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Journal of Fluorine Chemistry 80 (1996) 9–12

JOURNAL OF FLUORINE CHEMISTRY

Reactions of perfluoroalkylacetones with nucleophilic reagents

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Accepted 27 December 1995

Abstract

The interaction of perfluoroalkylacetones of formula $R_FCH_2COCH_3$ (R_F=*n*-C_3F_7, *n*-C_4F_9, *n*-C_6F_{13}, *n*-C_8F_{17}) with ammonia and primary and secondary amines has been studied. In all cases, nucleophilic reagents initially dehydrofluorinate the starting ketone, and then substitution of the vinyl fluorine atom by a nucleophile occurs to give aza analogues of β-dicarbonyl compounds $R_FC(NR_2)$=CH–C(O)CH_3; their hydrolysis yields the corresponding β-diketones under mild conditions.

Perfluoroalkylacetones react with sodium alkoxides to give compounds of formula $R_FC(OR)_2CH_2COCH_3$, whose acidic hydrolysis also results in β-diketones.

Keywords: Synthesis; Perfluoroalkylacetones; Nucleophilic reagents; NHR spectroscopy; IR spectroscopy; Mass spectrometry

1. Introduction

Previously we developed a technique for obtaining perfluoroalkylacetones by the radical perfluoroalkylation of isopropenylacetate [1].

There are considerable synthetic opportunities for perfluoroalkylacetones determined by the combination of several active centres in the molecule: the activated carbonyl group, the mobile hydrogen atoms, and the adjacent CF_2 and CH_2 groups which ensure easy dehydrofluorination of these compounds resulting in the formation of a reactive double bond.

2. Results and discussion

In this paper we report data on the reactions of perfluoroalkylacetones with O- and N-nucleophiles.

As expected, perfluoroalkylacetones **I** can be very easily dehydrofluorinated by the action of triethylamine in ether at 0 °C. In this case, α,β-unsaturated ketones **II** are isolated in quantitative yields:

$$R_F-CF_2-CH_2-\underset{\underset{O}{\|}}{C}-CH_3 \xrightarrow{Et_3N}$$

(I)

$$R_FCF{=}CH-\underset{\underset{O}{\|}}{C}-CH_3$$

(II)

where R_F=C_2F_5 (**a**), *n*-C_3F_7 (**b**), *n*-C_5F_{11} (**c**) or *n*-C_7F_{15} (**d**).

The interaction of ketones **I** with ammonia, primary and secondary amines does not stop at the point of formation of α,β-unsaturated ketones but yields aza analogues of β-diketones:

$$\mathbf{I} \xrightarrow{RR'NH} R_F-C(NR_2){=}CH-\underset{\underset{O}{\|}}{C}-CH_3$$

[R=R′=H (**III**), R_F=C_2F_5 (**a**), *n*-C_3F_7 (**b**), *n*-C_5F_{11} (**c**), *n*-C_7F_{15} (**d**); R=H, R′=CH_3, R_F=C_2F_5 (**IV**); R=R′=CH_3, R_F=C_2F_5 (**V**); R,R′=$(CH_2)_5$, R_F=C_2F_5 (**VI**)]

$$R_F-C(NRR'){=}CH-\underset{\underset{O}{\|}}{C}-CH_3$$

(III)

$$\xrightarrow{H_2SO_4} C_2F_5-\underset{\underset{O}{\|}}{C}-CH_3$$

(VII) ($R_F = C_2F_5$)

$$\xrightarrow{H_2O/H^+} R_F-\underset{\underset{O}{\|}}{C}-CH_2-\underset{\underset{O}{\|}}{C}-CH_3$$

(VIII)

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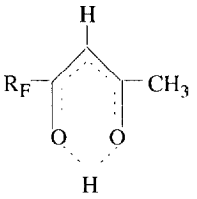
Elsevier Science S.A.
PII S0022-1139(96)03451-3

We could expect that acid hydrolysis of compounds **III**, **IV**, **V** and **VI** would lead to β-diketones. However, heating β-aminovinylketones with conc. H_2SO_4 gives pentafluoroethylmethylketone (**VII**) as the sole product in quantitative yield. Hydrolysis carried out under milder conditions (shaking with dilute HCl at room temperature) makes it possible to proceed from aminovinylketones to β-diketones **VIII**.

As expected, all the β-diketones **VIII** obtained are pure enols and a chelate structure was assigned to them based on ^1H and ^{19}F NMR spectra.

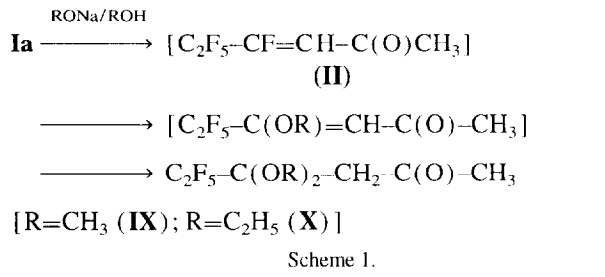


However, we would emphasize that the NMR spectra of compound **VIIIa** ($R_F = C_2F_5$) contain the signals of the corresponding diketone form, whose content is 1.5%–2%.

Like trifluoroacetylacetone, the first representative of this series, β-diketones **VIII**, are pale coloured liquids with a characteristic odour which are stable on storage. Low-temperature distillation in vacuo allowed us to isolate colourless samples, but these samples became coloured within several days even if they were stored at low temperature although no changes were recorded in the IR and NMR spectra.

Like aliphatic β-dicarbonyl compounds, β-diketones **VIII** formed chelates when shaken with an aqueous solution of copper(II) acetate. We note that the colour of the β-diketonates depends on the length of the perfluorocarbon chain (for $R_F = C_2F_5$, the colour is lilac; for $R_F = C_7F_{15}$, the colour is bright blue).

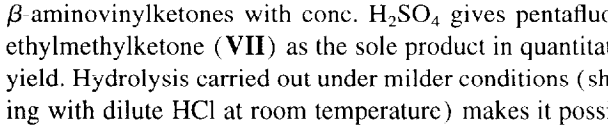
Sodium alkoxides react with ketone **Ia** at room temperature in a solution of the corresponding alcohol. This reaction is likely to proceed in accordance with Scheme 1 presented for the reaction of ketones **I** with amines. Hydrogen fluoride is eliminated to give a α,β-unsaturated ketone **II**, followed by nucleophilic substitution of the vinyl fluorine atom by an alkoxy group.



Scheme 1.

We isolated the corresponding ketals as reaction products in both the cases we studied. These ketals are formed as a result of the addition of an alcohol to the intermediate ether.

Heating ketals **IX** and **X** with P_2O_5 leads to elimination of one molecule of alcohol to give the alkyl ethers of the β-diketone enols **XI** and **XII** in almost quantitative yield. Hydrolysis of the products **XI** and **XII** also allowed us to obtain β-diketone **VIIIa** (even under vigorous conditions) in high yield.



3. Experimental details

^1H and ^{19}F NMR spectra were recorded on a Bruker AC-200 X instrument (200 MHz for ^1H and 188.3 MHz for ^{19}F), with TMS and CF_3COOH as references. Mass spectra were obtained on a VG 7070E spectrometer (70 eV). IR spectra were recorded on an UR-20 instrument.

*3.1. Preparation of the α,β-unsaturated ketones **II** (general procedure)*

A solution of ketone **I** (1 mol) and triethylamine (1.1 mol) in dry diethyl ether (ca. 1 g of solvent per 1 g of ketone **I**) was refluxed for 5–7 min and cooled to room temperature. Then the liquid part of the reaction mixture was separated, washed with dilute HCl (1:1) and water, and dried over $MgSO_4$. After removing solvent, enone **II** was isolated by distillation (see data in Table 1).

*3.2. Preparation of aminoenones **III** (general procedure)*

Ammonia (3 mol) was introduced into a solution of ketone **I** (1 mol) in dry diethyl ether (ca. 10 g of solvent per 1 g of **I**); NH_3 was passed over the surface of the solution with vigorous stirring. The thickened reaction mixture was then cooled to room temperature and stirred for 1 h. The liquid part of the reaction mixture was separated, poured into water (the water volume was four-times greater than the ether volume), the organic layer separated and the aqueous layer extracted twice with ether. The ether extracts were combined with the organic layer and dried over K_2CO_3. After removal of the solvent, the residue was recrystallized from hexane or distilled to give **III** (Table 1).

*3.3. Preparation of 4-methylamino-5,5,6,6,6-pentafluoro-3-hexene-2-one (**IV**)*

Product **IV** (9.0 g, 84%) was obtained from ketone **Ia** (11.3 g, 0.05 mol) and methylamine (5.0 g, 0.16 mol) using the procedure reported in Section 3.2 (Table 1).

*3.4. Preparation of 4-dimethylamino-5,5,6,6,6-pentafluoro-3-hexene-2-one (**V**)*

Product **V** (19.2 g, 84%) was obtained from ketone **Ia** (22.6 g, 0.1 mol) and dimethylamine (15.0 g, 0.33 mol) using the procedure reported in Section 3.2 (Table 1).

Table 1
Properties and spectral data for compounds R_F–CX = CH–CO–CH_3

Compound No.	R_F	X	Yield (%)	Bp/mmHg (m.p.) (°C)	^{19}F NMR δ (ppm); J (Hz)	^{1}H NMR δ (ppm); J (Hz)	IR (ν, cm^{-1})	MS (m/z, %)	Found/Calculated %			
									C	H	F	N
IIa	C_2F_5	F	47	99–102	8.3 (3F); 38.2 (1F, J = 35.0 Hz); 46.7 (2F)	2.7 (3H); 6.5 (1H, J = 35.0 Hz)	1695 (C–C); 1730 (C=O)	206 (M^+, 24)	34.8/35.0	1.8/1.9	55.6/55.3	
IIb	n-C_3F_7	F	82.5	119.5–122	4.6 (3F); 36.7 (1F, J = 36 Hz); 43.8 (2F); 51.6 (2F)	2.2 (3H); 6.0 (1H, J = 36.0 Hz)	1700 (C=C); 1732 (C=O)	256 (M^+, 16)	32.8/32.8	1.6/1.6	59.7/59.4	
IIc	n-C_5F_{11}	F	86	70–72/27	4.7 (3F); 36.8 (1F, J = 33.5 Hz); 42.5 (2F); 46 8 (4F); 50.5 (2F)	2.4 (3H); 6.2 (1H, J = 33.5 Hz) [a]	1700 (C=C); 1730 (C=O)	356 (M^+, 19)	30.0/30.3	1.0/1.1	63.4/64.1	
IId	n-C_7F_{15}	F	83.3	85–86/12	5.4 (3F); 36.9 (1F, J = 34.0 Hz); 42.8 (2F); 45.8–46.8 (8F); 51.5 (2F)	2.4 (3H); 6.1 (1H, J = 34.0 Hz)	1700 (C=C); 1730 (C=O)	456 (M^+, 12)	28.9/29.0	0.8/0.9	66.3/66.7	
IIIa	C_2F_5	NH_2	89	152–154 (42–44) [b]	6.8 (3F); 45.5 (2F)	2.2 (3H); 5.6 (IH); 8.7 (2H)	1547 (C=C); 1610 (C=O)	203 (M^+, 18)	35.8/35.5	2.9/3.0	46.9/46.8	7.2/6.9
IIIb	n-C_3F_7	NH_2	88	162–164 (44–46) [b]	3.6 (3F); 42.7 (2F); 50.0 (2F)	2.1 (3H); 5.4 (1H); 8.8 (2H)	1560 (C=C); 1646 (C=O)	253 (M^+, 20)	33.6/33.2	2.6/2.4	53.4/52.6	5.6/5.5
IIIc	n-C_5F_{11}	NH_2	82	78–79/10 [b]/(37–38)	4.7 (3F); 42.0 (2F); 46.3 (4F); 50.0 (2F)	2.8 (3H); 6.1 (1H); 8.7 (2II)	1560 (C=C); 1650 (C=O)	353 (M^+, 16)	30.6/30.6	1.7/1.7	59.3/59.2	4.0/4.0
IIId	n-C_7F_{15}	NH_2	60	99–101/12	4.7 (3F); 41.9 (2F); 46.0 (8F); 50.0 (2F)	2.8 (3H); 6.2 (1H); 8.8 (2H)	1555 (C=C); 1645 (C=O)	453 (M^+, 16)	29.1/29.1	1.2/1.3	63.3/62.9	3.2/3.1
VIIIa	C_2F_5	OH	80	111.5–112	6.4 (3F); 47.8(2F)	2.4 (3H); 6.2 (1H); 14.5 (1H)		204 (M^+, 26)	35.2/35.3	2.4/2.5	46.9/46.6	
VIIIb	n-C_3F_7	OH	76	133–134[c]	3.0 (3F); 44.5 (2F); 50.0 (2F)	2.4 (3H); 6.3 (1H); 14.6 (1H)		254 (M^+, 25)				
VIIIc	n-C_5F_{11}	OH	78	162–164	4.4 (3F); 43.5(2F); 45.7 (4F); 50.0 (2F)	2.5 (3H); 6.5 (1H); 14.8 (1H)		354 (M^+, 23)				
VIIId	n-C_7F_{15}	OH	62	187–189	4.5 (3F); 43.5 (2F); 45.5 (8F); 50.0 (2F)	2.5 (3H); 6.5 (1H); 14.7 (1H)		454 (M^+, 24)				
IV	C_2F_5	$NHCH_3$	83	73–75/38	6.4 (3F); 38.0 (2F)	2.2 (3H); 3.2 (3H); 5.6 (1H); 10.7 (1H)	1610 (C=C); 1633 (C=O)	217 (M^+, 14)	38.9/38.7	3.6/3.7	43.6/43.8	6.7/6.5
V	C_2F_5	$N(CH_3)_2$	83	77–78.5/37	6.1 (3F); 34.4 (2F)	2.1 (3H); 2.9 (6H); 5.7 (1H)	1590 (C=C); 1660 (C=O)	231 (M^+, 11)	41.0/41.6	3.9/4.3	41.4/41.1	6.1/6.1
VI	C_2F_5	$N(CH_2)_5$	78	85.5–87/10	5.6 (3F); 35.8 (2F)	1.6 (6H); 2.2 (3H); 3.1 (4H); 5.8 (1H)	1580 (C=C); 1680 (C=O)	271 (M^+, 12)	48.6/48.7	5.1/5.2	35.0/35.1	5.6/5.2
XI	C_2F_5	OCH_3	74	139–142	7.2 (3F); 40.5 (2F)	2.0 (3H); 3.4 (3H); 5.3 (1H)	1595 (C=C); 1710 (C=O)	218 (M^+, 28)	38.4/38.5	3.0/3.2	44.0/43.6	
XII	C_2F_5	OC_2H_5	81	151–153	7.2 (3F); 40.3 (2F)	1.5 (3H), J = 7.6); 2.4 (3H); 4.2 (2H, J = 7.6); 5.4 (1H)	1600 (C=C); 1717 (C=O)	232 (M^+, 30)	41.5/41.4	3.9/3.9	41.0/40.9	

[a] Cf. Ref. [2].
[b] Cf. Ref. [3].
[c] Cf. Ref. [4].

3.5. Preparation of 4-piperidino-5,5,6,6,6-pentafluoro-3-hexene-2-one (VI)

To a solution of ketone **Ia** (11.3 g, 0.05 mol) in 100 ml of dry ether, a solution of freshly distilled piperidine (15.0 g, 0.18 mol) in 20 ml of dry ether was added dropwise with vigorous stirring. A temperature of 15–25 °C was maintained. After addition of piperidine was complete, the reaction mixture was stirred for 2 h at room temperature. The liquid part of the reaction mixture was separated, poured into cold water (500 ml), the organic layer separated, washed with water (3×20 ml) and dried over $MgSO_4$. The solvent was removed, and distillation gave **VI** (10.5 g, 78%) (Table 1).

3.6. Reactions of heptafluoropropylacetone with alkoxides

To a solution of ketone **Ia** (22.6 g, 0.1 mol) in 50 ml of dry methanol, a solution of sodium methoxide [prepared by dissolution of Na (4.6 g, 0.2 mol) in 100 ml of dry methanol] was added dropwise at 10 °C for 2 h with vigorous stirring. The reaction mixture was warmed to room temperature and stored overnight. The reaction mixture was then poured into cold water (2 l, 0 °C), the organic layer separated and dried over K_2CO_3. The solvent was removed and distillation gave **IX** (16.6 g, 66%, b.p. 122 °C/140 mmHg). MS, m/z: 219 ($M-OCH_3$). ^{19}F NMR δ: 2.7 (3F); 43.8 (2F) ppm. ^1H NMR δ: 2.2 (3H); 2.9 (2H); 3.4 (6H) ppm. IR (υ, cm^{-1}): 1728 (C=O). Analysis: Found: C, 38.2; H, 4.3; F, 39.4%. $C_8H_{11}F_5O_3$ requires: C, 38.4; H, 4.4; F, 38.0%.

Product **X** (16.8 g, 60%, 186–188 °C) was obtained from **Ia** (22.6 g, 0.1 mol) by a procedure similar to that described above. **X**: MS, m/z: 233 ($M-OC_2H_5$)$^+$. ^{19}F NMR δ: 2.4 (3F); 44.2 (2F) ppm. ^1H NMR δ: 1.3 (6H, J=7.6 Hz); 2.3 (3H); 3.1 (2H); 3.9 (4H, J=7.6 Hz) ppm. IR (υ, cm^{-1}): 725 (C=O). Analysis: Found: C, 43.0; H, 5.6; F, 34.0%. $C_{10}H_{15}F_5O_3$ requires: C, 43.2; H, 5.4; F, 34.2%.

3.7. Synthesis of β-diketones VIII from β-aminovinylketones (method A) and β-alkoxyvinylketones (method B)

Method A

A mixture of β-aminovinylketone **III** was refluxed with dilute (1:1) HCl for 1 h and cooled to room temperature. The organic layer was separated, washed with water and distilled over P_2O_5 (Table 1).

β-Diketone **VIIIa** was obtained in a similar manner from other derivatives **IV**, **V** and **VI** in 57%, 40% and 75% yield, respectively.

Method B

β-Alkoxyvinylketone (**XI** or **XII**) (obtained by heating ketals **IX** or **X** with excess P_2O_5) was heated with an equal volume of conc H_2SO_4. Distillation gave pure **VIIIa** in 94% and 89% yield from **XI** and **XII**, respectively.

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