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SHORT COMMUNICATIONS

Difluoromethylation of 5-Sulfanyltetrazoles

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We previously [1, 2] studied difluoromethylation of some 2-sulfanylazoles which are heterocyclic compounds having an N–C–S ambident nucleophilic center. However, we failed to obtain N-difluoromethyl derivatives from 1-aryl-2-sulfanylimidazoles despite wide variation of the reaction conditions. In the reaction with 1-aryl-2-sulfanyl-1,3,4-triazoles, in which the heteroring is a stronger electron acceptor than imidazole ring, the corresponding N^4–CHF_2 derivatives were isolated in up to 25% yield [2].

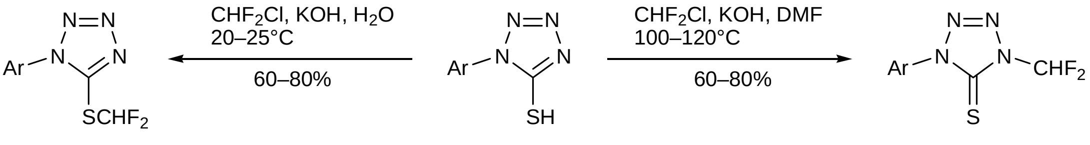
The present communication reports on difluoromethylation of 1-aryl-5-sulfanyltetrazoles **Ia**–**Ie** which possess even more acceptor heteroring. By reaction of compounds **Ia**–**Ie** with chlorodifluoromethane and KOH in DMF at 100–120°C we obtained the corresponding N-difluoromethyl derivatives **IIa**–**IIe** in 60–80% yield. When the reaction was carried out under milder conditions, in a solution of potassium hydroxide in aqueous dioxane at 20–25°C (reaction time 20 min), the products were S-difluoromethyl derivatives **IIIa**–**IIIe** (yield 60–80%; see table).

Presumably, increase in the electron-acceptor power of the heteroring makes the C–F bond in the N–CHF_2 group stronger, so that the products are more stable under conditions of alkaline hydrolysis. Difluoromethylation of 2-sulfanylazoles with $CHClF_2$ under drastic alkaline conditions involves concurrent transfer of the difluoromethyl group from sulfur to nitrogen and vice versa [1]. In the reaction with 1-aryl-5-sulfanyltetrazoles, the equilibrium is displaced toward more stable N-difluoromethyl derivatives.

The ^1H and ^{19}F NMR spectra were recorded from solutions in $CDCl_3$ on a Varian VXR-300 spectrometer at 300 and 282.2 MHz, respectively, using TMS (^1H) and $CFCl_3$ (^{19}F) as internal references.

1-Aryl-4-difluoromethyltetrazole-5-thiones IIa–IIe. A solution of 0.01 mol of tetrazole **Ia**–**Ie** in 10 ml of distilled DMF was saturated with chlorodifluoromethane at room temperature, and 6 g of finely powdered KOH was added under vigorous stirring. The mixture strongly warmed up. Passing of $CHClF_2$ was continued until it no longer absorbed at 100–120°C (for about 20 min). The mixture was poured into 100 ml of water, and the precipitate was filtered off, dried in air, and recrystallized from CCl_4–hexane (2:1). Yield of **IIa**–**IIe** 40–60%. The mother liquor was subjected to chromatography to isolate an additional amount (~20%) of product **IIa**–**IIe** and a small amount (5–10%) of isomer **IIIa**–**IIIe**.

1-Aryl-5-difluoromethylsulfanyltetrazoles IIIa–IIIe. A mixture of 5 ml of dioxane (freed from peroxy compounds) and a solution of 6 g of potassium hydroxide in 10 ml of water was saturated with chlorodifluoromethane under stirring, 0.01 mol of 5-sulfanyltetrazole **Ia**–**Ie** was added, and passing of $CHClF_2$ was continued for 20 min under stirring. The mixture was diluted with 100 ml of water, and the oily material was extracted into diethyl ether (3 × 30 ml). The combined extracts were washed with water (3 × 50 ml), dried over



IIIa–**IIIe** **Ia**–**Ie** **IIa**–**IIe**

Ar = C_6H_5 (**a**), 2-MeC_6H_4 (**b**), 4-MeC_6H_4 (**c**), 2,4-$Me_2C_6H_3$ (**d**), 2,5-$Me_2C_6H_3$ (**e**).

Yields, melting or boiling points, elemental analyses, and ^{1}H and ^{19}F NMR parameters of compounds **IIa**–**IIe** and **IIIa**–**IIIe**

Comp. no.	Yield, %	mp, °C, or bp, °C (*p*, mm)	Found, %			Formula	Calculated, %			NMR spectra		
			C	H	N		C	H	N	$\delta(\mathrm{C}\mathbf{H}\mathrm{F}_2)$	$\delta_\mathrm{F}(\mathrm{CH}\mathbf{F}_2)$	J_{HF}, Hz
IIa	83	93–94	41.96	2.56	24.37	$C_8H_6F_2N_4S$	42.10	2.65	24.55	7.96 t	–103.88 d	57
IIb	87	56–57	44.64	3.12	23.41	$C_9H_8F_2N_4S$	44.62	3.33	23.13	7.94 t	–103.36 d	57
IIc	68	126–127	44.92	3.01	23.22	$C_9H_8F_2N_4S$	44.62	3.33	23.13	8.00 t	–103.74 d	57
IId	70	75–76	47.15	4.05	21.72	$C_{10}H_{10}F_2N_4S$	46.87	3.93	21.86	8.07 t	–103.38 d	57
IIe	72	115–116	46.81	3.72	21.91	$C_{10}H_{10}F_2N_4S$	46.87	3.93	21.86	7.92 t	–103.40 d	57
IIIa	81	117–120 (0.5)	42.13	2.44	24.78	$C_8H_6F_2N_4S$	42.10	2.65	24.55	7.64 t	–92.39 d	56
IIIb	62	125–127 (0.3)	44.55	3.52	23.18	$C_9H_8F_2N_4S$	44.62	3.33	23.13	7.70 t	–92.64 d	56
IIIc	69	120–122 (0.3)	44.30	3.28	23.07	$C_9H_8F_2N_4S$	44.62	3.33	23.13	7.71 t	–92.69 d	56
IIId	68	136–136 (0.5)	46.69	3.60	22.13	$C_{10}H_{10}F_2N_4S$	46.87	3.93	21.86	7.64 t	–92.41 d	56
IIIe	67	125–127 (0.3)	46.98	3.81	22.04	$C_{10}H_{10}F_2N_4S$	46.87	3.93	21.86	7.66 t	–92.43 d	56

magnesium sulfate, and evaporated, and the residue was distilled under reduced pressure.

The yields, melting or boiling points, elemental analyses, and some NMR spectral parameters of compounds **IIa**–**IIe** and **IIIa**–**IIIe** are given in table.

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