C-ALKYLATION OF N-ALKYLANILINES BY POLYFLUOROKETONES

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Aniline reacts vigorously with highly electrophilic polyfluoroketones to form N-alkylation products, namely, geminal aminohydroxy compounds, which are stable under ordinary conditions [1, 2]. However, the reaction of hexafluoroacetone with aniline and N-alkylanilines at 170-200°C leads to C-alkylation products [1, 3], which are also formed upon heating anilines with hexafluoroacetone hydrate at reflux [4]. The C-alkylation of aniline by hexafluoroacetone has been considered a stepwise process involving N-alkylation and a subsequent shift of the  $\alpha$ -hydroxyhexafluoroisopropyl group from the nitrogen atom initially to the ortho position relative to the amino group and then to the para position.

On the other hand, the formation of C-alkylation products in the reaction of an aromatic amine and polyfluoroketone may be considered as a radical—ion process. The high electrophilicity of polyfluoroketones would lead us to expect the formation of radical—ion pairs under mild conditions. The homolytic transformations of such pairs usually occur with zero activation energy. Thus, the C-alkylation of anilines by polyfluoroketones by a radical—ion mechanism should occur under extremely mild conditions. In the present work, the conditions for the C-alkylation of N-alkylanilines by polyfluoroketones were found.

The C-alkylation of N-ethylaniline by hexafluoroacetone occurs smoothly in chloroform. Only N-ethyl-4-( $\alpha$ -hydroxyhexafluoroisopropyl)aniline (I) was obtained quantitatively upon mixing equivalent amounts of the reagents in CHCl<sub>3</sub> at -60° to -50° and subsequent spontaneous warming of the mixture to 20°C after maintenance for 1 h. Under analogous conditions, Nmethyl-4-( $\alpha$ -hydroxyhexafluoroisopropyl)-o-substutited anilines (II) and (III) were formed in high yield regiospecifically from N-methyl-o-toluidine and N,N-dimethylaniline. Under the

$$R' = Et, R' = R'' = H (I); R = R'' = Me, R' = H (II); R = R'' = H (III).$$

same conditions, the reaction of N-ethylaniline with 2.2 equivalents of hexafluoroacetone gives N-ethyl-2,4-di( $\alpha$ -hydroxyhexafluoroisopropyl)aniline (IV). However, even in the pres-C(CF<sub>3</sub>)<sub>2</sub>OH

-NHEt + (CF<sub>3</sub>)<sub>2</sub>CO 
$$\xrightarrow{-c_0 \rightarrow 20^{\circ}}_{\text{CHCl}_3}$$
 HO(CF<sub>3</sub>)<sub>2</sub>C -  $\bigvee$  -NHEt (IV) (80,6%)

ence of a large excess of hexafluoroacetone in CHCl<sub>3</sub>, N,N-dimethylaniline gives only monosubstituted product (III).

Methyl trifluoropyruvate reacts with N,N-dimethylaniline in  $CHCl_3$  similarly to hexa-fluoroacetone to form the 4-substituted aniline (V)

$$\sum -N(CH_3)_2 + CF_3COCO_2Me \xrightarrow{-60 \rightarrow 20^\circ}_{CHCl_3} HO(CF_3)C - \sum_{\substack{i \\ CO_2Me}} -N(CH_3)_2$$

The mild conditions and regiospecificy for the C-alkylation of anilines by polyfluoroketones are in accord with a radical—ion mechanism for these reactions. However, proof for this hypothesis requires special spectral studies.

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TABLE 1	ຕ໌ 1	U	NMR	Spectra	of	-(I)	(II)

		Che	mical shif	ts (ô, ppm)				Chemical s	hifts (δ, pl	)m)		13C-19F	soupling
Compound		1	63	en la constante da constante	4	5	9		∞	4,	4"	ULUSIAILIS,	2J
$CH_{3}-CH_{3}-HN-\overbrace{2}^{5}-C-OH$	(I)	150,6	111.7	128,1	117,8	128,1	111.7	37,9	14,2	78,1	124,5	286,9	27,1
CH <sub>3</sub> -HN- CH <sub>3</sub> -HN- CH <sub>3</sub> -COH CF <sub>3</sub> CF <sub>3</sub> CF <sub>3</sub>	(11)	149,4	122,7	129,0	119.6	126,8	109,4	30,6	17,4	78,3	124,5	286,7	27,2
$\begin{array}{c} CH_{3} \\ 7\\ CH_{3} \\ CH_{3} \end{array} \xrightarrow{5} \begin{array}{c} CF_{3} \\ C-OH \\ CH_{3} \\ CF_{3} \\ CF_{3} \end{array}$	(111)	152,3	112,4	128,3	118,2	128,3	112,4	40,1	1	78,1	124,4	286,8	29.6
$ \begin{array}{c} \mathrm{CH}_3 - \mathrm{CH}_3 - \mathrm{CH}_3 - \mathrm{HN} - \underbrace{5}_{\mathrm{CH}_3} - \underbrace{6}_{\mathrm{CH}_3} - \underbrace{6}_{\mathrm{C}_3} - \underbrace{6}_{\mathrm{C}_3} - \underbrace{6}_{\mathrm{C}_3} - \underbrace{6}_{\mathrm{C}_3} - \underbrace{6}_{\mathrm{C}_3} \\ \mathrm{CH}_3 - \underbrace{6}_{\mathrm{C}_3} - \underbrace{6}_{\mathrm{C}_3} - \underbrace{6}_{\mathrm{C}_3} - \underbrace{6}_{\mathrm{C}_3} - \underbrace{6}_{\mathrm{C}_3} \\ \mathrm{CH}_3 - \underbrace{6}_{\mathrm{C}_3} - \underbrace{6}_{\mathrm{C}_3} - \underbrace{6}_{\mathrm{C}_3} - \underbrace{6}_{\mathrm{C}_3} - \underbrace{6}_{\mathrm{C}_3} \\ \mathrm{CH}_3 - \underbrace{6}_{\mathrm{C}_3} - $	(1V)	150,5	113,4	129,7	119,0	127,8	115,4	39,5	14,0	77.5 81,3(2')	123.7 123.9(2'')	287,8 288,8	27.2 27.4
$ \begin{array}{c} \begin{array}{c} \begin{array}{c} \begin{array}{c} \begin{array}{c} \begin{array}{c} \begin{array}{c} \end{array}\\ \end{array}\\ \end{array}\\ \end{array} \end{array} $ $ \begin{array}{c} \begin{array}{c} \end{array}\\ \end{array} $ $ \begin{array}{c} \end{array} $ $ \end{array} $ $ \begin{array}{c} \end{array} $ $ \begin{array}{c} \end{array} $ $ \end{array} $ $ \begin{array}{c} \end{array} $ $ \begin{array}{c} \end{array} $ $ \end{array} $ $ \end{array} $ $ \begin{array}{c} \end{array} $ $ \end{array} $ $ \begin{array}{c} \end{array} $ $ \end{array} $ $ \end{array} $ $ \begin{array}{c} \end{array} $ $ \end{array} $ $ \begin{array}{c} \end{array} $ $ \end{array} $ $ \end{array} $ $ \end{array} $	* (V)	152,5	112.6	128,2	121,8	128,2	112,6	40,3	I	79,4	124,6	287.5	43.2
*ôMe 57.7, ôC = 0 169.	9 ppm.												

Com-	Vield	% mp. °G	P.		Found, %			
pound		·		п <sub>f</sub>	с	Н	N	F
(I)	92,0	93-94		),53	46,32	3,81	4,80	39,14
(11)	88,9	100-101		),68	46,07	3,69	4,78	39,34
(III)	90,2	80-81 *		),46	36,76	$2,\!45$	2,92	50,15
(IV)	80,6	136-137						
(V)	93,3	112-113		),57	51,90	4,93	4,97	20,97
	Com-	Chemical	M+		Ca	alc., %		
	pound	formula		C	н	N	F	
	(I)	C11H11NOF6	287	45,99	3,83	4,88	39,72	
	(II)	$C_{11}H_{11}NOF_6$	287	45,99	3,83	4,88	39,72	
	(III)							
	(IV)	$\mathrm{C}_{14}\mathrm{H}_{11}\mathrm{NO}_{2}\mathrm{F}_{12}$	453	37,10	2,43	3,09	50,33	
	(V)	C <sub>12</sub> H <sub>14</sub> NO <sub>3</sub> F <sub>3</sub>	277	51,98	5,05	5,05	20,57	

TABLE 2. Physical Indices of (I)-(VI)

\*See the work of Gilbert [3].

Products (I)-(V) are white crystalline compounds which are stable under ordinary conditions. The structures of these products were established by <sup>13</sup>C NMR spectroscopy and mass spectroscopy as well as by elemental analysis.

Table 1 indicates that the <sup>13</sup>C NMR spectra of (I), (III), and (V) have two signals corresponding to two pairs of magnetically equivalent nuclei, which is evidence for 1,4substitution of the benzene ring. Comparison of the  $\delta C^4$  values in N-ethylaniline (115.7 ppm) [5] and in (I) (117.8 ppm) indicates that the replacement of a hydrogen atom by the  $\alpha$ -hydroxyhexafluoroisopropyl group does not have a significant effect on the chemical shift of the corresponding carbon nucleus. Hence, we were able to determine the position of the hydroxyhexafluoroisopropyl group in (II) and (V). The  $\delta^{13}C$  values given in Table 1 are evidence for the correctness of the signal assignment.

## EXPERIMENTAL

The <sup>13</sup>C NMR spectra were taken on a Bruker WP-200 spectrometer at 50.31 MHz, 3 sec relaxation hold, and TMS as standard. The mass spectra were taken on an AEI MS-30 spectrometer. The R<sub>f</sub> values were determined on Kavalier Silufol UV-254 (manufactured in Czechoslovakia) using 5:1 CCl<sub>4</sub>—acetone as the eluent. The spots were detected by UV light. The physical indices of (I)-(VI) are given in Table 2.

<u>N-Ethyl-4-( $\alpha$ -hydroxyhexafluoroisopropyl)aniline (I)</u>. A solution of 5.11 g N-ethylaniline in 20 ml CHCl<sub>3</sub> was placed in a glass ampul, cooled to -60°C, and then 6.95 g hexafluoroacetone was condensed into this ampul. The ampul was sealed and left at 20°C to warm. The ampul was opened 1 h after warming, the solvent was evaporated, and the residue was crystallized from hexane to yield 11.1 g white crystalline (I).

 $\frac{N-Methyl-4-(\alpha-hydroxyhexafluoroisopropyl)-o-toluidine (II)}{2.24 g N-methyl-o-toluidine and 3.35 g hexafluoroacetone.}$  The yield of (II) was 5.1 g.

<u>N,N-Dimethyl-4-( $\alpha$ -hydroxyhexafluoroisopropyl)aniline (III)</u> was obtained analogously from 2.42 g dimethylaniline and 3.35 g hexafluoroacetone. The yield of (III) was 5.18 g.

<u>N-Ethyl-2,4-di( $\alpha$ -hydroxyhexafluoroisopropyl)aniline (IV)</u> was obtained analogously from 2.8 g ethylaniline and 8.3 g hexafluoroacetone. The yield of (IV) was 8.4 g.

<u>N,N-Dimethyl-4-( $\alpha$ -hydroxy- $\alpha$ -carbomethoxytrifluoroethyl)aniline (V).</u> A solution of 2.42 g N,N-dimethylaniline in 10 ml CHCl<sub>3</sub> was added to a solution of 3.12 g methyl trifluoropyruvate in 10 ml CHCl<sub>3</sub> at -60°C. The mixture was stirred and let warm at 20°C. The solvent was evaportated 3 h after warming and the residue was crystallized from hexane to give 5.2 g white crystalline (V).

## CONCLUSIONS

Conditions were found for the mild C-alkylation of secondary and tertiary aromatic amines by hexafluoroacetone and methyl trifluoropyruvate. The regiospecific formation of the products of C(4)-alkylation was demonstrated.

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## TEMPERATURE DEPENDENCE OF THE RATE OF THE CATALYTIC OXIDATION

OF 1-HEXENE IN THE PRESENCE OF NEUTRAL SALTS

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In our previous work [1-3], we showed that dehydration of the catalyst occurs in the catalytic oxidation of olefins by molecular  $O_2$  in the presence of manganese tetra-p-methoxy-phenylporphyrinatochloride (TPPMnCl) and excess NaBH<sub>4</sub>, which results, after long periods, in a decrease in the catalytic activity of TPPMnCl. The corresponding rate constants  $k_4$  and  $k_5$  of the catalyst dehydration steps were found in our previous work [3] in a study of the oxidation kinetics of 1-hexene. We found times t  $\sim \max\{1/k_4; 1/k_5\}$ , beginning at which the rate of product formation is given by the constant  $\lambda_1$  [3] proportional to  $k_4$  and  $k_5$ . In order to elucidate the nature of the processes determining the observed rate constants, we studied the temperature dependence of the observed rate constant  $\lambda_1$  in the oxidation of 1-hexene (for oxidation  $\leq 20\%$ ) and the effect of the presence of neutral salts in the reaction system on this constant [4].

The oxidation of 1-hexene was carried out in the presence of LiF in N,N-dimethylformamide at 278-310°K. The reaction kinetics was studied by gas-liquid chromatography relative to the consumption of 1-hexene [3]. The characteristic dependence of the effective rate constant  $\lambda_1$  [3], which describes the kinetics of product formation for t >30 min on the LiF concentration is given in Fig. 1. Analysis of the temperature dependences of  $\lambda_1$  in the presence of LiF (Fig. 2) gave an empirical equation

$$Q(C) = 9 \cdot (1 + 48 \cdot C) \text{ kJ/mole}$$
 (1)

for the effective activation energy Q(C), where C is the salt concentration in moles/liter. If C is given in terms of the mean distances between catalyst molecules and the closest salt anions (according to Chandrasekar [5],  $C \simeq 0.21/R^3$ , where R is given in nm), then the observed increase in Q(C) with increasing C (decrease in R) may be related to an increase in the mean coulombic ion-dipole interaction in the associated species consisting of the reduced catalyst molecule and the salt anion, with which both the reagents (O<sub>2</sub> and the olefin) and destructive agents may react.

The relatively low values of Q found in this work indicate the transport nature of the steps determining the effective rate constant for product formation at long reaction times (including catalyst destruction), while the form of the dependence of Q on C(R) indicates the coulombic nature of the interactions determining these steps.

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