Tetrahedron Letters,Vol.26,No.31,pp 3743-3744,1985 0040-4039/85 $3.00 + .00
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REGIOSELECTIVE ONE-STEP γ-CHLORINATION OF ALKANESULFONAMIDES. PREPONDERANCE OF 1,5-H MIGRATION FROM SULFONYL VERSUS AMIDE MOIETY IN SULFONYLAMIDYL RADICALS

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Summary. Alkanesulfonamides **1** are converted regioselectively into 3-chloroalkanesulfonamides **2** in one-pot reaction with $Na_2S_2O_8$-$CuCl_2$. N-Amylbutanesulfonamide **7** is substituted predominantly on sulfonyl moiety.

In course of our investigations of one-step remote oxidative functionalization of ketones[1], alkanoic acids and their amides[2] at non-activated C-atom we have found recently that N-methanesulfonylalkylamines cyclize regiospecifically into N-methanesulfonylpyrrolidines by oxidation with $Na_2S_2O_8$-$CuCl_2$[3].

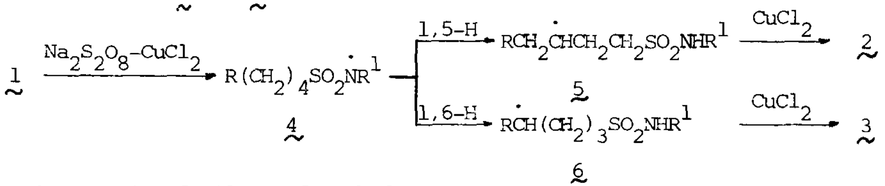
The subject of present communication is direct oxidative chlorination of alkanesulfonamides **1** into 3- and 4-chloroalkanesulfonamides **2** and **3**, the first strongly predominating (Table), by treatment with $Na_2S_2O_8$-$CuCl_2$ (molar ratio **1**:$Na_2S_2O_8$:$CuCl_2$=1:1:1)[4].

$$\underset{\mathbf{1a\text{-}d}}{R(CH_2)_4SO_2NHR^1} \xrightarrow{Na_2S_2O_8\text{-}CuCl_2} \underset{\mathbf{2a\text{-}d}}{RCH_2CHClCH_2CH_2SO_2NHR^1} + \underset{\mathbf{3a\text{-}d}}{RCHCl(CH_2)_3SO_2NHR^1}$$

a R=R^1=H; b R=H, R^1=Me; c R=Me, R^1=H; d R=Et, R^1=Me.

Sulfonamide	Conversion,%	Products[5], yields (%) based on **1** converted	
1a	47	**2a**, 54	**3a**, 17
1b	50	**2b**, 65	**3b**, 10
1c	43	**2c**, 40	**3c**, 30
1d	20	**2d**, 62	**3d**, 23

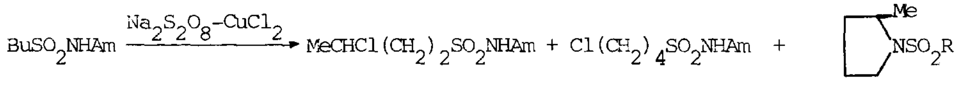
The observed regioselectivity of oxidative chlorination is in accordance with the mechanism involving generation of N-centred sulfonylamidyl radicals **4** undergoing 1,5- and 1,6-H shifts to C-centred radicals **5** and **6**. Subsequent oxidation of **5** and **6** with chlorine-transfer affords **2** and **3**.



$$\mathbf{1} \xrightarrow{Na_2S_2O_8\text{-}CuCl_2} \underset{\mathbf{4}}{R(CH_2)_4SO_2\dot{N}R^1} \left[\begin{array}{l} \xrightarrow{1,5\text{-}H} \underset{\mathbf{5}}{RCH_2\dot{C}HCH_2CH_2SO_2NHR^1} \xrightarrow{CuCl_2} \mathbf{2} \\ \xrightarrow{1,6\text{-}H} \underset{\mathbf{6}}{R\dot{C}H(CH_2)_3SO_2NHR^1} \xrightarrow{CuCl_2} \mathbf{3} \end{array} \right.$$

Comparative facility of H shift from sulfonyl vs. amide moiety in sulfonylamidyls[6], being principle matter for amidyl radicals in general[7], has not been studied previously.

We have found that N-amylbutanesulfonamide 7 by oxidation with $Na_2S_2O_8$-$CuCl_2$ is converted in chloroalkanesulfonamides 8 and 9 along with sulfonylpyrrolidines 10 (R=Bu) and 11 (R = $MeCHClCH_2CH_2$) (^1H NMR, g.l.c.-m.s.), the yields being 40, 5, 35 and 10% on converted 7 respectively, conversion 30%).



$$BuSO_2NHAm \xrightarrow{Na_2S_2O_8-CuCl_2} MeCHCl(CH_2)_2SO_2NHAm + Cl(CH_2)_4SO_2NHAm +$$

7 8 9 10,11

Thus the sulfonylamidyls $BuSO_2\dot{N}Am$ 12 generated from 7 are rearranged predominantly through H shift from sulfonyl moiety with formation of 9 and 8, the latter being evidently the precursor of 11. Pyrrolidine 10 is formed as a result of competitive 1,5-H shift from amide moiety in 12 [3].

The prevalence of 1,5-H shift from sulfonyl moiety is observed also in competitive oxidation of 1b and $MeSO_2NHAm$ 13 into 2b, 3b and N-methanesulfonyl-2-methylpyrrolidine (yields being 27, 5 and 10% respectively on starting 1b or 13, their conversions 45 and 11%). The most probable reason for this preponderance is conformationally and energetically advantageous (5- or 6-membered cyclic form) participation of SO_2-group O-atoms in stabilization of rearranged radicals such as 5 and 6. This stabilization could not take place in rearranged radicals forming by H shift from amide moiety (7-membered cycle).

Typical procedure. A solution of 11.9 g (0.05 mole) of $Na_2S_2O_8$ in 50 ml of water was added dropwise to a stirred mixture of 6.85 g (0.05 mole) of 1a and 8.55 g (0.05 mole) of $CuCl_2 \cdot 2H_2O$ in 100 ml of water at 90°C. The mixture was kept at the same temperature for 5 h, cooled to 20°C and extracted with ether (3 x 100 ml), extracts were dried ($MgSO_4$). The residue after solvent removal was analysed with ^1H NMR (250 MHz), g.l.c., and g.l.c.-m.s. The mixture of 2a and 3a was obtained after removal of unreacted 1a by fractional distillation.

References and Notes.

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(Received in UK 21 May 1985)