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NEW FACILE SYNTHESIS OF N-SULFINYLAMINE DERIVATIVES USING N,N'-SULFINYLBISIMIDAZOLE AND N-(CHLOROSULFINYL)IMIDAZOLE

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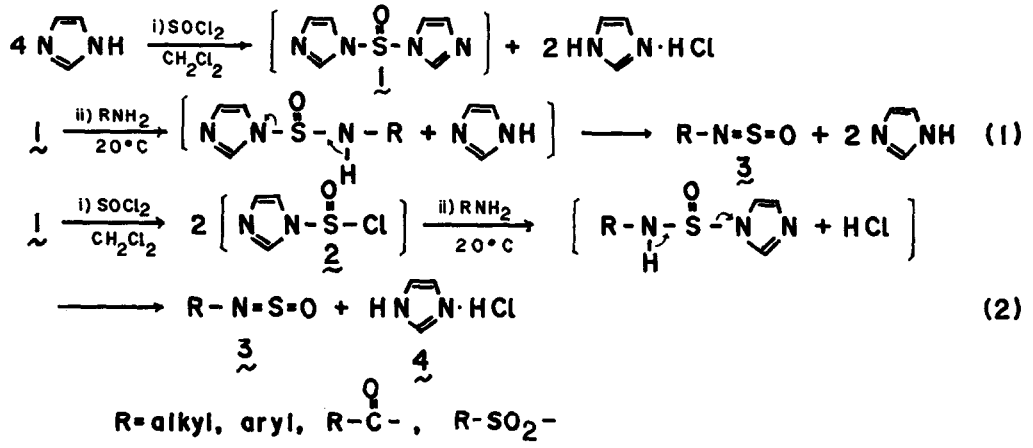
Summary. Treatment of amine derivatives such as amines, sulfonamides, and amides with N,N'-sulfinylbisimidazole (1) and N-(chlorosulfinyl)imidazole (2) *in situ* respectively gives the corresponding N-sulfinylamine derivatives (3): the latter reaction using N-(chlorosulfinyl)imidazole (2) yields 3 in almost quantitative yields at 20°C under mild conditions.

N-sulfinylamines have been known relatively to be unstable, but important heterocumulenes containing a sulfur-centered structure of great synthetic utility.[1]

Several papers on the preparation of 3 have been reported by the reaction of amines,[1,2] bistrimethylsilylamines[3] or amides[4] with thionyl chloride, by the reaction of lithioamides[5] or trimethylsilylamines in the presence of base[6] with sulfur dioxide, and by the reaction of arylazides with sulfur monoxide[7]. Sensitive unstable N-sulfinylamines were synthesized by a trans-sulfinylation using N-sulfinylsulfonamide.[1a] The known methods are successful to some extent, but not sufficient both in yields and reaction conditions.

We report a new facile synthetic method for the preparation of 3 using 1 and 2 as a sulfinylation reagent. N,N'-sulfinylbisimidazole (1)[8] was prepared by the treatment of imidazole with thionyl chloride, and N-(chlorosulfinyl)imidazole (2) was prepared by a direct treatment of 1 with thionyl chloride or by the treatment of imidazole with excess amount of thionyl chloride.[9] Without isolation of 1 or 2, they were used for the synthesis of 3 *in situ* as shown in Scheme I.

Scheme I



In a typical run, from 1 (method A): thionyl chloride (1.2g, 0.01 mole) distilled freshly was added to imidazole solution (2.72g, 0.04 mole, CH_2Cl_2; 30 ml) at -10°C under dry nitrogen atmosphere. The reaction mixture was stirred at 20°C for 10 min to form imidazolium chloride precipitation (2.05g, 98%) which was filtered and washed with dry dichloromethane (15 ml). The filtrate(1) collected was added to aniline solution (0.93g, 0.01 mole, CH_2Cl_2, 10 ml) at -40°C. The reaction mixture was stirred at 20°C for 0.5h and distilled under reduced pressure to give N-sulfinylaniline, which was purified by re-distillation. (1.02g, 73%, bp 40-43°C/1 mmHg [lit.,[6] bp 80°C/12 mmHg], IR (neat; ν_{NSO}) 1280, 1160 cm^{-1}). The results obtained are summarized in Table I.

From 2 (method B): thionyl chloride (0.6g, 5 mmole) was added to imidazole solution (1.36g, 0.02 mole, CH_2Cl_2; 20 ml) at -10°C. The reaction mixture was stirred at 20°C for 10 min to form imidazolium chloride (1.03g, 98.5%), which was filtered off. Thionyl chloride (0.6g, 5 mmole) was added to the filtrate (1) at -10°C and stirred at 20°C for 10 min to give 2 solution which was directly used *in situ* for the preparation of 3. The 2 solution was added to p-toluidine solution (1.07g, 0.01 mole, CH_2Cl_2; 10 ml) at -40°C immediately to give N-sulfinyl p-toluidine and imidazolium chloride solid. After being stirred at 20°C for 0.5h, imidazolium chloride (1.02g, 98%) was removed by filtration and washed with dichlorometnane (10 ml). The filtrate was concentrated to give highly pure N-sulfinyl p-toluidine (1.47g, 96%), which was purified by vacuum distillation to compare the boiling point (1.32g, 86%, bp. 50-53°/1 mmHg [lit.,[6] 47-50°/0.8 mmHg), IR (neat; ν_{NSO}) 1280, 1155 cm^{-1}). All the data obtained were summarized in Table 2.

Table 1. Preparation of 3 by the Reaction of Amines with 1 (Method A)

Run	Amines	Reaction Time(min)	Reaction Temp.(C°)	3	Yield (%)[a]	bp./mmHg[b](°C)	Reference
1	$PhNH_2$	30	20	Ph-N=S=O	73	40-43/1	6
2	$p\text{-}MeC_6H_4NH_2$	25	20	p-Me-C_6H_4-N=S=O	72	50-53/1	6
3	$p\text{-}ClC_6H_4NH_2$	20	20	p-Cl-C_6H_4-N=S=O	69	60-63/1	6

a) Isolated yields determined by re-distillation
b) Boiling points met reported values

Table 2. Preparation of 3 by the Reaction of Amines with 2 (Method B)

Run	Amines	Reaction Time(h)	Reaction Temp.(°C)	3	Yields(%)[a]( )[b]	bp/mmHg or mp (°C)	References
1	$PhNH_2$	0.5	20	Ph-NSO	100 (89)[b]	40-43/1	6
2	$p\text{-}MeC_6H_4NH_2$	0.5	20	pMeC_6H_4-NSO	96 (86)	50-53/1	6
3	$p\text{-}ClC_6H_4NH_2$	0.4	20	p-ClC_6H_4-NSO	98 (87)	60-63/1	6
						mp.32-34	10
4	$p\text{-}MeOC_6H_4NH_2$	0.5	20	p-$MeOC_6H_4$-NSO	95 (86)	80-84/1	5
						mp.24-25	10
5	$p\text{-}NO_2\text{-}C_6H_4NH_2$	0.5	20	p-NO_2-C_6H_4-NSO	89 (80)	mp.67-69	10
6		0.3	20		85 (77)	59-61/17	6
7	t-$BuNH_2$	0.3	20	t-Bu-NSO	83 (63)	27-29/23, 98-99/760[c]	11
8	n-$BuNH_2$	0.3	20	n-Bu-NSO	72 (53)	30-32/23,115-116/760[c]	2
9	$PhNHNH_2$	0.2	0	Ph-NH-NSO	94 (78)	mp.103-105	12
10	p-Me-$PhSO_2NH_2$	1	25	p-Me-Ph-SO_2-NSO	97 (86)	mp. 50-52	1b
11	Ph-SO_2NH_2	1	25	Ph-SO_2-NSO	97 (89)	mp. 67-69	1b
12	Ph-C(=O)-NH_2	0.5	25	Ph-C(=O)-NSO	98 (81)	70-75/0.15	4
13	CH_3-C(=O)-NH_2	0.5	25	CH_3-C(=O)-NSO	87 (79)	40-45/17	4

a) Isolated crude yield without distillation or recrystallization: t.l.c (silica gel, solvent: CH_2Cl_2) showed only one spot.
b) The yields in the parenthesis are obtained by distillation or recrystallization.
c) Product was observed to be decomposd by ditillation at 760 mmHg.

The products 3 are generally purified by the distillation, but it has been problem because 3 is sensitive to high temperature and moisture. Trials to purify 3 by the silica gel column or preparative thin layer chromatographys were failed since the products are readily converted to the corresponding amines in the column during chromatography. In the method A, it was difficult to separate 3 from imidazole by ditillation: redistillation is usually necessary for the purification. However, method B does not contain free imidazole: most imidazolium chloride salt 4 (in equation 2) formed can be removed by filtration to give almost quantitative yields of pure 3.

The method B has advantages over the known method for the preparation of 3; for instance, N-sulfinyl p-toluenesulfonamide (low yield) was prepared by the reaction of p-toluenesulfonamide with thionyl chloride in dry benzene under reflux for 5 days,[13] while our method requires 1h at 20°C to give the product in 97% yield (Run 10 in Table 2).

Thus, the new method for the preparation of various N-sulfinylamine derivatives described here will be widely usable for the preparation of 3 including unstable N-sulfinylalkyl amines. The scope and utility of 3 are being investigated.

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