	71	

References and note

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- A mixture of 2-phenyl-1-(phenylsulfonyl)indole (**1a**) (150 mg, 0.5 mmol), TBAF 1.0M solution in THF (0.5 ml, 0.5 mmol), and THF (20 ml) was refluxed for 1.5 hours. After cooling, the reaction mixture was evaporated *in vacuo*, and H₂O (20 ml) was added to the residue. The mixture was extracted with Et₂O (20 ml x 2), dried over MgSO₄ and evaporated *in vacuo*. The crude product was recrystallized from acetone - hexane to give colorless prisms (96 mg, 100%). mp 178 - 180°C. (lit.⁴ 175 - 179°C). ¹H-NMR (CDCl₃) δ: 6.83 (1H, s), 7.10 - 7.22 (2H, m), 7.30 - 7.47 (4H, m), 7.62 - 7.69 (3H, m), 8.30 - 8.45 (1H, br). Ms, *m/z*: 193 (100, M⁺).
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