12. H. Gross, J. Gloede, and D. Kunath, Tetrahedron Lett., 4089 (1967).
13. M. V. Urushadze, E. G. Abduganiev, Z. E. Samoilova, Kh. Khafizov, E. M. Rokhlin, and R. G. Kostyanovskii, Izv. Akad. Nauk SSSR, Ser. Khim., 176 (1973).
14. I. L. Knunyants, Yu. V. Ziefman, and L. T. Lantseva, Dokl. Akad. Nauk SSSR, 254, 117 (1980).

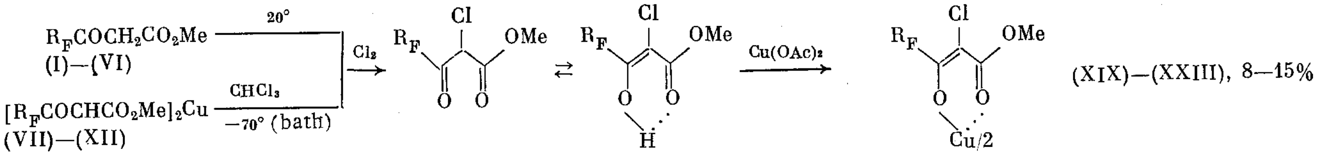
HALOGENATION OF FLUOROALKYL-SUBSTITUTED β-KETOESTERS

V. I. Saloutin, Z. É. Skryabina,
M. N. Rudaya, and K. I. Pashkevich

UDC 542.944:547.484'161

In the present work, we studied the chlorination and bromination of fluoroalkyl-substituted β-ketoesters (β-FKE) (I)-(VI) (Table 1) by molecular chlorine and bromine.

Weygand [1] and Hill [2] found that the chlorination and bromination of ethyl trifluoroacetoacetate (ETFAA) lead to the β-chloro and β-bromo derivatives on the basis of elemental analysis of the reaction products. However, the chlorination and bromination of β-FKE (I)-(VI) gave products differing in stability. The chlorination of (I)-(VI) or their copper chelates (VII)-(VII) (Table 2) indeed gives stable α-chloro derivatives of β-FKE (XIII)-(XVIII) (Table 3).



(XII)—(XVIII), 50—80%

$R_F = HCF_2$ (I), (VII), (XIII), (XIX); CF_3 (II), (VIII), (XIV), (XX); $H(CF_2)_2$ (III), (IX), (XV), (XXI); C_3F_7 (IV), (X), (XVI), (XXII); $H(CF_2)_4$ (V), (XI), (XVII); C_4F_9 (VI), (XII), (XVIII), (XXIII).

Products (XIII)-(XVIII) do not undergo significant decomposition upon distillation and storage and, similar to β-FKE (I)-(VI), they react with cupric acetate to give copper chelates (XIX)-(XXIII) (Table 4). The formation of copper chelates, (XIX)-(XXIII) in addition to IR and PMR spectral data (see Table 3), indicates that (XIII)-(XVIII) exist as tautomeric mixtures of keto and enol forms.

In an attempt to obtain α-bromo derivatives of β-FKE (I)-(VI) by the reaction of (I)-(VI) or their copper chelates (VII)-(XII) with Br_2, we found that the α-bromo derivatives formed under the conditions of Weygand [1] and Hill [5] which give one gas—liquid chromatographic peak and PMR spectrum with δCHBr 5.45-5.90 and δOMe 3.91-4.03 ppm are converted upon vacuum distillation into a 1:1 mixture of starting (I)-(VI) and dibromo derivatives of β-FKE (XXIV)-(XXIX) (Table 5).

$$\text{(I)—(VI)} \xrightarrow{Br_2} [R_FCOCHBrCO_2Me] \rightarrow \text{(I)—(VI)} + \underset{\text{(XXIV)—(XXIX)}}{R_FCOCBr_2CO_2Me}$$

$R_F = HCF_2$ (XXIV); CF_3 (XXV); $H(CF_2)_2$ (XXVI); C_3F_7 (XXVII); $H(CF_2)_4$ (XXVIII); C_4F_9 (XXIX).

Gas—liquid chromatography and PMR spectroscopy were used to identify (I)-(VI) and (XXIV)-(XXIX) by comparison with authentic samples obtained either according to Mosby [3] by the bromination of (I)-(VI) using excess Br_2 in chloroform—pyridine or by bromination of the copper chelates (VII)-(XII). In the latter case, the yields of (XXIV)-(XXIX) were higher by 20-25%.

Thus, we may say that the intermediate α-bromo derivatives of β-FKE are unstable and are brominating agents. The mechanism for this reaction may be represented as the bromination of an α-bromo derivative molecule by a second such molecule, apparently by halophilic attack of

---

Institute of Chemistry, Urals Science Center, Academy of Sciences of the USSR, Sverdlovsk. Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 5, pp. 1106-1114, May, 1984. Original article submitted March 23, 1983.

0568-5230/84/3305-1016$08.50

TABLE 1. Fluorine-Containing β-Ketoester $R_FCOCH_2CO_2Me$

Compound	R_F	Yield, %	bp, °C (p, mm Hg)	$\frac{\text{Found}}{\text{Calculated}}$, %			Chemical formula	IR spectrum, ν, cm^{-1}, CCl_4					PMR spectrum, δ, ppm, J, Hz, TMS, CCl_4 (50%)					
				C	H	F		C=O K†	CO_2Me K	CO_2Me E†	C=C E	OH E	CH_2 K	CH E	Me	OH E	$H(CF_2)_n$	J_T, Hz
(I)	HCF_2	64	149 (747)	39,90 39,48	3,70 3,98	24,26 24,98	$C_5H_6F_2O_3$	1765	1745	1675	1650	3100	3,72	5,60	3,81 K 3,87 E	11,97	6,17 K 6,07 E	51,4
(II)	CF_3	49	116 (745)	35,79 35,31	3,20 2,96	33,11 33,51	$C_5H_5F_3O_3$	1760	1725	1680	1655	3140	3,72	5,65	3,79 K 3,86 E	11,92	–	–
(III)	$H(CF_2)_2$	60	156 (751)	35,93 35,66	3,00 2,99	36,94 37,60	$C_6H_6F_4O_3$	1765	1747	1677	1650	3135	3,42	5,57	3,71 K 3,76 E	11,97	5,97 K 5,94 E	54,0 4,7
(IV)	C_3F_7	46	144 (742)	31,06 31,13	2,13 1,87	48,70 49,23	$C_7H_5F_7O_3$	1773	1753	1677	1650	3135	3,64	5,55	3,70 K 3,77 E	11,92	–	–
(V)	$H(CF_2)_4$	53	63 (5)	31,20 31,80	1,88 2,00	49,73 50,31	$C_8H_6F_8O_3$	1770	1750	1680	1650	3135	3,67	5,61	3,72 K 3,79 E	11,99	6,00	53,2 5,18
(VI) *	C_4F_9	55	78 (36)	30,54 30,02	2,45 1,57	53,21 53,41	$C_8H_5F_9O_3$	1775	1750	1680	1650	3140	3,33	5,82	3,76 K 3,87 E	11,95	–	–

---

*100 MHz, Joel-100, in CD_3COCD_3.

†K) keto form, E) enol form.

TABLE 2. Copper Chelates of Fluorine-Containing β-Ketoesters $[R_FCOCHCO_2Me]_2Cu$

Compound	R_F	Yield, %	mp, °C (from aq. MeOH)	Found/Calculated, %			Chemical formula	IR spectrum, ν, cm^{-1}, vaseline oil	
				C	H	F		$\diagdown\underset{\underset{\cdots O}{\|}}{C}{-}OMe$	$>C{=}C<$
(VII)	HCF_2	75	185–186	32,52/32,84	2,68/2,76	20,52/20,78	$C_{10}H_{10}F_4O_6Cu$	1615	1555
(VIII)	CF_3	70	180–181	29,32/29,90	2,27/2,01	28,43/28,40	$C_{10}H_8F_6O_6Cu$	1610	1575
(IX)	$H(CF_2)_2$	65	171–173	31,28/30,95	2,29/2,16	32,43/32,63	$C_{12}H_{10}F_8O_6Cu$	1630	1565
(X)	C_3F_7	50	85–86	28,25/27,94	1,60/1,34	44,68/44,20	$C_{14}H_8F_{14}O_6Cu$	1635	1555
(XI)	$H(CF_2)_4$	55	80–81	28,77/28,87	1,69/1,51	45,50/45,70	$C_{16}H_{10}F_{16}O_6Cu$	1630	1565
(XII)	C_4F_9	58	88–89	27,76/27,38	1,54/1,15	48,61/48,73	$C_{16}H_8F_{18}O_6Cu$	1615	1550

TABLE 3. Fluorine-Containing α-Chloro-β-ketoesters $R_FCOCHClCO_2Me$

Compound	R_F	Yield, %	bp, °C (p, mm Hg)	Found/Calculated, %				Chemical formula	IR spectrum, ν, cm^{-1}, neat				PMR spectrum, δ, ppm, J, Hz			
				C	H	Cl	F		$R_F-\underset{\underset{O}{\Vert}}{C}$ К	CO_2Me	C=C E	OH E	Me	CHCl К	OH	$H(CF_2)_n$
(XIII)	HCF_2	51	60(15)	31,97 32,19	3,03 2,70	18,77 19,01	20,28 20,37	$C_5H_5ClF_2O_3$	1750 1770 **sh**	1740 К 1650E	1630	3470	3,96 К 4,03 E	5,35	12,37	6,57 J_t=56,44
(XIV) *	CF_3	54	57(10)	13,30 13,00	3,02 2,77	15,98 16,22	26,00 26,08	$C_7H_6ClF_3O_3$	1760 1780 **sh**	1740 К 1660 E	1630	3460	1,31 К J_t=7,18, 1,41 E, J_t=7,18, 4,1 К, J_q=7,18, 4,58 К J_q=7,18	5,46	13,17	–
(XV)	$H(CF_2)_2$	55	75(10)	30,05 30,05	2,38 2,13	15,05 15,00	32,40 32,13	$C_6H_5ClF_4O_3$	1750 1770 **sh**	1740 К 1660 E	1620	3500	3,94 К 4,04 E	5,39	12,78	6,32, J_t=55,4, J_t=4,7
(XVI)	C_3F_7	48	60–62(10)	27,63 27,61	1,48 1,32	11,92 11,64	43,79 43,67	$C_7H_4ClF_7O_3$	1760 1780	1740 **sh** К 1660 E	1620	3500	3,97 К 4,07 E	5,35	13,20	–
(XVII)	$H(CF_2)_4$	56	85–87(10)	28,20 28,55	1,89 1,50	10,20 10,53	45,07 45,16	$C_8H_5ClF_8O_3$	1760 1780	1740 К 1660 E	1620	3500	3,96 К 4,05 E	5,37	–	6,24 J_t=62,41, J_t=4,7
(XVIII)	C_4F_9	84	80(8)	27,41 27,10	1,64 1,20	10,24 10,00	47,95 48,22	$C_8H_4ClF_9O_3$	1770 1790 **sh**	1750пл К 1670 E	1620	3450	3,96 К 4,05 E	5,36	12,93	–

---

*$CF_3COCHClCO_2C_2H_5$.

TABLE 4. Copper Chelates of Fluorine-Containing α-Chloro-β-ketoesters $[R_FCOCClCO_2Me]_2Cu$

Compound	R_F	Yield, %	mp, °C, H_2O	Found/Calculated, %				Chemical formula	IR spectrum, ν, cm^{-1}, vaseline oil	
				C	H	Cl	F		$\diagdown\underset{\underset{\cdots O}{\|}}{C}{-}OMe$	C=C
(XIX)	HCF_2	15,4	168–170	27,61/27,54	1,70/1,86	16,80/16,32	17,18/17,49	$C_{10}H_8Cl_2F_4O_6Cu$	1600	1520
(XX) *	CF_3	12,3	163–164	28,53/28,90	1,90/2,02	13,96/14,22	22,51/22,86	$C_{12}H_{10}Cl_2F_6O_6Cu$	1610	1520
(XXI)	$H(CF_2)_2$	9,8	149–150	27,48/26,96	2,01/1,51	13,27/13,26	28,76/28,43	$C_{12}H_8Cl_2F_8O_6Cu$	1610	1530
(XXII)	C_3F_7	7,8	90–91	25,07/25,07	1,32/0,90	10,51/10,57	39,90/39,60	$C_{14}H_6Cl_2F_{14}O_6Cu$	1620	1520
(XXIII)	C_4F_9	8,0	81–83	24,95/24,94	1,07/0,79	9,11/9,20	44,36/44,37	$C_{16}H_6Cl_2F_{18}O_6Cu$	1610	1520

---

*$[CF_3COCClCO_2C_2H_6]_5Cu$.

TABLE 5. Fluorine-Containing α,α-Dibromo-β-ketoesters $R_FCOCBr_2CO_2Me$

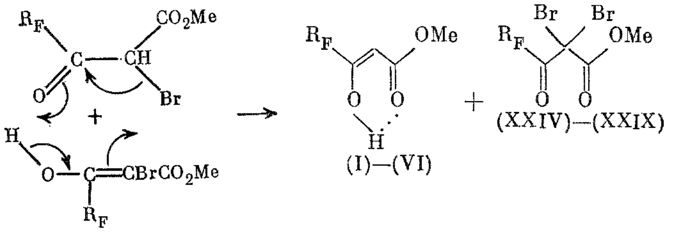
Compound	R_F	Yield, %†	bp, °C (p, mm Hg)	Found/Calculated, %				Chemical formula	IR spectrum, ν, cm⁻¹, neat			PMR spectrum, δ, ppm, J, Hz	
				C	H	Br	F		$R_F-\overset{\|\|}{C}$ O	CO_2Me	CO_2Me	Me	$H(CF_2)_n$
(XXIV)	HCF_2	20	105(8)	19,75/19,38	1,84/1,30	51,60/51,57	12,23/12,26	$C_5H_4Br_2F_2O_3$	1780 **sh**	1760	1740	3,96	6,23
(XXV) *	CF_3	35	68(15)	21,43/21,10	1,61/1,47	46,30/46,74	15,94/16,67	$C_6H_5Br_2F_3O_3$	1780 **sh**	1760	1740	1,38, J_t=7,04 5,13, J_t=7,04	–
(XXVa)	CF_3	30	47(5)	18,59/18,32	1,47/0,92	49,15/48,74	17,37/17,38	$C_5H_3Br_2F_3O_3$	1780 **sh**	1760	1740	3,97	–
(XXVI)	$H(CF_2)_2$	24	76(15)	19,95/20,02	1,18/1,12	44,30/44,41	20,75/21,11	$C_6H_4Br_2F_4O_3$	1780	1750	1740 **sh**	4,04	6,34 J_t=55,24, J_t=5,69
(XXVII)	C_3F_7	32	85(15)	19,25/19,65	1,00/0,71	37,37/37,35	31,03/31,08	$C_7H_3Br_2F_7O_3$	1780	1760	1740	4,02	–
(XXVIII)	$H(CF_2)_4$	31	118(5)	20,82/20,89	1,30/0,90	34,69/34,75	33,56/33,05	$C_8H_4Br_2F_8O_3$	1780	1760	1740	4,01	6,22 J_t=54,71, J_t=5,85
(XXIX)	C_4F_9	36	65(10)	19,88/20,10	0,84/0,63	33,41/33,44	35,08/35,78	$C_8H_3Br_2F_9O_3$	1790	1770	1750	0,04	–

---

*$CF_2COCBr_2CO_2C_2H_5$.

†Yield given for the case of the bromination of β-FKE (I)-(VI).

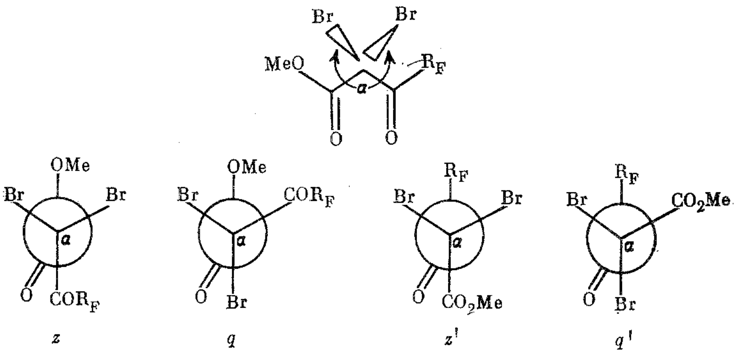
the enol form of an α-bromo derivative molecule at the bromine atom of the keto form of the second molecule which gives the enol form of β-FKE (I)-(VI) and the α-dibromo derivative of β-FKE (XXIV)-(XXIX).



These results are in accord with the lability of the bromine atom in the α-position of acetoacetate esters, which under go intramolecular rearrangement with the formation of γ-bromo isomers [4]. In our case, intermolecular rearrangement is impossible due to the presence of the fluoroalkyl substituent and the reaction proceeds by an intermolecular pathway.

We studied the IR spectra and dipole moments (DM) of (XXIV)-(XXIX) in order to establish their structure.

The presence of two geminal internal rotation axes at the tetrahedral α-carbon atom permits several isomers of (XXIV)-(XXIX) with overlapping of both carbonyl groups by either the C_α—C bond (z and z') or by the C_α—Br bond (q and q'). In this regard, we might expect four types of C=O stretching vibrations in the IR spectra of (XXIV)-(XXIX): two types for COR_F and two types for CO_2Me since overlapping by a bromine atom leads to a shift toward higher frequencies by 20-30 cm^{-1} [5]. The experimental IR spectra of (XXIV)-(XXIX) have three C=O bands (see Table 5). However, the strongest of these bands at 1760-1770 cm^{-1} may be assigned to the



total absorption of the CO(OMe)-q band as in bromomethyl acetate (1764 cm^{-1} [5]) and the $CO(R_F)$-z' band as in trifluoromethyl ethyl ketone (1765 cm^{-1} [5]). The band at 1740-1750 cm^{-1} may be assigned to the carbonyl band of the ester group in the z-conformation, while the band at 1780-1790 cm^{-1} may be assigned to the $CO(R_F)$-q' band.

The formation of the z- and q-isomers due to rotation of the CO Me group may also be demonstrated by the dipole moment method in the case of XXVa with $R_F = CF_3$. Since the direction of the dipole moment of the $COCF_3$ group in light of the equal values of μ_{C-CF_3} and $\mu_{C-C(O)}$ [2.3 D [6]) coincides with the direction of the axis of rotation (the C_α-C(O)CF_3 bond) the z'- and q'-conformers for this compound will have the same DM and the experimental DM (μ_{exp}) should depend only on the ratio of the z- and q-isomers. The value of μ_{exp} for (XXVa) is 2.68 D, while $\mu_{calc_z} = 3.18$ D and $\mu_{calc_q} = 200$ D. The ratio of the z- and q-isomers is thus 0.48 [n = 0.48 from the equation $\mu_{exp}^2 = \mu_{calc_z}^2 \cdot n + \mu_{calc_q}^2 \cdot (1 - n)$].

Thus, two orientations of the ester C=O bond are realized for α,α-dibromo derivatives (XXIV)-(XXIX) with overlapping both by the C—C and C—Br bonds in contrast to the ketone bromo derivatives for which conformers with overlapping of the carbonyl group by the C—H or C—C bond are more stable [7].

EXPERIMENTAL

The IR spectra were obtained on a UR-20 spectrometer. The PMR spectra were taken on a Perkin-Elmer R-12B spectrometer at 60 MHz with HMDS as internal standard. The gas—liquid chromatographic analysis was carried out on an LKhM-72 chromatograph with a katharometer detector, helium gas carrier on a 2-m steel column packed with 5% SE-30 on Chromatone N-AW-DMS.

The experimental dipole moment values were calculated using the Guggenheim–Smith equation [8]. The dielectric susceptibility (ε) of the 0.01-0.05 M benzene solutions was measured at 25°C on a Tangens-2M dielcometer at 1 MHz. The reflection indices (n_D) were taken on an IRF-22 refractometer. The theoretical dipole moments were calculated using a vector additive scheme for the tetrahedral α-carbon atom (109.5°C bond angle) using the following group moments: $\mu_{C-CO_2Me} = 1.83$ D, $\theta = 99°$ [9]; $\mu_{C-COCF_3} = 2.3$ D (from $\mu_{C-CF_3} = 2.3$ D and $\mu_{C-C(O)} = 2.3$ D, $\angle$ CCC 120°), $\mu_{C_\alpha-Br} = 1.12$ D (as in dibromomethane) [6].

α,α-Dibromo-β-ketoesters (XXIV)-(XXIX). A solution of 25 g dry pyridine and 43.3 g (0.272 mole) dry Br_2 in chloroform was added dropwise to a solution of 0.036 mole β-FKE (I)-(VI) cooled to –78°C. After the addition was completed, the reaction mass was stirred for the time required for spontaneous heating to about 20°C and then for 4 h at 55-60°C. Most of the chloroform was distilled off in vacuum. The orange residue was heated and mixed with 220 ml dry petroleum ether (bp 20-40°C). The solution was filtered off and distilled in vacuum. Products (XXIV)-(XXIX) were obtained upon double vacuum distillation through a column with traces of zinc powder (see Table 2). Higher yields (54-58%) were obtained in the bromination of the copper chelates of β-FKE (VII)-(XII). A sample of 0.5 mole Br_2 was added dropwise with stirring and cooling to a suspension of 0.1 mole copper chelate in chloroform. Cupric bromide was filtered off and the solvent was distilled off in vacuum. The residue was vacuum distilled to give (XXIV)-(XXIX) (see Table 5).

α-Chloro-β-ketoesters (XIII)-(XVIII) were obtained by passing 0.155 mole gaseous chlorine through 0.155 mole β-FKE (I)-(VI) with cooling of the solution to 20°C with subsequent removal of HCl by passing argon through the reaction mixture and vacuum distillation of the residue or by passing 0.2 mole chlorine through a suspension of 0.1 mole copper chelate (VII)-(XII) in 250 ml $CHCl_3$ at –70°C bath temperature. In the latter case, the cupric chloride precipitate was filtered off prior to distillation of the reaction mixture. The indices of (XIII)-(XVIII) are given in Table 3.

CONCLUSIONS

1. The bromination of fluoroalkyl-substituted β-ketoesters using bromine gives unstable α-bromo derivatives which undergo intermolecular rearrangement to yield the starting β-ketoesters and α,α-dibromo-β-ketoesters.

2. An IR spectroscopic and dipole moment study showed that the z- and q-conformers relative to the ester C=O bond are equally probable for the fluoroalkyl-substituted β-ketoesters.

LITERATURE CITED

1. H. Dworschak and F. Weygand, Chem. Ber., 101, 302 (1968).
2. H. M. Hill, E. B. Towne, and J. B. Dickey, J. Am. Chem. Soc., 72, 3289 (1950).
3. W. L. Mosby, J. Am. Chem. Soc., 74, 844 (1952).
4. M. S. Kharasch, E. Sternfeld, and F. R. Mayo, J. Am. Chem. Soc., 59, 1655 (1937).
5. L. Bellamy, New IR Spectral Data for Complex Molecules [Russian translation], Izd. Mir, Moscow (1971), p. 167.
6. V. I. Minkin, O. A. Osipov, and Yu. A. Zhdanov, Dipole Moments in Organic Chemistry [in Russian], Khimiya, Moscow (1968), pp. 79, 171.
7. B. A. Arbuzov and I. I. Lapkin, Izv. Akad. Nauk SSSR, Ser. Khim., 70 (1978).
8. E. A. Guggenheim and J. W. Smith, Trans. Faraday Soc., 46, 394 (1950).
9. J. W. Le Fevre and A. Lundarum, J. Chem. Soc., 3904 (1962).