



## Supporting Information

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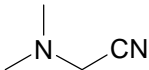
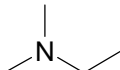
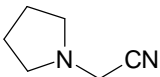
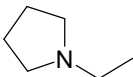
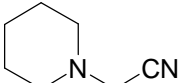
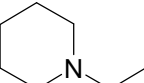
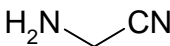
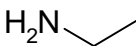
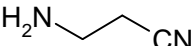
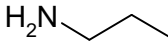
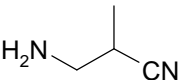
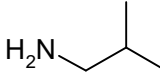
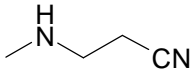
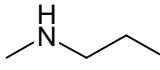
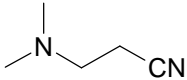
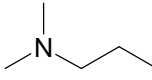
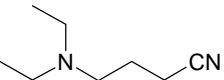
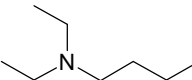
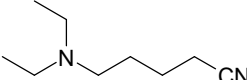
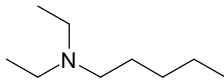
Supplementary Material to

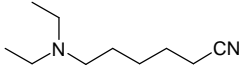
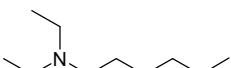
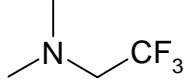
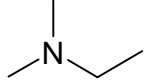
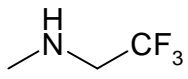
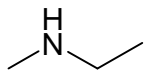
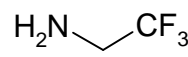
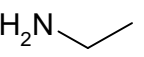
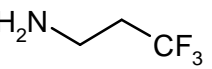
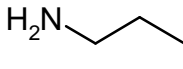
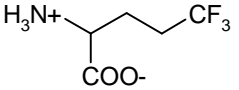
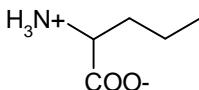
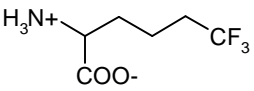
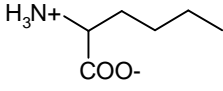
**Remote Modulation of Amine Basicity  
by a Phenylsulfone and a Phenylthio Group**

Rainer E. Martin, Baptiste Plancq, Olivier Gavelle,  
Björn Wagner, Holger Fischer, Stefanie Bendels, and Klaus Müller

Table S1:

For the estimates of  $\Delta pK_a$  decrements, the following data from the MedChem DB<sup>[1]</sup> were used:

compound	$pK_a$	Ref.compound	$pK_a$ (ref)	$\Delta pK_a$
	4.2		10.2	-6.0
	4.8		10.3 <sup>(a)</sup>	-5.5 <sup>(a)</sup>
	4.6		10.4	-5.8
	5.3		10.7	-5.4
	7.7		10.7	-3.0
	7.7		10.7	-3.0
	8.1		10.9	-2.8
	7.0		10.2	-3.2
	9.3		10.8 <sup>(b)</sup>	-1.5 <sup>(b)</sup>
	10.1		10.8 <sup>(b)</sup>	-0.7 <sup>(b)</sup>

	10.5		<i>10.8</i> <sup>(b)</sup>	<i>-0.3</i> <sup>(b)</sup>
	4.8		10.2	-5.4
	6.1		10.9	-4.8
	5.7		10.7	-5.0
	8.7		10.7	-2.0
	8.9		9.8	-0.9
	9.5		9.8	-0.3

### Comments:

The  $pK_a$  shifts are estimated for a replacement of a methyl group by either a CN or a  $CF_3$  group. Figures in italics are estimated  $pK_a$  values:

(a)  $pK_a$  value of *N*-propyl-pyrrolidine which is expected to be the same as that of *N*-ethyl-pyrrolidine, as judged from the  $pK_a$ 's of acyclic ethyl- and *n*-propyl-amines, as well as *N*-ethyl- and *N*-propyl-piperidine;

(b) The  $pK_a$  values are derived from the corresponding values for *N,N*-dimethyl amines ( $pK_a = 10.2$ ), corrected by  $\Delta pK_a$  upshifts of +0.3 for each replacement of a methyl by an ethyl group.<sup>[2]</sup>

**Table S2:** Experimental basicities for amines with phenylsulfone, phenylsulfoxide, and phenylthio groups at different topological distances from the amine function, as well as calculated  $pK_a$  values,  $CpK_a$ , and differences  $CpK_a - pK_a$  obtained by the two methods  $CpK_a$  by ACD<sup>[3]</sup> and  $pkalc$  Version 3.1.<sup>[4]</sup>

Parent Compound	Compd	n	$pK_a$	$CpK_a$ (ACD)	Diff (ACD)	$CpK_a$ (CD)	Diff (CD)
thiomorpholine-1,1-dioxide	<b>1</b>	-	5.4	6.5	+1.1	7.8	+2.4
thiomorpholine	<b>4</b>	-	9.0	9.1	+0.1	9.0	0.0
PhSO <sub>2</sub> -(CH <sub>2</sub> ) <sub>n</sub> -NH <sub>2</sub>	<b>5a</b>	2	7.8	7.2	-0.6	8.5	+0.7
	<b>6a</b>	3	9.2	8.9	-0.3	9.5	+0.3
	<b>7a</b>	4	10.0	9.8	-0.2	10.2	+0.2
	<b>8a</b>	5	10.4	10.3	-0.1	10.9	+0.5
PhSO <sub>2</sub> -(CH <sub>2</sub> ) <sub>n</sub> -NHCH <sub>3</sub>	<b>6b</b>	3	9.3	9.8	+0.5	9.7	+0.4
	<b>7b</b>	4	10.2	10.3	+0.1	10.4	+0.2
	<b>8b</b>	5	10.6	10.6	0.0	11.1	+0.5
PhSO <sub>2</sub> -(CH <sub>2</sub> ) <sub>n</sub> -N(CH <sub>3</sub> ) <sub>2</sub>	<b>7c</b>	4	9.3	9.4	+0.1	9.2	-0.1
	<b>8c</b>	5	9.8	9.6	-0.2	10.0	+0.2
PhSO-(CH <sub>2</sub> ) <sub>n</sub> -N(CH <sub>3</sub> ) <sub>2</sub>	<b>7g</b>	4	9.4	9.5	+0.1	9.2	-0.2
PhS-(CH <sub>2</sub> ) <sub>n</sub> -NH <sub>2</sub>	<b>5d</b>	2	9.0	8.7	-0.3	9.2	+0.2
	<b>6d</b>	3	9.9	9.7	-0.2	9.8	-0.1
	<b>7d</b>	4	10.4	10.3	-0.1	10.2	-0.2
	<b>8d</b>	5	10.5	10.5	0.0	10.9	+0.4
PhS-(CH <sub>2</sub> ) <sub>n</sub> -NHCH <sub>3</sub>	<b>7e</b>	4	10.5	10.6	+0.1	10.4	-0.1
	<b>8e</b>	5	10.9	10.7	-0.2	11.1	+0.2
PhS-(CH <sub>2</sub> ) <sub>n</sub> -N(CH <sub>3</sub> ) <sub>2</sub>	<b>7f</b>	4	9.8	9.6	-0.2	9.2	-0.6
	<b>8f</b>	5	10.0	9.7	-0.3	10.0	0.0

## References:

- [1] MedChem DB Version 06, Daylight Chemical Information Systems Inc., Aliso Viejo, CA 92656, USA; this database contains currently >60'000 entries.
- [2] D. D. Perrin, B. Dempsey, E. P. Serjeant, *pKa Prediction for Organic Acids and Bases*, Chapman and Hall, London and New York, **1981**.
- [3] ACD/pKa Predictor, Version 8.19, Advanced Chemistry Development, Inc., Toronto ON, Canada.
- [4] pkalc, Version 3.1, CompuDrug Inc., Sedona AZ, USA.