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A NEW SULFOXIMINE SYNTHESIS

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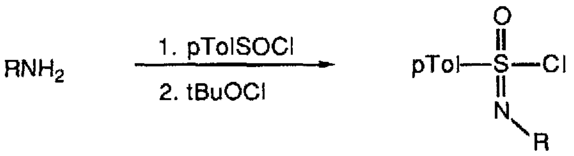
Summary: Selected sulfonimidoyl halides react with ethylaluminum dichloride to give S-ethyl sulfoximines in good yields.

The sulfoximine functional group is a versatile, species of great utility in organic synthesis.[1] The preparation of sulfoximines has been accomplished by a variety of processes including the reaction of sulfoxides with hydrazoic acid[2] or p-toluenesulfonyl azide,[3] the oxidation of sulfilimines with hydrogen peroxide[4] or sodium hypochlorite,[5] and the reaction of sulfonimidates[6] or sulfonimidoyl fluorides[7] with organolithium reagents.

While these methods often serve well in sulfoximine synthesis we thought it appropriate to attempt to develop a simple one step synthesis of sulfoximines from easily accessible sulfonimidoyl chlorides. Our recent foray into the chemistry of sulfonimidoyl chlorides[8] led us to the conclusion that organometallic compounds which were also Lewis acids might serve well in the conversion of sulfonimidoyl chlorides into sulfoximines. Our work has borne out this supposition.

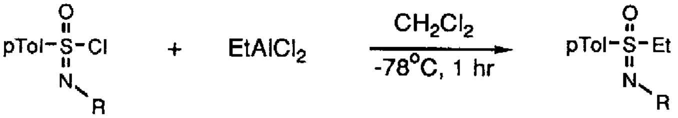
In this preliminary study we began by converting a small number of amines to sulfinamides by reaction with p-toluenesulfinyl chloride. Oxidation to sulfonimidoyl chlorides with t-butyl hypochlorite[9] in methylene chloride at -78°C proceeded smoothly (equation 1). Removal of solvent and excess t-butyl hypochlorite in vacuo was followed by dissolution in methylene

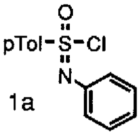
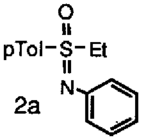
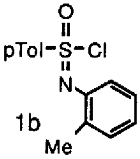
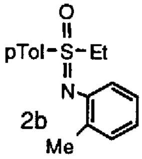
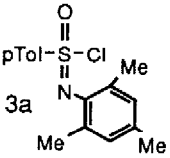
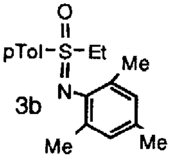
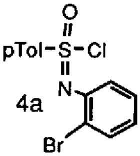
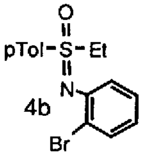
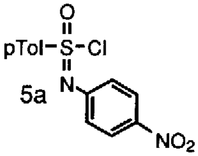
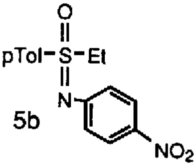
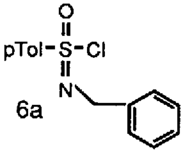
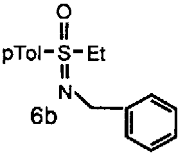


$$RNH_2 \xrightarrow[2.\ tBuOCl]{1.\ pTolSOCl} pTol-\overset{O}{\overset{\|}{S}}(=NR)-Cl$$

Eq. 1

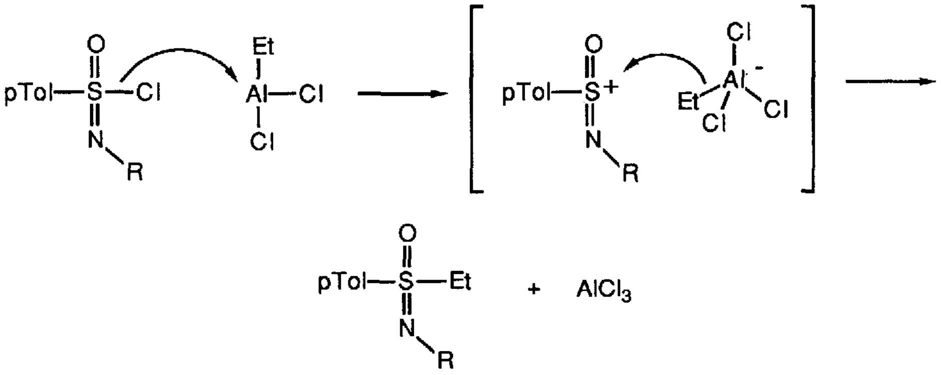
Table



Entry	Sulfoximidoyl Chloride	Sulfoximine	Yield(%)
1	 1a	 2a	94
2	 1b	 2b	75
3	 3a	 3b	41
4	 4a	 4b	83
5	 5a	 5b	76
6	 6a	 6b	63

chloride (~.2M) and addition of 2 equivalents of a 1M solution of ethylaluminum dichloride in methylene chloride (Aldrich) at -78°C. After stirring for one hour the reaction was quenched with 1N HCl and worked up. Flash chromatographic purification gave the sulfoximines in good yield. The results are shown in the Table. The process has not yet been optimized. Entries 1-5 demonstrate the synthesis of N-aryl sulfoximines by this methodology.[10] The survival of the para nitro substituent (entry 5) is significant as it is doubtful that this functionality would survive treatment with organolithium reagents. While the synthesis of N-alkyl sulfoximines has not been rigorously tested, entry 6 in the Table illustrates that this should not be problematical. Finally, it should be pointed out that macroscopically these reactions are often quite colorful (purple, blue, brown), presumably due to Lewis acid induced decomposition of small amounts of the sulfonimidoyl chlorides, but that this does not seriously affect the yield of the process.

A plausible mechanism for the process is shown in Scheme 1. Reaction of ethylaluminum dichloride with the sulfonimidoyl chloride proceeds with chloride abstraction to produce an ion pair which ultimately collapses to sulfoximine and aluminum chloride. Surprisingly, aromatic sulfonyl chlorides apparently react with organoaluminum compounds by a reductive alkylation process to produce sulfoxides rather than the expected sulfones.[11] In general, this type of process did not appear to be present to a significant extent in our systems.



Scheme 1

This methodology greatly increases the accessibility of sulfoximines for use in organic synthesis. Efforts to expand the scope of this reaction and to develop sulfoximine based organometallic reagents capable of delivering a general variety of alkyl groups to pi systems with enantiofacial discrimination are under way.[12,13]

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12. All new compounds exhibited acceptable 1H NMR and IR spectra as well as satisfactory combustion analysis or HRMS data. All yields are for chromatographically purified materials.
13. Data for S-ethyl-S-(4-methylphenyl)-N-phenylsulfoximine (**2a**): oil, 1H NMR (90 MHz, CDCl$_3$) 7.79 (d, 2H, J=8), 7.30 (d, 2H, J=8), 7.12-6.69 (m, 5H0, 3.32 (q, 2H, J=7.5), 2.40 (s, 3H), 1.29 (t, 3H, J=7.5). IR (neat) 626m, 641m, 695s, 733s, 757s, 803m, 815m, 893w(br), 977w, 995m, 1013s, 1039s, 1074m, 1094s, 1153w, 1194s, 1266s, 1295s(br), 1380w, 1406m, 1448m, 1487s, 1572m, 1595s, 2875w, 2938m, 2976w, 3028w, 3060w, 3077w. HRMS Calcd. for $C_{15}H_{17}NOS$: 259.1031. Found: 259.1030.

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