Decomposition Studies of N-([^{19}F, Br)halogenoalkyl-N-nitroso-4-methyl-benzenesulfonamides

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Introduction

^{18}F-fluoroalkylation is a useful alternative method for introducing the ^{18}F-label into polyfunctional molecules like radiopharmaceuticals for positron-emission-tomography (PET). [1] Especially for H-acidic compounds, which do not lend themselves to direct nucleophilic fluorination, fluoroalkylation makes it possible to introduce [^{18}F]fluoralkyl groups, such as C_2H_4[^{18}F]F into NH, OH, and SH functionalities applying 2-[^{18}F]fluoroethyltosylate. Bifunctional alkanes like 1-bromo-2[^{18}F]fluoroethane and analogues can also be applied as precursors for ^{18}F-fluoroalkylations, which are easily made via anion activated nucleophilic ^{18}F-substitution of the corresponding di-bromoalkanes. Furthermore, ^{18}F-fluorobenzylation applying 4-[^{18}F]fluorobenzylbromide has been used for the syntheses of fluorinated radiopharmaceuticals.

Results and Discussions

The syntheses of all halogenated compounds is shown in fig. 1.
To obtain data about the time-dependent decomposition of the ^{19}F-standard compounds 11-13 under typical labelling conditions (acetonitile as solvent, Kryptofix 2.2.2./K_2CO_3 to avoid liberation of HF, radioactivity adsorption on the vessel surface and to enhance the nucleophilicity of [^{18}F]fluoride), ^{1}H NMR experiments were performed at 75°C as well as 25°C. Additionally to the performed decomposition studies of the fluoro compounds at typical labelling conditions, the stability of the bromo bearing precursors which are also from general interest for the planned labelling reaction was conducted. Therefore, decomposition studies at 25°C and 75°C in acetonitrile with Kryptofix® 2.2.2./K_2CO_3 were monitored with ^{1}H NMR experiments. The focus was on the aromatic- and alkyl protons. Plots (Figure 2) of the decomposition data applying ln (% N-bromooalkyl-N-nitroso-4-methylbenzenesulfonamides) vs time (min) gave straight lines reflecting first order decomposition kinetics. The product distribution after the decomposition experiments were performed with ^{1}H NMR as well as MS (EI, FD).

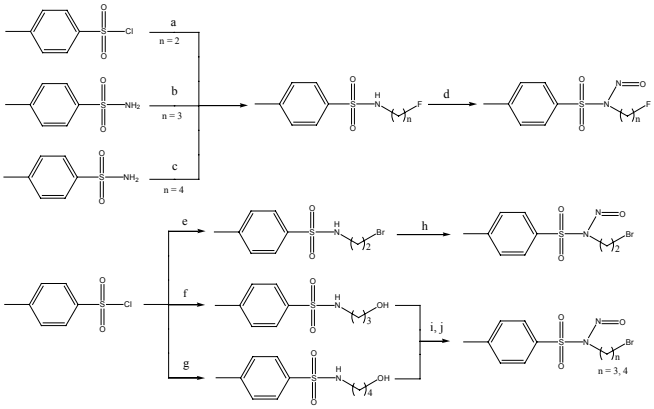
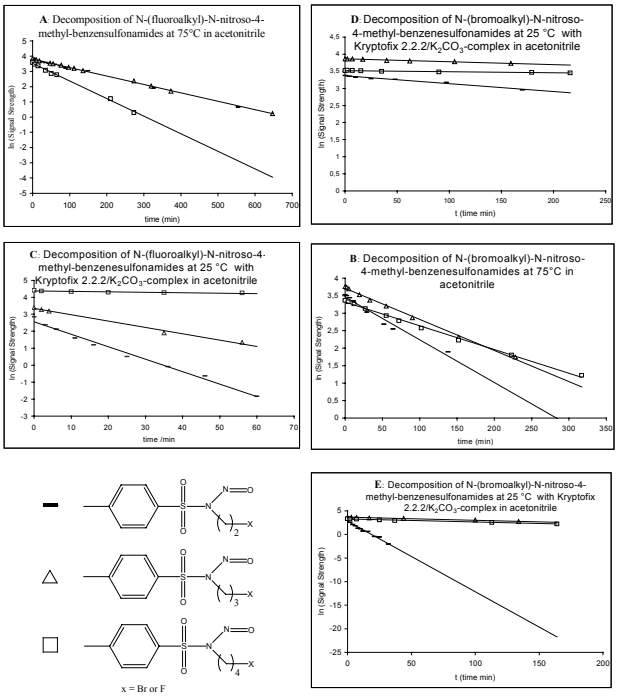


fig. 1: Syntheses of halogenated compounds



compound entries

n	F	Br	OH	F	Br
2	3	6		11	14
3	4	7	9	12	15
4	5	8	10	13	16

Fig. 2: Decomposition kinetics in acetonitrile and compound entries

Conclusion

The graphical data suggest that the bromo-compounds are sufficiently stable under labeling conditions whereas the corresponding fluoro-derivatives decompose rapidly by liberating nitrogene within 1-2 min at 75°C. With regard to the planned radioactive labeling, these experimental results demand a modified labeling technique that includes an alternative setup. Research concerning this problem is straight forward.

[1] D. Block, H.H. Coenen, G. Stöcklin, J. Labelled Compd. Radiopharm. 1987, 25, 201