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NUCLEOPHILIC SUBSTITUTION IN FLUOROOLEFINS. I

Reactions of Amines with Alkoxyfluorocycloolefins

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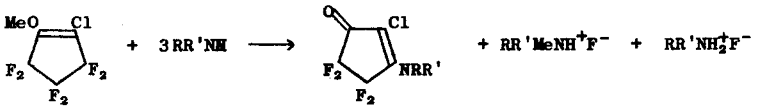
Primary and secondary amines react rapidly with perfluoro- and halofluoroolefins to give aminofluoroalkanes and fluorovinylamines by addition and addition-elimination reactions.[1] We report here on the reaction of several alkoxyfluorocycloolefins with primary and secondary amines to give alkylamino-unsaturated cyclic ketones.

1-Methoxy-2-chlorohexafluorocyclopentene (I) reacts rapidly and smoothly at 25° with primary and secondary amines to give the corresponding 1-alkylamino-2-chloro-3-ketotetrafluorocyclopentenes (II). The reaction of (I) with diethylamine was studied in some detail: on mixing 6 g (25 mmoles) of (I) and 7.3 g (100 mmoles) of diethylamine in 50 ml of ether at 25°, there was immediate precipitation of amine hydrofluoride salts; reaction was complete in five hours. The salt was filtered from the mixture, washed with ether and dissolved in D_2O. The H^1 n.m.r. spectrum of the salt solution showed a $C\underline{H}_3N<$ singlet at 6.97 τ, a $CH_3C\underline{H}_2N<$ quartet centered at 6.92 τ, and a $C\underline{H}_3CH_2N<$ triplet at 8.70 τ. The latter resonance bands were in an approximate area ratio of 2:3; no integral ratio was found for $C\underline{H}_3N<$ resonance to either of



I II

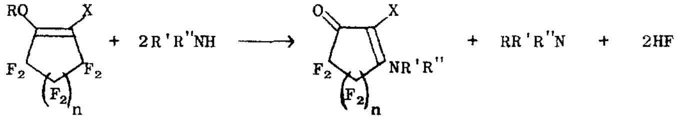
the other bands because of the presence of diethyl ammonium fluoride.

Evaporation of the ethereal reaction mixture gave 5.8 g of crude product. Recrystallization of the white solid from cyclohexane gave 4.9 g (19 mmoles, 75% yield) of 1-diethylamino-2-chloro-3-ketotetrafluorocyclopentene (IIa, R = R' = Et), m.p. 57-8°; IR (CCl_4): (C = O) 5.7 μ, (C = C) 6.25 μ; H^1 n.m.r. (CCl_4): $CH_3\underline{CH_2}N$, 6.28 τ; $\underline{CH_3}CH_2N<$, 8.63 τ; calculated for $C_9H_{10}ONClF_4$: C 41.65; H 3.86; N 5.40; Cl 13.7. Found: C 42.0; H 4.09; N 5.59; Cl 13.3. Independent synthesis of IIa from 1,2-dichloro-3-ketotetrafluorocyclopentene[2] and diethylamine gave a product identical in spectral features, m.p. and m.m.p. with IIa.

Other ketones formed by the reaction of primary and secondary amines with several methoxyfluoroolefins were characterized by their infrared spectra and elemental analyses. Results are summarized in Table I.

Table I

Reaction of Amines with Alkoxyfluorocycloolefins[a]



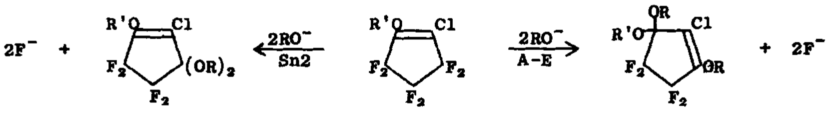
R, X	Amine	Product (1-alkylamino-2-X-3-ketotetra(di)-fluorocycloolefin): m.p.[b]; IR[c] (μ)	% Yield
(n = 1)			
MeO, Cl	Et_2NH	57-58°; 5.7, 6.22	75
" "	$C_6H_5NH_2$	150-151°; 5.75, 6.38	73
" "	$n-BuNH_2$	64-65°; 5.70, 6.20	53
" "	$(n-Bu)_2NH$	65-66°; 5.8, 6.28	69
EtO, Cl	Et_2NH	same as for R = MeO, X = Cl;	20
iPrO, Cl	Et_2NH	no reaction	
MeO, MeO	Et_2NH	52-53°; 5.82, 6.15, 6.25	18
(n = 0)			
MeO, Cl	Et_2NH	b.p. 70°/0.4 mm; 5.62, 6.24	38

[a] Method of preparation of these olefins is described in ref. 3.
[b] Not corrected.
[c] In CCl_4.

1-Ethoxy-2-chlorohexafluorocyclopentene reacts very slowly with diethylamine or n-butylamine at 25°. The rate is only about 1/20th the rate observed for the corresponding reaction with the methoxyolefin. 1-Isopropoxy-2-chlorohexafluorocyclopentene and either n-butylamine or diethylamine in excess amine solvents gives no reaction up to the boiling points of the solvents (78° or 56°). Triethylamine reacts readily with I to give a dark oil which has not been characterized.

Direct displacement by amine at the alkyl C-O bond would lead to an intermediate ketone which would give the observed final product on reaction with additional amine. However, this mechanism is contraindicated by the demonstrated ease of reaction of alkoxide ion with these same alkoxyfluoroolefins to give trialkoxyolefins, not alkoxyketoolefins.[1c, 3]

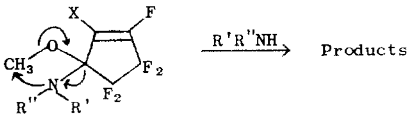
An independent study[4] of the reaction of alkoxide ion (methoxide, ethoxide, isopropoxide) with 1-alkoxy-2-chlorohexafluorocyclopentene and the 1-methoxycyclobutene homolog was made using n.m.r. to distinguish between isomeric trialkoxyolefins (III or IV).



IV III

In every case only isomer III was found, indicating the reaction proceeds through a series of addition-elimination (A-E) reactions.[5]

This result requires that amines react with these same 1-alkoxy-2-chlorohexafluorocyclopentenes to give a 1-alkoxy-1-alkylamino intermediate addition product (V). Either concurrent with or subsequent to reaction with more amine, V undergoes internal elimination of a secondary or tertiary amine to form a carbonyl group. Presumably formation of a conjugated, amino-olefin-carbonyl system is the driving force for this reaction.[7]



V

Thus the order of reactivity of alkoxyolefins towards an amine found in this system: MeO > EtO ≫ i-PrO, must be associated with steric hindrance at the double bond, not at the alkyl C-O bond, for which this order is commonly observed.[8]

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2. D. H. Campbell, Thesis, Purdue Univ., 1955, p. 83.

3. J. D. Park, C. M. Snow and J. R. Lacher, J. Am. Chem. Soc., 73, 2342 (1951).

4. Results of this study, including rates of substitution by methoxide ion in various chlorofluorocycloolefins, will be published separately.

5. Although these data permit no distinction between a concerted (Sn2') or stepwise mechanism (addition-elimination) with formation of an intermediate carbanion, we believe the stepwise mechanism is more consistent with the observations that (1) nucleophilic substitution in 1,2-dichloroperfluoroolefins always leads to C-Cl cleavage, never C-F cleavage; and (2) at $pH < 10$, base-catalysed addition rather than substitution occurs.[1a, 6]

6. A. P. Stefani, J. R. Lacher and J. D. Park, J. Org. Chem., 25, 676 (1960).

7. 1,3,3-Trimethoxy-2-chlorotetrafluorocyclopentene does not rearrange to the ketone at 200°; 1-diethylamino-3,3-dimethoxy-2-chlorotetrafluorocyclopentene does give some ketone when heated but it could be formed by an acid-catalysed hydrolysis.

8. A. Streitweiser, Jr., Chem. Rev., 56, 584 (1956).