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SULFONAMIDES AS PHOTOLABILE PROTECTING GROUPS FOR AMINES

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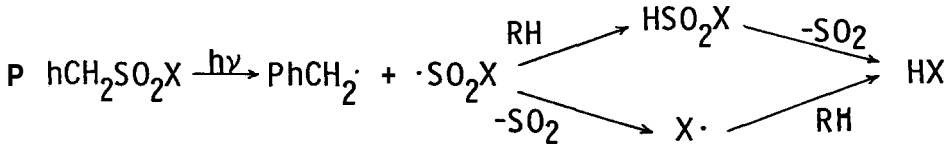
As Hendrickson has emphasized (1), sulfonamides serve as excellent protecting groups for amines because they lower the nucleophilicity of the nitrogen and as well allow conversion of primary amines to secondary amines by alkylation. They can be prepared in high yields and are relatively resistant to acid and base hydrolysis and oxidation. To solve the problem of deprotection, Hendrickson designed a phenacylsulfonamide which could be removed by Zn/HCl at room temperature. Clearly these conditions are incompatible with some functional groups.

In recent publication (2), we have shown that the photochemistry of benzylsulfonyl systems is characterized by homolytic cleavage to benzyl and sulfonyl radicals. The final products are dependent on the stability of the sulfonyl radical to loss of SO_2 and the solvent used. We now report an extension of this photochemistry to the protection of amines with a



sulfonyl group which meets Hendrickson's requirements but is removable under neutral conditions.

As shown in the Table, photolysis of the benrylsulfonamides of both primary and secondary amines gives high yields of the free amine. Entries l-3 indicate that the yield is increased, at least for secondary amines, if the hydrogen atom donating ability of the solvent is improved. For primary amines (entries 4 and 5) both methanol and 2-propanol are satisfactory Since the other products of these reactions are sulfur dioxide and toluene or diphenylethane isolation of the amine is possible by solvent evaporation and extraction into dilute HCl. Although these photoreactions are characterized by excited state carbon-sulfur bond cleavage, it is not obvious whether loss of sulfur dioxide occurs before or after trapping by the solvent since no information is available on the S-N bond strength in sulfonamides(3). Entry 6 demonstrates that the method is not suitable for aromatic amines presumably because the more strongly absorbing aniline chromophore changes the nature of &he excited state process. An initial attempt to circumvent this problem using 4-nitrobenzyl as the chromophore was unsuccessful (entry 7). Even after long irradiations only starting material was recovered suggesting that the lower excitation energy does not lead to $C\text{-}SO_2$ bond cleavage.

In the Table, entries 8-11 demonstrate that this photolability of sulfonamides can also be useful for benzene rather than benzyl derivatives. Now, however, excitation leads to sulfur-

Table

	Sulfonamide[a]	Solvent	Yield of Amine[b]
1.	$PhCH_2SO_2N(C_4H_9)_2$	Benzene:10% CH_3OH	40%
2.	"	CH_3OH	61%
3.	"	$(CH_3)_2CHOH$	78%
4.	$PhCH_2SO_2NH(CH_2)_8CH_3$	$(CH_3)_2CHOH$	81%(70%)[c]
5.	$PhCH_2SO_2NHC_6H_{11}$	CH_3OH	98%
6.	$PhCH_2SO_2NHPh$	$(CH_3)_2CHOH$	10%
7.	$4\text{-}NO_2\text{-}C_6H_4CH_2SO_2NHC_6H_{11}$	$(CH_3)_2CHOH$	0%
a.	$PhSO_2NH(C_4H_9)_2$	CH_3OH	63%
9.	"	$(CH_3)_2CHOH$	80%
10.	"	$(CH_3)_2CHOH$:3% in NaOH	81%
11.	$PhSO_2NHC_6H_{11}$	"	96%

[a] All photolyses were on 300 mg of sulfonamide in 300 ml of solvent using a 200 W medium-pressure vycor filtered mercury lamp for 2-4 hr; run 7 was with a pyrex filter

[b] Yields by calibrated glc

[c] By isolation of amine

nitrogen bond cleavage. Trapping of the radicals formed by the solvent gives benzene sulfinic acid and the free amine. This leads to complications since the salt precipitates and interferes with the photolysis and the analysis for amine liberated. Precipitation can be avoided by performing the photolysis in slightly basic solution (entries 10 and 11) and again the yields are excellent.

Preliminary experiments suggest that benzylsulfonyl derivatives of amino acids (4) can also be deprotected photochemically. However, the requirement for short enough wavelengths for the benzene chromophore leads to show photodegradation of the amino acids liberated and yields go through a maximum (~85% for glycine and ~70% for leucine as determined colorimetrically (5)). Since photodegradation will be more serious for other amino acids (phenylalanine, histidine, etc.) the procedure can only be general if a longer wavelength chromophore is available. This problem has been solved previously using nitrobenzene derivatives (6) but entry 7 suggests this will not be possible here. Other variations are currently being examined.

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