253. Photoreduction of Cyclic α-Fluoroketones

by **Karin Reinholdt**[1] and **Paul Margaretha***

Institut für Organische Chemie und Biochemie, Universität, D-2000 Hamburg 13

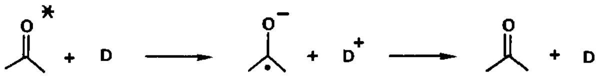
(26.IX.83)

Summary

Irradiation of the α-fluoroketones **1a** and **6a** in i-PrOH selectively affords the parent ketone **1b** and **6b**, respectively. It is concluded that in this solvent heterolytic C–F bond cleavage of the anion radical – formed by electron transfer to the excited fluoroketone – is a faster process than the subsequent protonation by the cation radical of the solvent. In cyclohexane **1b** and **6b** are only formed in minor amounts, the fluorinated *RH*-reduction product **4** now being the major product from **1a**. In non-reducing solvents as *t*-BuOH or benzene 2-fluorocyclohexanone (**1a**) exhibits a similar behavior as cyclohexanone (**1b**) on excitation. The quantum yields for α-cleavage are alike for both compounds, but oxetane formation with 2-methylpropene as olefinic component occurs much more readily with **1a** than with **1b**.

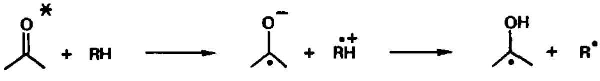
Photoreduction of a ketone consists of electron transfer from a donor molecule to the excited carbonyl compound [1] [2]. In the absence of any further chemical transformation back electron transfer occurs, this sequence represents the quenching of the excited ketone by the donor *(Scheme 1)*.

Scheme 1



When the cation radical of the donor acts as a proton source the overall reaction corresponds to an H-abstraction by the excited carbonyl compound *(Scheme 2)*.

Scheme 2



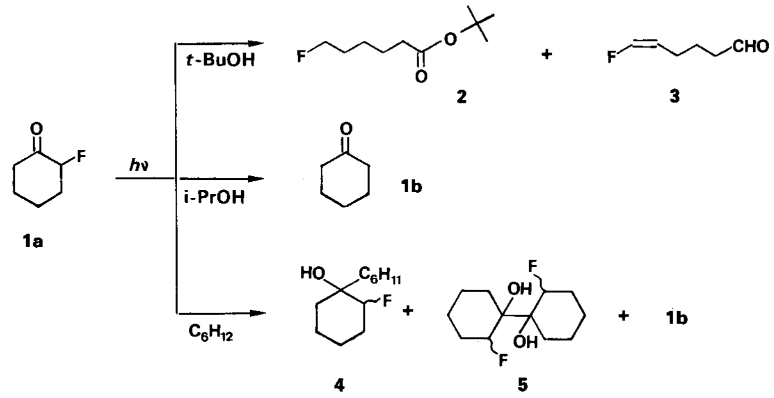
---

[1] Part of the planned doctoral thesis, University of Hamburg.

The possibility of observing the intermediate radical ion pair in this sequence depends on the relative rates of electron transfer *vs.* proton transfer. For aliphatic ketones and amines, evidence for such a sequence has been established [3] [4] [5], while for alcohols or hydrocarbons the two steps usually occur in an almost synchronous fashion (H-atom transfer). α-Fluoroketones being reduced at *ca.* 0.5 V less cathodic potentials than the parent ketones [6] are consequently better oxidizing agents in their excited states. This feature applies to other α-haloketones as well, but in chloro-, bromo- and iodoketones the excitation energy ($\approx$ 80 kcal/mol) is already sufficient to induce homolytic C-halogen bond cleavage [7], while no homolytic C–F bond cleavage (D = 116 kcal/mol) is expected to occur in α-fluoroketones. We now present evidence for the distinct intermediacy of anion radicals in the light-induced reaction of aliphatic α-fluoroketones with i-PrOH.

Irradiation (λ = 300 nm) of 2-fluorocyclohexanone (**1a**)[2]) in *t*-BuOH affords *t*-butyl 6-fluorohexanoate (**2**) in 30% yield. Traces (8%) of 6-fluoro-5-hexenal (**3**) are also formed in this reaction. In i-PrOH α-cleavage products are not observed, instead cyclohexanone (**1b**) is formed selectively (60–65% at low degrees of conversion). In cyclohexane the RH-reduction product 2-fluoro-1-cyclohexylcyclohexanol (**4**) is formed as the main product (58%) besides **1b** (22%). Structure **5** is tentatively assigned to a higher molecular weight product formed in 15% yield *(Scheme 3)*.

Scheme 3



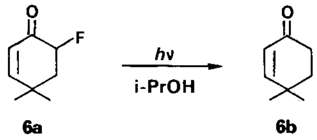
A similar solvent-dependent selectivity is observed in the irradiation of 6-fluoro-4,4-dimethyl-2-cyclohexenone (**6a**). Slow degradation without detection of any products is observed in *t*-BuOH while in i-PrOH the parent enone **6b** is formed selectively (37%). In cyclohexane **1b** is again a minor product (10%). No other products have been detected *(Scheme 4)*.

The strong influence of the α-fluoro substituent in oxetane-forming [2+2]-photocycloadditions for **6a** as compared to **6b** has already been discussed in detail [9] [10] [11].

---

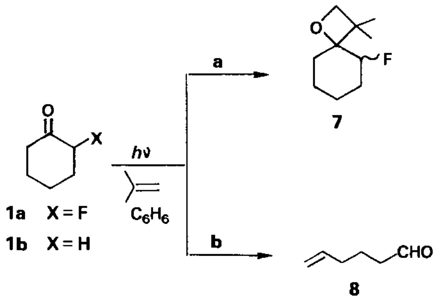
[2]) Irradiation of **1a** in MeOH afforded methyl 6-fluorohexanoate in very modest yields (GC) [8].

Scheme 4



A similar increase in efficiency in oxetane formation is also observed in the irradiation of **1a** and **1b** in benzene with 2-methylpropene as olefinic component. For **1a** the oxetane **7** is obtained in 51 % isolated yield while **1b** only gives the α-cleavage product **8** *(Scheme 5)*.

Scheme 5



The quantum yields for the photoreactions are summarized in *Table 1* and the spectroscopic data of the photoproducts in *Table 2*.

The results of the light-induced experiments in *t*-BuOH or benzene confirm the expectation that the C–F bond in **1a** is not cleaved in the absence of a reducing agent, as in these solvents **1a** exhibits similar behavior as the parent ketone **1b**. Fluoroenone **6a** does not seem to undergo the lumiketone rearrangement as does enone **6b**. The enhanced

Table 1. *Quantum Yields for Photoreactions of* **1a** *and* **6a** *(10^{-1} M, λ = 300 nm)*

Solvent	Φ_{-} a)		Φ_{+} b)			
i-PrOH	**1a**	0.29	**1b**	0.18		
	6a	0.08	**6b**	0.03		
	1b	0.39		[12]		
	6b	0.04		[13]		
Cyclohexane	**1a**	0.38	**1b**	0.08,	**4**	0.20
	6a	0.07	**6b**	0.007		
	1b	0.19		[14]		
	6b	< 0.001		–		
t-BuOH + C_6H_6 (95:5)	**1a**	0.27	**2**	0.12,	**3**	0.02
	6a	0.01		–		

a) Loss of starting material.
b) Product formation.

Table 2. *Spectroscopic Data of Photoproducts*

Compound	IR (CCl_4)	^1H-NMR ($CDCl_3$)	MS
2	1730, 1150	4.42 (*t*, $J = 48$, 6 and 6, 2H) 2.20 (*t*, $J = 8$, 2H) 1.8 – 1.3 (*m*, 6H) 1.40 (*s*, 9H)	190 (M^+) **57**
3	1712, 1685	9.30 (*t*, $J = 1$, 1H) 6.45 (*m*, $J_{HF} = 84$, 1H) 4.80 (*m*, $J_{HF} = 44$, 1H) 2.4 – 1.5 (*m*, 6H)	116 (M^+) **72** ($M^+ - CH_3CHO$)
4			200 (M^+) **98**
5			194 ($M^+ - 2HF$) **98**
7	1020, 980	4.70 (*ddd*, $J = 48$, 8 and 4, 1H) 4.36 (*d*, $J = 6$, 1H) 3.98 (*d*, $J = 6$, 1H) 2.1 – 1.5 (*m*, 8H) 1.24 & 1.18 (*s*, CH_3)	142 ($M^+ - CH_2O$) **56**

oxetane formation from **1a** and 2-methylpropene as compared to **1b** and the same olefin parallels the differential behavior of **6a** and **6b**, respectively, in the reaction with 2,3-dimethyl-2-butene [9] [10].

In a comparative study on the photoreduction of 1,1,1-trifluoroacetophenone (TFA) and acetophenone by toluene – both compounds affording pinacols and *RH*-reduction products – *Wagner & Leavitt* [15] have suggested that acetophenone is reduced *via* direct H-abstraction while the low reduction potential of TFA enhances the rate of charge-transfer interaction. The intermediacy of the anion radical of TFA was suggested by the lack of any isotope effect when $CD_3C_6H_5$ is substituted for toluene. H-abstraction and electron transfer are discussed as two distinct processes.

The electrochemical reduction of α-haloketones on Hg affords the parent carbonyl compound [16] [17]. The overall reaction involves cleavage of the C-halogen bond in a two-electron sequence to give the enolate and the halide anion. The anion radical formed by the first electron transfer usually undergoes a very fast cleavage into a free radical and halide anion and the free radical is further reduced at the same potential *(Scheme 6)*.

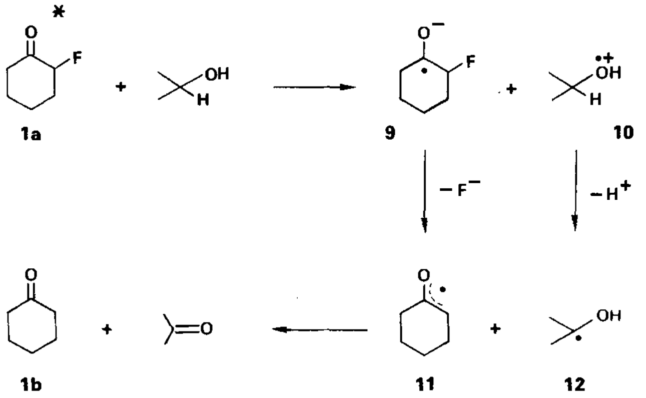
Scheme 6

$$RX + e \longrightarrow RX^{\overset{\bullet}{-}} \longrightarrow R^{\bullet} + X^-$$

$$R^{\bullet} + e \longrightarrow R^-$$

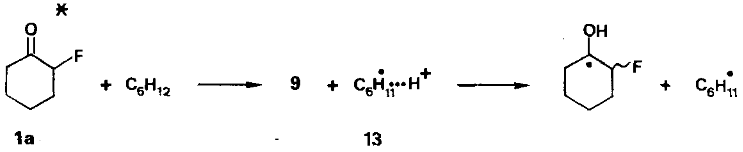
The selective formation of **1b** from **1a** or **6b** from **6a** by photoreduction in i-PrOH strongly suggests the intermediacy of an anion radical, *e.g.* **9**. Loss of F^- from **9** and of H^+ from the cation radical of i-PrOH (**10**) afford the radicals **11** and **12**, which disproportionate to give the parent ketone and acetone *(Scheme 7)*.

Scheme 7



In cyclohexane the conversion of **9** to **11**, *i.e.* cleavage of the C–F bond, is apparently only a minor process, the major product from **1a** now being the *RH*-reduction product **4**. Assuming that H-transfer is not an alternative mechanism to electron transfer, but that these two processes represent two extremes of a mechanistic continuum, as already proposed by *Cohen & Cohen* [18], this difference in reactivities of **1a** or **6a** in i-PrOH on the one side and cyclohexane on the other side has to be correlated with intrinsic differences between **10** and the cation radical of cyclohexane (**13**) *(Scheme 8)*.

Scheme 8



In a study on the $\mathrm{p}K_a$ of cation radicals *Nicholas & Arnold* [19] proposed that for compounds with very similar bond dissociation free energies a difference in their respective standard oxidation potentials of 0.1 V corresponds to a difference of ≈ 2 $\mathrm{p}K_a$-units in the acidities of their cation radicals. For i-PrOH and cyclohexane ($\Delta E_{1/2} = 0.5$ V [20] [21], it follows, that **10** is expected to be a weaker acid by ≈ 10 $\mathrm{p}K_a$-units than **13**. Unfortunately neither for i-PrOH nor cyclohexane cation radical proton-loss rates have been measured, but it can be assumed that the net efficiency of proton transfer from **10** to **9** is smaller than that from **13** to **9**, as the *p*-acid **10** also undergoes fast proton exchange with other molecules of i-PrOH in a similar way as tertiary aminylium radicals do with a variety of protic species [22]. Proton transfer from the σ-acid **13** to cyclohexane will not compete with the protonation of **9**, which therefore is now an efficient enough process to prevent the competing heterolytic C–F bond cleavage **9** → **11**.

Financial support by *Deutsche Forschungsgemeinschaft* and *Fonds der Chemischen Industrie* is gratefully acknowledged.

Experimental Part

General. Absorptions in the IR spectra are given in cm^{-1}. Chemical shifts in the 400-MHz ^1H-NMR spectra are given in ppm relative to TMS (= 0 ppm) as internal standard. The GC/MS analyses were carried out on a *Varian MAT CH7* instrument using a 2-m column of 3% SE 30 on *80/100 Suppelcoport.*

Starting Materials. 6-Fluoro-4,4-dimethyl-2-cyclohexenone (**6a**) was synthesized according to [9]. *2-Methylpropene* was purchased from *Fluka AG.* All solvents used were of spectral grade.

2-Fluorocyclohexanone (**1a**). A mixture of 10 g (0.16 mol) well-dried KF and 11 g (0.08 mol) 2-chlorocyclohexanol in 60 ml diethyleneglycol is stirred at 140° for 5 h. After filtration of the KCl distillation affords 5.7 g (60%) 2-fluorocyclohexanol, b.p. 71°/15 mm ([23]: 68–69°/14 mm). The fluoroalcohol is added to a suspension of 25 g pyridinium chlorochromate in 150 ml CH_2Cl_2 and the mixture stirred for 24 h at r.t. The mixture is filtered and the filtrate concentrated to a volume of 50 ml. Chromatography on 100 g SiO_2 (CH_2Cl_2), evaporation of the solvent and distillation affords 3.7 g (65%) **1a**, b.p. 71°/16 mm ([24]: 69°/14 mm).

Photolyses. Irradiations ($\lambda = 300$ nm) were performed in a *Rayonet RPR-100* photoreactor. For analytical purposes degassed 1-ml solutions of **1a** and **6a** (10^{-1} M) were irradiated in quartz tubes in a merry-go-round apparatus.

t-Butyl 6-Fluorohexanoate (**2**) *and 6-Fluoro-5-hexenal* (**3**). 1 g **1a** in 100 ml *t*-BuOH/C_6H_6 (95:5) was irradiated under N_2 for 65 h. Evaporation of the solvent and chromatography (SiO_2, CH_2Cl_2) affords 80 mg (8%) **3** and then 490 mg (30%) **2**.

5-Fluoro-3,3-dimethyl-1-oxaspiro[3.5]nonane (**7**). A solution of 500 mg **1a** in 50 ml benzene saturated with 2-methylpropene is irradiated for 48 h. Evaporation of the solvent and chromatography (SiO_2, CH_2Cl_2) affords 380 mg (51%) **7**.

Actinometry of **1a** *and* **6a** *in i-PrOH or Cyclohexane.* Irradiations of 10^{-1} M solutions were carried out in a merry-go-round apparatus, valerophenone [25] being used as actinometer. The degrees of conversion were determined by GC with decane as internal standard. The products were analysed by GC/MS.

REFERENCES

[1] *P.J. Wagner*, Topics Curr. Chem. *66*, 1 (1976).
[2] *P. Margaretha*, in 'Houben-Weyl, Methoden der Organischen Chemie', Vol. 6/Ib, in press.
[3] *S.G. Cohen, A. Parolan & G.H. Parsons*, Chem. Rev. *73*, 141 (1973).
[4] *R.F. Davidson & P.F. Lambeth*, Chem. Commun. *1968*, 511.
[5] *R. Ghaffari-Tabrizi & P. Margaretha*, Helv. Chim. Acta *65*, 1029 (1982).
[6] *J. Casanova & L. Eberson*, in 'The Chemistry of the Carbon-Halogen Bond', ed. S. Patai, J. Wiley, New York, 1973, p. 979.
[7] *P.C. Purohit & H.R. Sunawane*, Tetrahedron *37*, 873 (1981).
[8] *H.G. Ferguson, P. de Mayo, F.L.M. Pattison & T. Tabata*, Can. J. Chem. *41*, 2099 (1963).
[9] *V. Desobry & P. Margaretha*, Helv. Chim. Acta *58*, 2161 (1975).
[10] *G. Vo Thi & P. Margaretha*, Helv. Chim. Acta *59*, 2236 (1976).
[11] *G. Jones II*, in 'Organic Photochemistry', Vol. 5, ed. A. Padwa, M. Dekker, New York, 1981, p. 1.
[12] *R. Simonaitis, G.W. Cowell & J.N. Pitts Jr.*, Tetrahedron Lett. *1967*, 3751.
[13] *D.I. Schuster, I.M. Nunez & C.B. Chan*, Tetrahedron Lett. *1981*, 1187.
[14] *J.C. Dalton, K. Dawes, N.J. Turro, D.S. Weiss, J.A. Barltrop & J.D. Coyle*, J. Am. Chem. Soc. *93*, 7213 (1971).
[15] *P.J. Wagner & R.A. Leavitt*, J. Am. Chem. Soc. *95*, 3669 (1973).
[16] *P.J. Elving & J.T. Leone*, J. Am. Chem. Soc. *79*, 1546 (1957).
[17] *P. Tissot & P. Margaretha*, Helv. Chim. Acta *60*, 1472 (1977).
[18] *S.G. Cohen & J.I. Cohen*, J. Phys. Chem. *72*, 3782 (1968).
[19] *A.M.P. Nicholas & D.R. Arnold*, Can. J. Chem. *60*, 2165 (1982).
[20] *G. Sundholm*, Acta Chem. Scand. *25*, 3188 (1971).
[21] *M. Fleischmann & D. Pletcher*, Tetrahedron Lett. *1968*, 6255.
[22] *G.P. Gardini & J. Bargon*, J. Chem. Soc., Chem. Commun. *1980*, 757.
[23] *T. Ando, T. Ishihara, E. Ohtani & H. Sawada*, J. Org. Chem. *46*, 4466 (1981).
[24] *J. Julien & N. Thoi Lai*, Bull. Soc. Chim. Fr. *1970*, 3948.
[25] *P.J. Wagner, P.A. Kelso & R.G. Zepp*, J. Am. Chem. Soc. *94*, 7480 (1972).