HETEROCYCLES, Vol. 6, No. 1, 1977

THE STRUCTURE OF ALKYLATION PRODUCTS OF 2-SUBSTITUTED 3-METHYLBENZOTHIAZOLINES WITH MEERWEIN REAGENTS

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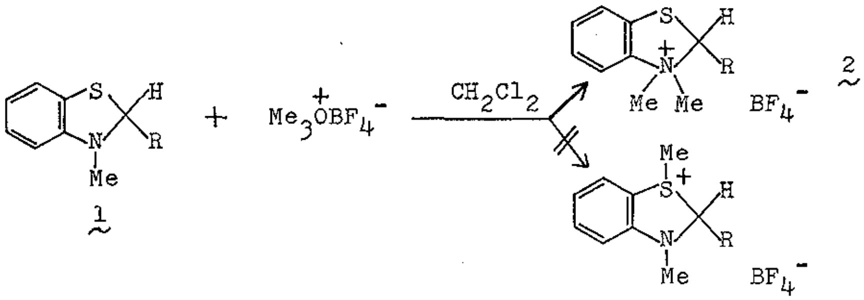
Methylation and ethylation of 2-substituted 3-methylbenzothiazolines with Meerwein reagents gave the corresponding ammonium fluoroborates. The configuration of two methyl groups on nitrogen was assigned, i. e., one at lower field (in NMR) is syn to 2-C-H and the other at higher field is syn to 2-C-R.

The selectivity of alkylation of a compound containing sulfur and nitrogen in a molecule has been studied by some groups and is still to be explored. Ethylation of morpholine sulfide with triethyloxonium fluoroborate gave the corresponding sulfonium salt in a moderate yield but alkylation with other reagents , even with trimethyloxonium fluoroborate, were unsuccessful.1) Methylation of sulfinamide took place on oxygen2) and that of sulfoximine on nitrogen.3)

In this paper, we report alkylation of benzothiazolines (1)4) with trialkyloxonium fluoroborate, which was disclosed to give the corresponding ammonium salts (**2**).

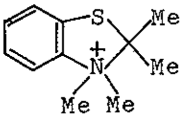
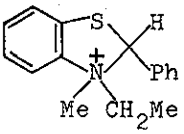


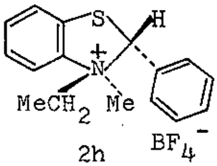
A typical example is shown below. 3-Methyl-2-phenylbenzothiazoline (**1c**: 1.14 g, 5.0 mmol) in anhydrous methylene chloride (15 ml) was added to a suspension of trimethyloxonium fluoroborate (0.888 g, 6.0 mmol) in methylene chloride (20 ml) at room temperature with stirring. After about 1 hr, the mixture was refluxed for 10 min to give clear orange-red solution. To the solution was added methanol (1 ml) at room temperature and the solvent was evaporated under reduced pressure. The residue was recrystallized twice from absolute ethanol to yield 3,3-dimethyl-2-phenylbenzothiazolinium fluoroborate (**2c**: 1.13 g, 69%, mp 178.5 -180.5 °C).

The yields and NMR data of **2** are shown in the Table.

It is clear by inspection of the Table that the fluoroborates (**2a**-**e**) show well separated two methyl signals with equal intensity. These methyl signals can be assigned to $\overset{+}{S}$-Me and N-Me groups, respectively. However, it was shown that they should belong to the dimethylammonium group because no spectral change could be observed by addition of trifluoroacetic acid to the fluoroborate (**2c**).

Table Characterization of 2-Substituted 3,3-dimethylbenzothiazolinium fluoroborate (δ from TMS in DMSO-d$_6$)

	2 R	mp (°C)	Yield %	2 C-H	N-Me (1 : 1)	
a)	p-MeOC$_6$H$_4$	165-167	65	6.94	3.12	3.65
b)	p-MeC$_6$H$_4$	195-197	59	6.94	3.10	3.66
c)*1	Ph	178.5-180.5	69	6.99	3.11	3.71
d)	p-ClC$_6$H$_4$	196-197	58	7.00	3.17	3.71
e)	Me	117.5-119.0	66	5.81*2	3.35	3.73
f)	H	172.0-173.5	77	5.34 (s,2H)	3.62 (s,6H)	
g)*1		177.0-178.5	72	1.95 (s,6H)	3.53 (s,6H)	
h)		148.0-149.5	34	6.93	3.12*3 (s,3H)	



2h

*1 No spectral change was observed by addition of trifluoroacetic acid.

*2 5.81 (1H, q, J=7.0 Hz); 1.86 (3H, d, J=7.0 Hz)

*3 N-Et 1.43 (3H, t, J=7.0 Hz)
3.5-4.5 (2H, m)

This result was supported by the fact that the fluoroborates (2f and g) which bear the same substituent at 2-C show a single N-methyl peak.

The chemical shifts of the lower field methyl of 2a-e show almost constant value (δ 3.7), on the other hand, those of the higher field methyl are constant for 2a-d (δ 3.12) but a distinct shift to lower field is observed when the substituent at 2-C is methyl. Hence, it can be concluded that the lower field methyl is assigned to lie syn to 2-C-H and the higher field methyl syn to 2-C-R.

According to the conclusion mentioned above, two isomers should be obtained by ethylation of 1, that is, one with the methyl syn to 2-C-H and the other with the methyl syn to 2-C-R. This was substantiated in ethylation of 1c.

Two methyl signals were observed at δ 3.12 and 3.27 (integral ratio, ca. 2:1) for the dried residue after evaporation of the solvent, where the reaction mixture was quenched with D_2O. One isomer (2h) was obtained as pure crystals after repeated recrystallization of the dried residue from absolute ethanol and its character is shown in the Table.

The methyl signal of 2h corresponds to the higher field one of the reaction mixture, so the methyl is syn to 2-C-Ph, if it can be taken for granted that the conclusion on the configuration of the methyl of 2a-e can also be held in this case.

References and Note

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3) C. R. Johnson, E. R. Janiga, and M. Haake, *J. Am. Chem. Soc.*, **90**, 3890 (1968).

4) K. Akiba, Y. Ohara, M. Hisaoka, and N. Inamoto, *Heterocycles*, **3**, 567 (1975).

5) All compounds (**2a**-**h**) gave correct elemental analysis and showed the presence of BF_4^- in IR (br and vs 1000-1100 cm^{-1} in KBr disc).

Received, 21st October, 1976