Supporting Information

1,2-Benzisothiazole Derivatives Bearing 4-, 5- or 6-alkyl/arylcarboxamide Moieties Inhibit Carbonic Anhydrase Isoform IX (CAIX) and Cell Proliferation under Hypoxic Conditions.

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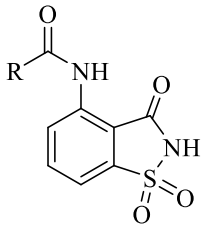
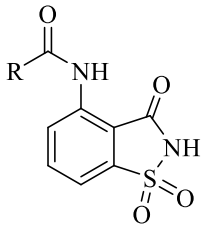
Table 1-SI. Physical Properties of N-(1,1-dioxide-3-oxo-2,3-dihydrobenzo[*d*]isothiazol-4-yl)arylamide, **4a,b,h**.



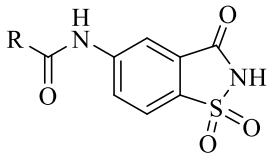
N	R	yield (%)	recryst solv	mp (°C)
4a	C_6H_5	62	Toluene	195-196
4b	C_6H_4-m-Br	42	Toluene	234 dec.
4h	C_6H_4-p-C_6H_5	35	Toluene	>300

Table 2-SI. Spectral Data of N-(1,1-dioxide-3-oxo-2,3-dihydrobenzo[*d*]isothiazol-4-yl)arylamide, **4a,b,h**.



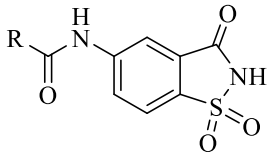
N	R	^{1}H-NMR (δ, ppm)
4a	C_6H_5	11.26 (s, 1H, exc.), 8.79 (d, 1H, J=8.0 Hz), 7.99-7.95 (m, 7H)
4b	C_6H_4-m-Br	12.72 (s, 1H, exc.), 8.61 (d, 1H, J=8.0 Hz), 8.09 (s, 1H), 7.96 (d, 1H, J=7.8 Hz), 7.87 (d, 1H, J=8.0 Hz), 7.66-7.55 (m, 2H), 7.39 (d, 1H, J=7.8 Hz)
4h	C_6H_4-p-C_6H_5	12.11 (s, 1H, exc.), 8.69 (d, 1H, J=8.2 Hz), 8.04 (d, 2H, J=8.0 Hz), 7.88 (d, 2H, J=8.2 Hz), 7.79-7.72 (m, 3H), 7.53-7.41 (m, 4H)

Table 3-SI. Physical Properties of N-(1,1-dioxide-3-oxo-2,3-dihydrobenzo[*d*]isothiazol-5-yl)arylamide, **5b-f,h** and N-(1,1-dioxide-3-oxo-2,3-dihydrobenzo[*d*]isothiazol-5-yl)acetamide, **5j**.



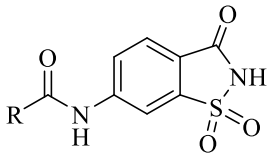
N	R	yield (%)	recryst solv	mp (°C)
5b	C_6H_4-m-Br	40	isPrOH	210 dec.
5c	C_6H_4-m-Cl	56	MeOH	>300
5d	C_6H_4-p-F	92	AcCN	>300
5e	C_6H_4-p-Cl	20	AcCN	>300
5f	C_6H_4-p-OCH_3	39	AcCN	>300
5h	C_6H_4-p-C_6H_5	19	AcCN	>300
5j	CH_3	47	isPrOH	225 dec.

Table 4-SI. Spectral Data of N-(1,1-dioxide-3-oxo-2,3-dihydrobenzo[*d*]isothiazol-5-yl)arylamide, **5b-f,h** and N-(1,1-dioxide-3-oxo-2,3-dihydrobenzo[*d*]isothiazol-5-yl)acetamide, **5j**.



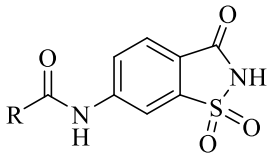
N	R	^{1}H-NMR (δ, ppm)
5b	C_6H_4-m-Br	10.65 (s, 1H, exc.), 8.17 (s, 1H), 8.04 (s, 1H), 7.99 (d, 1H, J=4.0 Hz), 7.96 (d, 1H, J=4.0 Hz), 7.84-7.48 (m, 3H)
5c	C_6H_4-m-Cl	10.96 (s, 1H, exc.), 8.45 (s, 1H), 8.16-7.66 (m, 6H)
5d	C_6H_4-p-F	10.88 (s, 1H, exc.), 8.47 (d, 1H, J=4.0 Hz), 8.27 (dd, 1H, J=12.0, 4.0 Hz), 8.14-8.07 (m, 3H), 7.42 (t, 2H, J=12.0 Hz)
5e	C_6H_4-p-Cl	10.86 (s, 1H, exc.), 8.35 (d, 1H, J=1.4 Hz), 8.19 (dd, 1H, J=8.0, 1.4 Hz), 8.05-7.96 (m, 3H), 7.65 (d, 2H, J=8.0 Hz)
5f	C_6H_4-p-OCH_3	10.73 (s, 1H, exc.), 8.32 (d, 1H, J=1.6 Hz), 8.10 (dd, 1H, J=8.0, 2.0 Hz), 7.97-7.89 (m, 3H), 7.04 (d, 2H, J=9.0 Hz) 3.79 (s, 3H, OCH_3)
5h	C_6H_4-p-C_6H_5	10.85 (s, 1H, exc.), 8.40 (s, 1H), 8.23 (d, 1H, J=8.4 Hz), 8.11 (d, 2H, J=8.4 Hz), 8.01 (d, 1H, J=8.6 Hz), 7.89 (d, 2H, J=8.0 Hz), 7.78 (d, 2H, J=7.4 Hz), 7.56-7.41 (m, 3H)
5j	CH_3	10.76 (s, 1H, exc.), 8.47 (s, 1H), 8.25 (d, 1H, J=4.2 Hz), 8.08 (d, 1H, J=4.2 Hz), 2.60 (s, 3H)

Table 5-SI. Physical Properties of N-(1,1-dioxide-3-oxo-2,3-dihydrobenzo[*d*]isothiazol-6-yl)arylamide, **6a-g**



N	R	yield (%)	recryst solv	mp (°C)
6a	C_6H_5	68	EtOH	>300
6b	C_6H_4-m-Br	58	$CHCl_3$	>300
6c	C_6H_4-m-Cl	65	CH_2Cl_2	275 dec.
6d	C_6H_4-p-F	33	MeOH	295 dec.
6e	C_6H_4-p-Cl	69	EtOH	>300
6f	C_6H_4-p-OCH_3	80	MeOH	>300
6g	C_6H_4-p-CH_3	68	MeOH	>300

Table 6-SI. Spectral Data of N-(1,1-dioxide-3-oxo-2,3-dihydrobenzo[*d*]isothiazol-6-yl)arylamide, **6a-g**.



N	R	^{1}H-NMR (δ, ppm)
6a	C_6H_5	10.86 (s, 1H, exc.), 8.51 (s, 1H), 8.19 (d, 1H, J=8.0 Hz), 8.03-7.89 (m, 3H), 7.59-7.50 (m, 3H)
6b	C_6H_4-m-Br	11.02 (s, 1H, exc.), 8.49 (s, 1H), 8.20-8.17 (m, 2H), 8.01 (d, 1H, J=4.2 Hz), 7.99 (d, 1H, J=4.2 Hz), 7.86 (d, 1H, J=4.0 Hz), 7.55 (t, 1H, J=4.0 Hz)
6c	C_6H_4-m-Cl	11.03 (s, 1H, exc.), 8.49 (s, 1H), 8.19 (d, 1H, J=4.0 Hz), 8.06 (s, 1H), 8.02 (d, 1H, J=4.2 Hz), 7.95 (d, 1H, J=4.0 Hz), 7.73 (d, 1H, J=4.0 Hz), 7.626 (t, 1H, J=4.0 Hz)
6d	C_6H_4-p-F	10.88 (s, 1H, exc.), 8.47 (s, 1H), 8.19 (d, 1H, J=8.0 Hz), 8.05-7.96 (m, 3H), 7.65 (d, 2H, J=8.0 Hz)
6e	C_6H_4-p-Cl	10.89 (s, 1H, exc.), 8.47 (s, 1H), 8.16 (d, 1H, J=8 Hz), 8.05-7.89 (m, 3H), 7.58 (d, 2H, J=8.0 Hz)
6f	C_6H_4-p-OCH_3	10.81 (s, 1H, exc.), 8.53 (s, 1H), 8.18 (d, 1H, J=6.6 Hz), 8.00 (d, 3H, J=8.4 Hz), 7.11 (d, 2H, J=8.6 Hz), 3.86 (s, 3H)
6g	C_6H_4-p-CH_3	10.79 (s, 1H, exc.), 8.47 (s, 1H), 8.14 (d, 1H, J=8.6 Hz), 7.96-7.86 (m, 3H), 7.37 (d, 1H, J=7.6 Hz), 2.38 (s, 3H)