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PRELIMINARY NOTE

Fluoroalkylation and Fluoroalkoxylation. Magnesium Single-Electron-Transfer Induced Synthesis of 2-Fluoroalkylpyrroles

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SUMMARY

An $S_{RN}1$ reaction, initiated by single electron transfer from magnesium, provides an efficient method for the regioselective synthesis of 2-fluoroalkylpyrroles from pyrrole and the corresponding fluoroalkyl iodides.

Direct fluoroalkylation of N-methyl pyrrole with fluoroalkyl iodides was first reported by Wakselman et al. at high temperature, but it was failed for pyrrole itself under similar conditions[1]. However, the latter reaction could be realized photochemically, although the yield was low (~30%)[2]. Recently, we observed that transition metals, e.g. zinc or copper, could induce the reaction, but the stoichiometric amounts of metal were necessary[3]. We now report that in the presence of catalytic amounts of magnesium turnings (25 mol%), pyrrole (2) can be fluoroalkylated by the reaction with fluoroalkyl iodides (1) in DMF under mild conditions, giving good yield of 2-fluoroalkylpyrrole (see Table).

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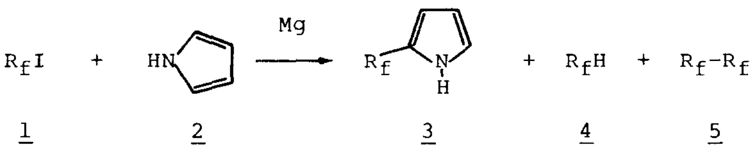
TABLE

Magnesium-catalysed fluoroalkylation reactions of pyrrole[e]

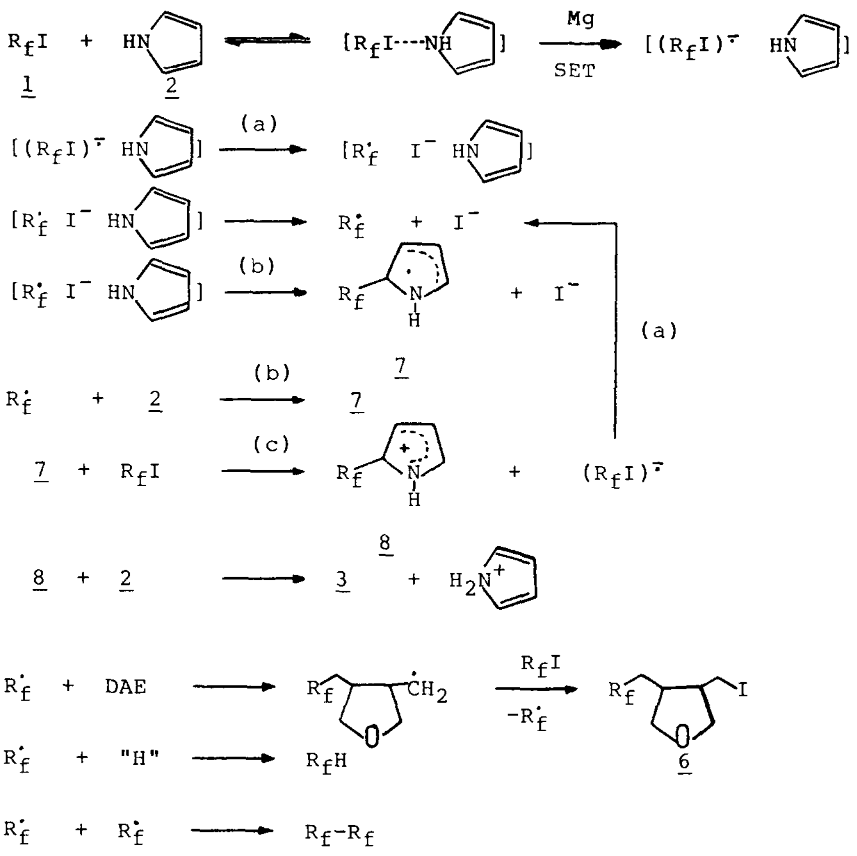
Run	Reactant	T(°C)	t(h)	Conv.(%)[f]	Products(%)[g]	
					3(b.p./mmHg)	5
1	1a	60	20	95	65(62°C/10)	18
2	1a	60	10	69.5	64	13
3	1a	90	10	100	54.6	21.6
4	1a	60	5	40	83	8.8
5	1b[h]	80	15	90	58(67°C/5)	15
6	1c	120	7	100	47(93°C/4)	36.5
7	1d[i]	60	20	100	53	22
8	1b, p-DNB (20 mol%)	80	15	30.1	67	15
9	1a	40	20	16.7	78	5.9
10	1a, DAE	60	15	100	28.4	61.7[j]
11	1a	120	20	58	72.3	13.5[k]

[e] Reactant ratio, 1:2:Mg=1:2:20% (unless otherwise specified); in DMF. [f] Determined by ^{19}F NMR. [g] The structure of 3 was determined by elemental analyses, IR, MS and ^{1}H, ^{19}F NMR; sometimes a small amount of R_fH (4) was detected by ^{19}F NMR. [h] 50 mol% of Mg was used. [i] 100 mol% of Mg was used. [j] 6(1a: 2:DAE=1:2:2). [k] product 4; reaction catalyzed by Al (50 mol%).



R_f: $Cl(CF_2)_n$, n=4(a), 6(b), 8(c); $CF_3(CF_2)_2$ (d)

The reaction was highly regioselective,and only one fluoroalkyl group was introduced into the 2-position of pyrrole. Increasing the amount of magnesium used from 20 to 100 mol% has little influence



Scheme

on the reaction. The aprotic polar solvent, such as DMF, seemed necessary; thus, only 1-hydrofluoroalkane (4) was obtained if acetic anhydride or tetrahydrofuran was used as the solvent instead of DMF. Raising the temperature slightly accelerated the reaction, but also increased the yield of the coupled products (5).

The possibility of forming the Grignard reagent (R_fMgI) in DMF has been excluded in our previous work [4]. On the other hand, the conversion was decreased to 30% compared with that of a control (95%) by the addition of p-dinitrobenzene (p-DNB). Furthermore, in the presence of diallyl ether (DAE), both fluoroalkylated pyrroles and tetrahydrofuran derivatives (6) were obtained. These results showed that a radical intermediate might be involved in the reaction.

The reaction Scheme suggested includes the cycle of the decomposition (or elimination) of the anion radical (a), radical addition (b) and electron transfer (c), as part of a typical $S_{RN}1$ mechanism [5] initiated by SET from magnesium. This means that stimulation by some metals may be a new initiation method for $S_{RN}1$ [6]. Aluminium has also been found able to induce the reaction at a higher temperature (120°C/20h) to give the product 3 in a yield of ~40%.

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1 I.Cantacuzene, C.Wakselman and P.Korme, J.Chem.Soc., Perkin Trans I., (1977) 1565.

2 Y.Kobayashi, I.Kumadaki, A.Ohsawa, S.Murakami and T.Nakano, Chem.Pharm.Bull., **26** (1978) 1247.

3 Q.Y.Chen and Z.M.Qiu, Youji Huaxue, (1987) 44; Acta. Chimica Sinica, to be published.

4 Q.Y.Chen and Z.M.Qiu, J.Fluorine Chem., **36** (1987) 149.

5 R.N.Russell, Preprints (Symoposia), Division of Petroleum Chemistry, INC, ACS, **29** (1984) 338.

6 R.A.Rossi and R.H.Rossi, 'Aromatic Substitution by the $S_{RN}1$ Mechanism', ACS Monograph 178, Am.Chem.Soc., Washington,D.C., 1983, p.161.