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VICARIOUS SUBSTITUTION OF HYDROGEN IN AROMATIC HETEROCYCLES WITH CARBANIONS OF CHLOROMETHYL SULFONYL COMPOUNDS[1]

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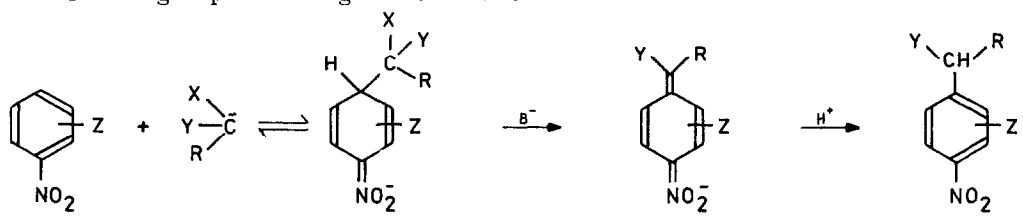
Summary: Carbanions of chloromethyl phenylsulfone and chloromethane sulfonmorpholide replace hydrogen in benzothiazole,acridine and variety of substituted 1,2,4-triazines giving corresponding sulfonyl methylderivatives.

Recently we have found[2-4] that a variety of carbanions containing leaving groups at the carbanionic centers react with aromatic nitro compounds replacing hydrogen atoms ortho or para to the nitro group according to the scheme:



where X=leaving group, Y=carbanion stabilizing group, R=substituent

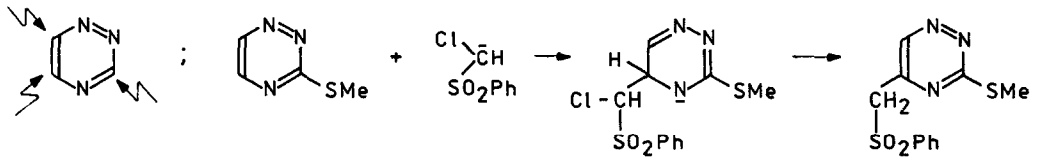
These reactions were named v i c a r i o u s nucleophilic substitution of hydrogen in order to specify that, although hydrogen atom in the nitroaromatic ring is replaced by the carbanion moiety, the leaving group departing from the intermediate σ-adduct, is that originally present in the reacting carbanion. Besides nitroarenes a variety of aromatic heterocycles exhibit strong electrophilic properties, hence one can expect that they should be able to react with such carbanions according to the vicarious nucleophilic substitution scheme. This process would provide a simple method for introduction of α-functionalized alkyl substituents into heteroarenes[5].

Unfortunately simple azines: pyridine, quinoline and also more electrophilic diazines do not react with carbanion of chloromethyl phenyl sulfone 1. On the other hand acridine, which is known to add readily nucleophilic reagents, reacts with 1 and chloromethane sulfomorpholide 2 in presence of KOH in DMSO yielding C-10 sulfonylmethyl derivatives. This reaction takes place also with benzothiazole and its oxygen analogue-benzoxazole; in both cases the hydrogen atom at C-2 is replaced by the sulfonylmethyl substituent.

Similarly 1,2,4-triazine derivatives react easily with 1. In this case there was a question of the orientation of the substitution since in this heterocycle nucleophiles can attack all three positions of the ring (3.5 and 6).

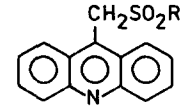
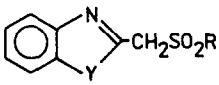
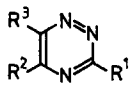
It was possible to establish using various substituted 1,2,4-triazine derivatives that the reactivity of these positions towards anionic nucleophiles decrease in the following order: 5>3>6. Thus for 6-phenyl-1,2,4-triazine the reaction takes place exclusively at C-5, for 3-phenyl and 3-methylthio derivatives the substitution occurs at C-5 and for 5-phenyl derivative at C-3. Only when both 3- and 5-positions are occupied as in 3-methylthio-5-phenyl--1,2,4-triazine the substitution of hydrogen takes place at C-6; besides the vicarious

substitution product also 3-(phenylsulfonyl)methyl-5-phenyl-1,2,4-triazine was formed apparently via the nucleophilic replacement of the methylthio group by the carbanion of 1 followed by reductive dechlorination of the product. The observed reactivity order for 1,2,4-triazine derivatives in vicarious nucleophilic substitution process is in agreement with the previous observations and theoretical considerations [6,7].



All compounds obtained in this work gave correct elemental analysis, their structure was confirmed by appropriate spectral data. Yields m.p. and ^{1}H NMR data are given in the table.

Table

	R	Y		Yield (%)	m.p. (°C)	^{1}H NMR (δ, in $CDCl_3$) CH_2	H in heterocyclic ring
	Ph	-		72	210	5.34	-
		-		76	220	5.34	-
		O		14	133	4.61	-
		S		67	153	4.80	-
	Ph	S		64	135	4.84	-
	R_1	R_2	R_3				
	H	$PhSO_2CH_2$	Ph	65	-[a]	4.80	9.60(H-3)
	Ph	$PhSO_2CH_2$	H	78	135-6	4.60	9.25(H-6)
	MeS	$PhSO_2CH_2$	H	76	151-2	4.55	9.15(H-6)
	$PhSO_2CH_2$	Ph	H	74	144-5	5.07	9.72(H-6)
	MeS	Ph	$PhSO_2CH_2$	56[b]	141-2	4.92	-

a) liquid, b) 3-CH_2SO_2Ph-5-Ph-1,2,4-triazine was also isolated in 23% yield

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