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Condensation of 2-Polyfluoroacylcycloalkanones with Aldehydes and Dimethylformamide–Dimethylacetal

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Polyfluorinated 1,3-diketones containing carbocycles react with aldehydes under Lewis-acid catalysis and also with dimethylformamide–dimetylacetal without catalysis, yielding exclusively (*E*)-configured condensation products involving the methylene group of the carbocycle. Novel trifluoromethylated chromenes are prepared from 2-trifluoroacetylcycloalkanones and salicylaldehyde. The structures of two new compounds, 2-(*E*)-benzylidene-6-trifluoroacetylcyclohexanone and 4-trifluoroacetyl-2,3-dihydro-1*H*-xantene, are confirmed by X-ray structure analysis.

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Introduction

The Knoevenagel condensation of linear 1,3-dicarbonyls with electrophiles like aromatic aldehydes, in the presence of bases, straightforwardly yields addition products involving the active methylene group of the nucleophile.[1] This reaction is considered an important method for the synthesis of highly reactive 2-aryliden-1,3-dicarbonyls.[2]

Using an unsymmetrical 1,3-diketone, e.g. 1,1,1-trifluoropentane-2,4-dione, as the nucleophile resulted in, along with the expected compound, products of condensation at the methyl group, and moreover, trifluoromethylstyryl ketones. The products' ratio depends on the reaction conditions and on the substituent properties in the aromatic aldehyde ring.[3] Only in the case of 4,4,4-trifluoro-1-phenylbutane-1,3-dione and 2,4,6-trimethylbenzaldehyde was the 'normal' Knoevenagel reaction observed to afford a trifluoromethylated 2-arylidene-1,3-diketone.[3]

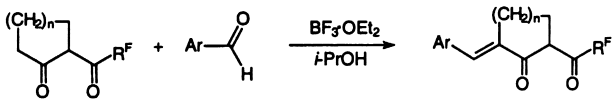
Non-fluorinated 2-acetylcycloalkanones, considered 1,3-diketones with an alkyl substituent in the 2-position at which condensation is not possible, react easily with aromatic aldehydes to give products of a twofold condensation at the activated methyl and methylene moiety.[4] Similar condensation products involving the methylene group in the γ-position of the β-dicarbonyl system have been obtained by treating 2-carbalkoxycyclopentanones with aromatic aldehydes and cinnamaldehyde.[5]

The reaction pathway in the case of dimethylformamide–dimethylacetal (DMF–DMA) depends mainly on the properties of the nucleophile; for non-fluorinated linear 1,3-diketones the condensation proceeds at the activated methylene fragment,[6,7] for non-fluorinated 2-acetylcycloalkane-1,3-diones[8] and for trifluoromethylated β-aminoenones[9] condensation at the methyl group was reported.

Recently, we showed[10] that 2-trifluoroacetylcyclohexanone and methyl trifluoroacetate give the Claisen-condensation product (at the 6-position of cyclohexanone) under base catalysis. In continuation of a systematic investigation of the chemical properties[11] of 2-polyfluoroacylcycloalkanones, we have studied their behavior in reactions with selected *C*-electrophiles.

Results and Discussion

2-Polyfluoroacylcycloalkanones (1–6) and the aromatic aldehydes (7–11,13) (in boiling propan-2-ol, $BF_3{\cdot}OEt_2$ catalysis) gave enediones (14–16,18–21,23–31) in good to excellent yields. Only the reaction with *o*-chlorobenzaldehyde (12) resulted in the formation of compounds (17) and (22) in 15 and 18% yields, respectively (Scheme 1, Table 1).



	n	R^F	Ar
(1)	1	CF_3	
(2)	2	CF_3	
(3)	2	CF_2CF_2H	
(4)	2	C_2F_5	
(5)	2	C_3F_7	
(6)	2	C_4F_9	
(7)			4-$(CH_3)_2NC_6H_4$
(8)			4-$(C_2H_5)_2NC_6H_4$
(9)			4-HOC_6H_4
(10)			4-$CH_3OC_6H_4$
(11)			C_6H_5
(12)			2-ClC_6H_4
(13)			2-C_4H_3O*
(14)	1	CF_3	4-$(CH_3)_2NC_6H_4$
(15)	1	CF_3	4-$CH_3OC_6H_4$
(16)	1	CF_3	C_6H_5
(17)	1	CF_3	2-ClC_6H_4
(18)	2	CF_3	4-$(CH_3)_2NC_6H_4$
(19)	2	CF_3	4-$(C_2H_5)_2NC_6H_4$
(20)	2	CF_3	4-$CH_3OC_6H_4$
(21)	2	CF_3	C_6H_5
(22)	2	CF_3	2-ClC_6H_4
(23)	2	CF_2CF_2H	4-$(C_2H_5)_2NC_6H_4$
(24)	2	CF_2CF_2H	4-$CH_3OC_6H_4$
(25)	2	CF_2CF_2H	C_6H_5
(26)	2	C_2F_5	4-HOC_6H_4
(27)	2	C_2F_5	2-C_4H_3O
(28)	2	C_3F_7	4-$(CH_3)_2NC_6H_4$
(29)	2	C_3F_7	4-$CH_3OC_6H_4$
(30)	2	C_3F_7	C_6H_5
(31)	2	C_4F_9	4-$(CH_3)_2NC_6H_4$

* Furfural

Scheme 1. Reaction of 2-polyfluoroacylcycloalkanones with aromatic aldehydes.

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Table 1. Preparation and properties of compounds (14–38,40)

	Compound	Starting Materials	M.p. (°C) (solvent)	Formula	Found/Calc. Anal. (%) or HRMS (*m/z*) C	H	F	N	Yield (%)	Reaction time (h)
(14)	5-Trifluoroacetyl-2-(*E*)-(*p*-dimethylaminobenzylidene)-cyclopentanone	(1) and (7)	182–183 (toluene)	$C_{16}H_{16}F_3NO_2$	61.9 61.7	5.3 5.2	17.8 18.3	4.7 4.5	92	5
(15)	5-Trifluoroacetyl-2-(*E*)-(*p*-methoxybenzylidene)cyclopentanone	(1) and (10)	94–95 (hexane)	$C_{15}H_{13}F_3O_3$	60.5 60.4	4.4 4.4	18.9 19.1	–	68	5
(16)	2-(*E*)-Benzylidene-5-trifluoroacetylcyclopentanone	(1) and (11)	102–103 (petroleum ether/toluene, 4:1)	$C_{14}H_{11}F_3O_2$	62.7 62.7	4.1 4.1	21.5 21.3	–	67	10
(17)	2-(*E*)-(*o*-Chlorobenzylidene)-5-trifluoroacetylcyclopentanone	(1) and (12)	115–117 (perfluoro-1,1-dimethylcyclohexane)	$C_{14}H_{10}ClF_3O_2$,	302.0318. 302.0321. 1.1 ppm (10.0), 0.3 mmu (30.0)				15	10
(18)	6-Trifluoroacetyl-2-(*E*)-(*p*-dimethylaminobenzylidene)-cyclohexanone	(2) and (7)	161–163 (petroleum ether/toluene, 4:1)	$C_{17}H_{18}F_3NO_2$	62.6 62.8	5.6 5.6	17.6 17.5	4.3 4.3	71	5
(19)	2-(*E*)-(*p*-Diethylaminobenzylidene)-6-trifluoroacetylcyclohexanone	(2) and (8)	96–97 (petroleum ether)	$C_{19}H_{22}F_3NO_2$	64.5 64.6	6.2 6.3	16.5 16.1	4 4	76	11
(20)	6-Trifluoroacetyl-2-(*E*)-(*p*-methoxybenzylidene)cyclohexanone	(2) and (10)	112–113 (toluene)	$C_{16}H_{15}F_3O_3$	61.4 61.5	4.9 4.8	18.5 18.3	– –	61	16
(21)	2-(*E*)-Benzylidene-6-trifluoroacetylcyclohexanone	(2) and (11)	110–111 (petroleum ether)	$C_{15}H_{13}F_3O_2$	63.9 63.8	4.7 4.6	20.2 20.2	– –	95	16
(22)	2-(*E*)-(*o*-Chlorobenzylidene)-6-trifluoroacetylcyclohexanone	(2) and (12)	57 (perfluoro-1,1-dimethylcyclohexane)	$C_{15}H_{12}ClF_3O_2$,	316.0484. 316.0478. –2.1 ppm (10.0), –0.6 mmu (10.0)				18	20
(23)	2-(*E*)-(*p*-Diethylaminobenzylidene)-6-(2,2,3,3-tetrafluoropropanoyl)cyclohexanone	(3) and (8)	92–93 (petroleum ether)	$C_{20}H_{23}F_4NO_2$	62.3 62.3	6.2 6	19.7 19.7	3.4 3.6	71	11
(24)	2-(*E*)-(*p*-Methoxybenzylidene)-6-(2,2,3,3-tetrafluoropropanoyl)cyclohexanone	(3) and (10)	76–78 (petroleum ether)	$C_{17}H_{16}F_4O_3$	59.3 59.3	4.6 4.7	22.3 22.1	– –	66	16
(25)	2-(*E*)-Benzylidene-6-(2,2,3,3-tetrafluoropropanoyl)cyclohexanone	(3) and (11)	64–65 (petroleum ether)	$C_{16}H_{14}F_4O_2$	61.8 61.2	5.1 4.5	– –	– –	72	16
(26)	6-Perfluoropropanoyl-2-(*E*)-(*p*-hydroxybenzylidene)cyclohexanone	(4) and (9)	90.0–90.5 (hexane)	$C_{16}H_{13}F_5O_3$	55 55.2	3.6 3.8	27.4 27.3	– –	78	10
(27)	6-Perfluoropropanoyl-2-(*E*)-(2-furfurylydene)cyclohexanone	(4) and (13)	67 (hexane)	$C_{14}H_{11}F_5O_3$	52.3 52.2	3.4 3.4	29.3 29.5	– –	70	10
(28)	6-Perfluorobutanoyl-2-(*E*)-(*p*-dimethylaminobenzylidene)cyclohexanone	(5) and (7)	126–127 (petroleum ether)	$C_{19}H_{18}F_7NO_2$	53.8 53.6	4.2 4.3	31.2 31.3	3.4 3.3	97	5
(29)	6-Perfluorobutanoyl-2-(*E*)-(*p*-methoxybenzylidene)cyclohexanone	(5) and (10)	77–78 (hexane)	$C_{18}H_{15}F_7O_3$	52.6 52.4	3.9 3.7	32.5 32.3	– –	73	5
(30)	2-(*E*)-Benzylidene-6-perfluorobutanoylcyclohexanone	(5) and (11)	Oil	$C_{17}H_{13}F_7O_2$	53.6 53.4	3.3 3.4	34.6 34.8	– –	56	5
(31)	2-(*E*)-(*p*-Dimethylaminobenzylidene)-6-perfluoropentanoylcyclohexanone	(6) and (7)	127–128 (hexane)	$C_{20}H_{18}F_9NO_2$,	475.1174. 475.1194. 4.1 ppm (10.0), 2.0 mmu (30.0)				64	5
(32)	4-Trifluoroacetyl-2,3-dihydro-1*H*-xanthene	(2) and salicylaldehyde	118–119 (petroleum ether)	$C_{15}H_{11}F_3O_2$	64.3 64.3	4 4	20.4 20.3	– –	30	10
(33)	5-Trifluoroacetyl-2-(*E*)-(*o*-hydroxybenzylidene)cyclopentanone	(1) and salicylaldehyde	>180[A] (toluene)	$C_{14}H_{11}F_3O_3$	60 59.2	3.9 3.9	– –	–	21	3
(34)	3-Trifluoroacetyl-2,3-dihydro-1*H*-cyclopenta-[b]-chromene	(33)	119.5–120.0 (petroleum ether)	$C_{14}H_9F_3O_2$,	266.0536. 266.0555. 7.2 ppm (20.0), 1.9 mmu (4.0)				21	1
(35)	2-(*E*)-Cinnamylidene-5-trifluoroacetylcyclopentanone	(1) and cinnamaldehyde	152–154 (hexane)	$C_{16}H_{13}F_3O_2$,	294.0861. 294.0868. 2.2 ppm (10.0), 0.6 mmu (5.0)				13	4
(36)	2-(*E*)-Cinnamylidene-6-trifluoroacetylcyclohexanone	(2) and cinnamaldehyde	124–126 (petroleum ether)	$C_{17}H_{15}F_3O_2$,	308.1012. 308.1024. 3.9 ppm (10.0), 1.2 mmu (5.0)				19	3
(37)	2-(*E*)-Dimethylaminomethylene-5-trifluoroacetylcyclopentanone	(1) and DMF–DMA	115–118 (hexane/ethanol, 10:1)	$C_{10}H_{12}F_3NO_2$	51.2 51.1	5.2 5.1	24.6 24.2	5.8 6.0	51	2
(38)	2-(*E*)-Dimethylaminomethylene-6-trifluoroacetylcyclohexanone	(2) and DMF–DMA	101–103 (hexane/ethanol, 10:1)	$C_{11}H_{14}F_3NO_2$	53.2 53.0	5.6 5.7	22.9 22.9	5.6 5.6	74	2
(40)	2-(*E*)-(*p*-Dimethylaminobenzylidene)-6-(2,2,3,3-tetrafluoropropanoyl)cyclohexanone	(39) and (7)	124–125 (petroleum ether)	$C_{18}H_{19}F_4NO_2$	60.7 60.5	5.2 5.4	20.9 21.3	3.9 3.9	52	6

[A] Sublimation point.

In the X-ray structure analysis (Table 2,3) of (21) two independent molecules, (A) and (B), were found. The existence of the *endo*-enol form (Fig. 1) was shown. The enol proton was found at O(2) [O(2A)], the C(2)–O(1) [C(2A)–O(1A)] distance is shorter than the C(8)–O(2) [C(8A)–O(2A)] distance, 125.8(3) [125.4(3)] pm and 133.8(3) [133.1(3)] pm, respectively. The phenyl ring is twisted with respect to the rest of the molecule with the torsion angle C(7)–C(9)–C(10)–C(15) 33.9° for (A) [–151.3° for the corresponding angle in molecule (B)]. The O(1)–C(2)–C(3)–C(8)–O(2)–H[O(2)] and O(1A)–C(2A)–C(3A)–C(8A)–O(2A)–H[O(2A)] systems are planar. The cyclohexane ring possesses a 'half-chair' conformation where C(5) [C(5A)] is above the ring atoms by 67.2 [65.4] pm. The calculated torsion angles are 2.6° for O(2)–C(8)–C(3)–C(2), –4.5° for C(8)–C(3)–C(2)–O(1), 1.4° for O(2A)–C(8A)–C(3A)–C(2A) and –1.0° for C(8A)–C(3A)–C(2A)–O(1A) (in contrast, the *endo*-enol form of 2-trifluoroacetylcyclohexanone (2) exhibits a non-planar chelate ring with the corresponding MINDO/3 calculated torsion angles[12] of 5.5° and 17.8°). In the O–H–O bridge of (21), [O(2)–O(1) 249.0 pm; O(2A)–O(1A) 247.8 pm], a small deviation from linearity was observed (O(1)–H(2)–O(2) = 164.2°, O(1A)–H(2A)–O(2A) = 151.7°), compared with the *endo*-enol form of 2-trifluoroacetylcyclohexanone with angle O–H–O = 122.0°.[12]

Table 2. Details of crystal data, measurement of intensities, and data processing of the X-ray diffraction investigation of compounds (21) and (32)

	(21)	(32)		(21)	(32)
FW	282.25	280.24	μ(Mo Kα) (mm^{-1})	0.126	0.129
Crystal size (mm)	0.6 × 0.5 × 0.4	0.9 × 0.7 × 0.5	2θ range (°)	2.59 to 27.50	2.40 to 25.00
Crystal system	Monoclinic	Monoclinic	F(000)	1168	576
Space group	$P2_1/n$	$P2_1/c$	Index range	$-13 \le h \le 1$, $-32 \le k \le 1$, $-13 \le l \le 13$	$-8 \le h \le 8$, $-21 \le k \le 21$, $-11 \le l \le 12$
a (pm)	1006.60 (10)	1011.30 (10)	Reflections collected	6486	8292
b (pm)	2495.8 (2)	1775.6 (4)	Independent reflections	5125 [R_{int} = 0.0246]	2176 [R_{int} = 0.0411]
c (pm)	1015.50 (10)	716.70 (10)	Completeness to θ_{max}	87.7%	99.9%
β (°)	91.460 (10)	106.710 (10)	Data/Restraints/Parameter	5125/0/372	2176/0/183
V (nm^3)	2.5504 (4)	1.2326 (3)	Goodness-of-fit at F^2	1.044	1.037
Z	8	4	Final *R* indiced [$I > 2\sigma(I)$]	R_1 = 0.0581, $wR2$ = 0.1275	R_1 = 0.0424, $wR2$ = 0.1090
D_c (Mg/m^3)	1.470	1.510	Largest diff. peak and hole ($e \cdot Å^{-3}$)	0.273 and –0.301	0.220 and –0.269

The two 2-trifluoroacetylcycloalkanones (1) and (2) react with salicylaldehyde differently; in the case of the cyclohexane derivative (2) the product of condensation and heterocyclization (32) was isolated (Scheme 2, Table 1). With the cyclopentane 1,3-diketone (1) the *o*-hydroxy-substituted enedione (33) is formed, which is transformed into the corresponding heterocycle (34) by heating in conc. H_2SO_4 (Scheme 2, Table 1).

The molecular structure of (32) (Fig. 2, Table 2,3) showed a planar chromene system. The cyclohexane ring has a twisted conformation with C(5) 47.7 pm above and C(7) 25.9 pm under the C(3)–C(4)–C(7)–C(8) plane. The trifluoroacetyl group is slightly twisted towards the conjugated C(3)–C(8)–C(7)–C(15) system with a torsion angle C(1)–C(2)–C(3)–C(8) of 9.8°.

Table 3. The selected bond lengths (pm) and angles (°) of compounds (21) and (32)

(21)		(32)	
C(2)–O(1)	125.8(3)	C(2)–O(1)	123.1(2)
C(2)–C(3)	140.8(4)	C(2)–C(3)	144.4(3)
C(3)–C(8)	139.5(3)	C(3)–C(8)	136.6(3)
C(8)–O(2)	133.8(3)	C(3)–C(4)	151.9(2)
C(2A)–O(1A)	125.4(3)	C(6)–C(7)	150.8(2)
C(2A)–C(3A)	141.6(4)	C(7)–C(15)	134.2(3)
C(3A)–C(8A)	138.9(3)	C(7)–C(8)	144.8(2)
C(8A)–O(2A)	133.1(3)	C(8)–O(2)	136.19(19)
O(1)–C(2)–C(3)	125.4(2)	O(1)–C(2)–C(3)	122.36(16)
C(8)–C(3)–C(2)	117.9(2)	C(8)–C(3)–C(2)	127.38(15)
O(2)–C(8)–C(3)	120.6(2)	C(5)–C(4)–C(3)	113.25(16)
O(1A)–C(2A)–C(3A)	125.1(2)	C(4)–C(5)–C(6)	110.79(16)
C(8A)–C(3A)–C(2A)	117.7(2)	C(7)–C(6)–C(5)	109.98(15)
O(2A)–C(8A)–C(3A)	120.7(2)	O(2)–C(8)–C(3)	118.22(15)

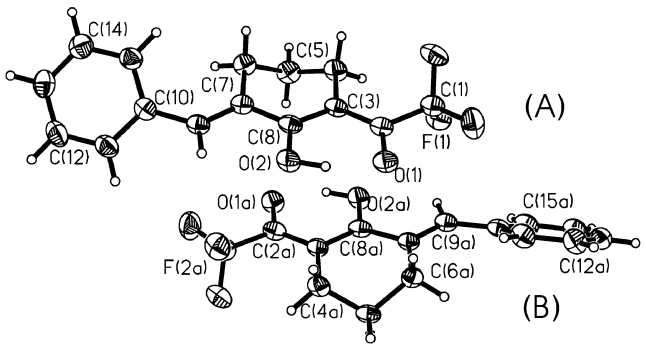


Figure 1. Molecular structure of (21) (with two independent molecules (A) and (B), thermal ellipsoids with 50% probability).

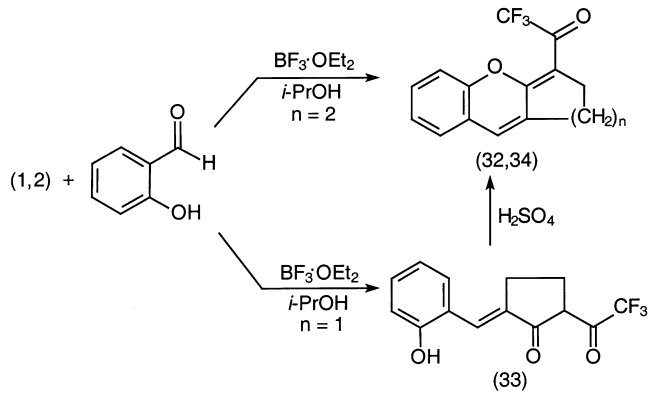
Reacting 1,3-diketones (1,2) with cinnamaldehyde under the conditions mentioned above, yellow crystalline (*E*)-cinnamylidene derivatives (35) and (36) were formed (Scheme 3, Table 1) with low yields [13% (35), 19% (36)], as in the case of the analogous cinnamylidene-2-carbalkoxy cyclopentanones.[5]

1,1,1,5,5,5-Hexafluoropentane-2,4-dione and DMF, when heated in acetic anhydride, gave straightforwardly the 3-dimethylaminomethylene-substituted derivative,[13] whereas 1,3-diketone (2) produced a complex mixture of several products. When one equivalent of 2-trifluoroacetylcycloalkanone (1) or (2) was reacted with 1.1 equivalents of DMF–DMA in boiling toluene, compounds (37) and (38) (51 and 74% yield, respectively) were obtained (Scheme 4, Table 1).

1,1,1-Trifluoropentane-2,4-dione and benzaldehyde (heating in propan-2-ol in the presence of $BF_3 \cdot OEt_2$, or DMF–DMA, heating in toluene) produce an inseparable mixture of compounds similar to a previous case.[3] Apparently, the condensation took place not only at the activated 1,3-diketone methylene group, but also at the methyl group, generating (*E*)- and (*Z*)-isomers with respect to the dimethylaminomethylene C–C double bond.

β-Aminoenone (39) [amino derivative of 1,3-diketone (3)] and *p*-dimethylaminobenzaldehyde (7) (Scheme 5, Table 1), under acid-catalysis, gave enedione (40) in 52% yield, which was formed by hydrolysis of the enamine function.

The ^1H and ^{19}F nuclear magnetic (NMR) spectra (Table 4) of compounds (37) and (38) in $CDCl_3$ exhibit only one set of signals. The data confirms the presence of an enol form, since the formation of an ammonium zwitter-ion[14] could be ruled out on the basis of the ^1H NMR data. There is a broad signal at $\delta_H > 14$ corresponding to the enol proton (the signal of the Me_2NH^+ group could be observed at *ca.* $\delta_H = 9.5$[15]). The enol tautomer was observed in the ^1H NMR spectra for compounds (14–31,33,35,36,40) in $CDCl_3$ (Table 5, 6) with



	n
32	2
34	1

Scheme 2. Reaction of 2-trifluoroacetylcycloalkanones with salicylaldehyde.

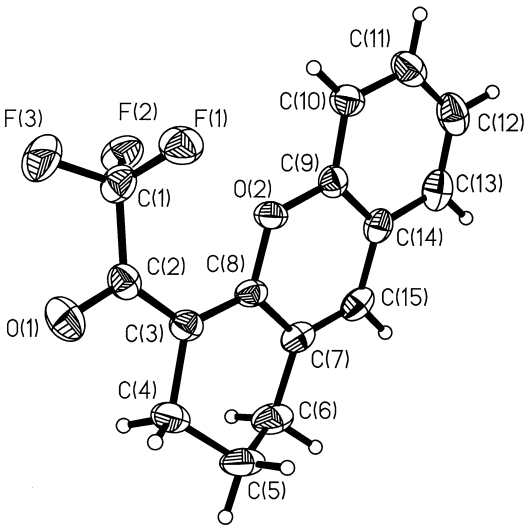
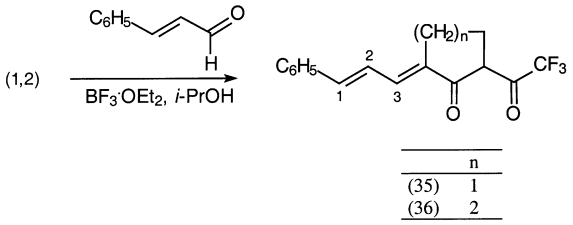
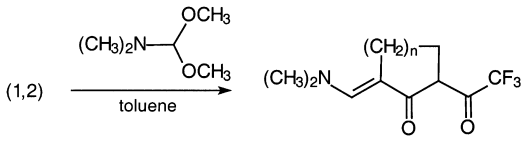


Figure 2. Molecular structure of compound (32) (thermal ellipsoids with 50% probability).



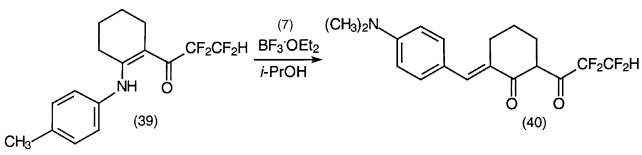
	n
(35)	1
(36)	2

Scheme 3. Reaction of 2-trifluoroacetylcycloalkanones with cinnamaldehyde.



	n
(37)	1
(38)	2

Scheme 4. Reaction of 2-trifluoroacetylcycloalkanones with DMF–DMA.



Scheme 5. Reaction of the 1-[*N*-(*p*-tolyl)-amino]-2-(2,2,3,3-tetrafluoropropanoyl)cyclohexene with *p*-dimethylaminobenzaldehyde.

Table 4. ^{1}H and ^{19}F NMR data of compounds (37) and (38)

Comp.	^{1}H NMR d, *J* (Hz)				^{19}F NMR δ
	$(CH_2)_{n+1}$	CH_3	=CH	OH	
(37)	2.58–2.72, 2.76–2.87, 2 × m, 2 × 2H	3.11, s	7.30, s	14.4, br s	–72.53, s
(38)	1.59–1.71, 2.38–2.48, 2 × m, 2 × 2H; 2.58, t, $^{3}J_{HH}$ = 6.2, 2H	3.16, s	7.68, s	17.3, br s	–71.16, s

δ_H = 11.1–16.5 (=C–OH). No resonance for the methine proton of the diketo tautomer was observed, although according to the ^{19}F NMR spectra it was present in low concentration (< 4%) (Table 6,7).

The most abundant tautomer was found to be the *cis*-enol,* the structure of which was confirmed from the ^{19}F NMR spectra of compounds (14) and (21), by analysis of the through-space spin–spin coupling of fluorine nuclei and the methylene protons of the substituent in the α-position of the β-diketone (Table 7). The shift range of the enolic protons (Tables 5,6) is due to the presence of intramolecular hydrogen bridges, which decrease in stability from the cyclohexane derivatives (18–31,36,40) (δ_H = 15.00–16.49) to the cyclopentane derivatives (14–17,33,35) (δ_H = 11.1–13.3), similarly to the starting diketones.[12,16] This stability difference is probably caused by the increase in O–O distance originating from the increase in ring strain when moving from cyclohexane to cyclopentane.[12,17] The same argument holds for compounds (37) and (38).

The arylidene proton resonances of compounds (32) and (34) [(*Z*)-configuration of arylidene C–C double bond] were observed at δ_H = 6.9. The respective resonances of 4-ene-1,3-diones (14–31,33,35,36,38,40) were found at lower field (δ_H = 7.5–7.8). This correlates well with the corresponding δ_H value of (21) [(*E*)-configuration of the arylidene C–C double bond was proved by X-ray analysis, see above], and also with the respective literature data of related (*E*)-configured

* The structures of all 4-ene-1,3-diones in this paper are given in the diketo-form, since we are not sure whether the compounds synthesized by us exist in the *endo*- or *endo*-cyclic enol tautomeric form.

Table 5. ^{1}H NMR data of compounds (14–34,40)

Comp.	^{1}H NMR δ, *J*(Hz)				
	$(CH_2)_{n+1}$	Ar	=C–H	R^F	OH
(14)	2.9, br s, 4H	3.05, s, 6H; 6.65–7.40, m, 4H	7.5, br s	–	13.3, br s
(15)	2.93, s, 4H	3.85, s, 3H; 6.89–7.44, m, 4H	7.55, s	–	12.5, br s
(16)	2.93–3.10, m, 4H	7.36–7.59, m, 6H; C_6H_5, =CH	–	–	12.9, br s
(17)	2.84–3.01, m, 4H	7.24–7.37, m, 2H; 7.45–7.49, m, 1H; 7.54–7.59, m, 1H	7.69, t, $^4J_{HH}$ = 2.5	–	12.7, br s
(18)	1.77–1.80, m, 2H; 2.59, m, 2H; 2.76–2.80, m, 2H	3.05, s, 6H; 6.69–6.73, m, 2H; 7.42–7.46, m, 2H	7.78, s	–	15.73, s
(19)	1.35–1.91, m, 2H; 2.51–2.87, m, 4H	1.20, t, $^3J_{HH}$ = 7.1, 6H; 3.42, q, $^3J_{HH}$ = 7.1, 4H; 6.61–7.47, m, 4H	7.76, t, $^4J_{HH}$ = 1.8	–	15.79, s
(20)	1.69–1.81, m, 2H; 2.58, t, $^3J_{HH}$ = 5.4, 2H; 2.70–2.78, m, 2H	3.84, s, 3H; 6.93, 7.41 AB-System, J_{HaHb} = 8.6, 4H	7.76, s	–	15.40, s
(21)	1.53–1.90, m, 2H; 2.54–2.84, m, 4H	7.38–7.43, m	7.80, t, $^4J_{HH}$ = 2.0	–	15.20, s
(22)	1.79–1.82 m, 2H; 2.58–2.63, m, 4H	7.28–7.48, m	7.89, s	–	15.00, s
(23)	1.60–1.90, m, 2H; 2.59–2.86, m, 4H	1.20, t, $^3J_{HH}$ = 7.1, 6H; 3.42, q, $^3J_{HH}$ = 7.1, 4H; 6.61–7.48, m, 4H	7.77, t, $^4J_{HH}$ = 1.8	6.25, tt, $^2J_{HF}$ = 52.8, $^3J_{HF}$ = 5.7	16.16, s
(24)	1.75–2.01, m, 2H; 2.53–3.02, m, 4H	3.85, s, 3H; 6.84–7.50, m, 4H	7.8, br s	6.24, tt, $^2J_{HF}$ = 52.8, $^3J_{HF}$ = 5.5	15.74, s
(25)	1.66–1.81, m, 2H; 2.62–2.84, m, 4H	7.41, s	7.80, t, $^4J_{HH}$ = 1.8	6.25, tt, $^2J_{HF}$ = 53.0, $^3J_{HF}$ = 5.5	15.55, s
(26)	1.59–1.90, m, 2H; 2.57–2.84, m, 4H	5.22, s, 1H; 6.81–7.44, m, 4H	7.78, s	–	15.83, s
(27)	1.71–1.94, m, 2H; 2.56–2.94, m, 4H	6.50–6.57, 6.68–6.72, 2 × m, both 1H; 7.49–7.82, m, 2H, C_4H_3O, =CH	–	–	15.66, s
(28)	1.66–1.89, m, 2H; 2.54–2.84, m, 4H	3.04, s, 6H; 6.66–7.80, m, 4H	7.79–7.82, m	–	16.47, s
(29)	1.52–1.89, m, 2H; 2.56–2.85, m, 4H	3.85, s, 3H; 6.88–7.50, m, 4H	7.82, s	–	16.1, br s
(30)	1.40–1.87, m, 2H; 2.34–2.83, m, 4H	7.24–7.58, m	7.84, s	–	15.9, br s
(31)	1.69–1.82, 2.59–2.70, 2.76–2.82, 3 × m, all 2H	3.05, s, 6H; 6.71, d, $^3J_{HH}$ = 9.2, 2H; 7.45, d, $^3J_{HH}$ = 9.2, 2H	7.8, br s	–	16.49, s
(32)	1.77–1.83, m, 2H; 2.59–2.65, m, 4H	7.16–7.37, m, 4H	6.91, s	–	–
(33)[A]	2.73–2.76, 2.84–2.86, 2 × m, both 2H	6.79–6.91, m, 2H; 7.14–7.22 m, 1H; 7.43, d, $^3J_{HH}$ = 8.0, 1H; 10.1 br s, 1H	7.62, t, $^4J_{HH}$ = 2.3	–	11.1, br s
(34)	2.82–2.94, m, 4H	7.14–7.40, m, 4H	6.9, br s	–	–
(40)	1.74–1.91, m, 2H; 2.53–2.93, m, 4H	3.04, s, 6H; 6.64–7.48, m, 4H	7.8, br s	6.24, tt, $^2J_{HF}$ = 52.8, $^3J_{HF}$ = 5.7	16.07, s

[A] In (D_6)-dimethylsulfoxide (DMSO).

compounds.[3,9,18] Thus, compounds (14–31,33, 35, 36,38,40) are (*E*)-configured at the *exo*-methylene C–C double bond.

The situation for (37) is not so clear, since the signal for the olefinic proton was observed at δ_H = 7.30. Since this resonance is found at a slightly higher field for the cyclopentane ring containing an aryl substituted 4-ene-1,3-dione than their cyclohexane analogues (see Table 5) an (*E*)-configuration is proposed for (37), as for (38).

There is additional confirmation for the enol form of 4-ene-1,3-diones present in the solid state from the infra red (IR) spectra (Table 8), where broad absorptions in the 3000–4000 cm^{-1} region were found, typical for hydrogen-bridged enolic hydroxy groups.[19,20]

In conclusion, ring-containing polyfluorinated 1,3-diketones underwent a condensation reaction with aldehydes and dimethylformamide–dimethylacetal to give novel 1-polyfluoroalkyl-2,4-oligomethylene-alk-4-(*E*)-ene-1,3-diones, which were present in their enol form both in solution and in the solid state. They are versatile synthons for further syntheses of potential bioactive compounds.

Experimental

Melting points are uncorrected. Mass-spectra (EI, 70 eV) were carried out on a MAT 8200 spectrometer (Table 9). NMR spectra [standards: TMS (^{1}H) and $CFCl_3$ (^{19}F)] were recorded in $CDCl_3$ solutions on a Tesla BS-587A instrument operating at 80.1 MHz (^{1}H) and 75.3 MHz (^{19}F)

Table 6. ^{1}H and ^{19}F NMR data of compounds (35) and (36)

Comp.	^{1}H NMR δ, *J* (Hz)				^{19}F NMR
	$(CH_2)_{n+1}$	C^1H=C^2H	=C^3H C_6H_5	OH	δ
(35)	2.82, s, 4H	6.89–7.12, m, 3H; 7.26–7.51, m, 3H		12.6, br s	–76.32, s
(36)	1.72–1.84, m, 2H; 2.53–2.65 m, 4H	6.93, d, $^3J_{HH}$ = 15.2, 1H; 7.11, dd, $^3J_{HH}$ = 15.2, $^3J_{HH}$ = 11.2, 1H	7.28–7.42, m, 3H; 7.46–7.51, m, 2H	15.14, s	–73.81, s

Table 7. ^{19}F NMR data of compounds (14–22,31,33)

Comp.	^{19}F NMR (major tautomer) δ, *J*(Hz)
(14)	–75.03, t, $^5J_{FH}$ = 1.6
(15)	–75.81, s
(16)	–76.26, s
(17)	–76.67, s
(18)	–73.29, s
(19)	–73.19, s
(20)	–73.70, s
(21)	–73.93, t, $^5J_{FH}$ = 1.2
(22)	–74.24, s
(31)	–126.59, –123.64, –115.48, 3 × m, all 2F; –82.11, t, $^4J_{FF}$ = 8.6, 3F
(33)[A]	–75.21, s

[A] In (D_6)-DMSO.

Table 8. IR data of compounds (14,19–21,23–26,28,30,40)

Comp.	IR, ν (cm^{-1}) C=C–C=O	O–H···O (br)
(14)	1570	3000–4000
(19)	1555	3000–4000
(20)	1560	3060–4000
(21)	1560	3000–4000
(23)	1555	3000–4000
(24)	1570	3000–4000
(25)	1580	3000–4000
(26)	1590	3000–4000
(28)	1580	3000–4000
(30)	1540	3000–4000
(140)	1540	3000–4000

and a Bruker DPX-200 spectrometer operating at 200.1 MHz (^{1}H) and 188.3 MHz (^{19}F). IR spectra were recorded in nujol on a Specord 75 IR spectrophotometer. Chromatography was performed on a silica gel column (normal phase, MATREX, Grace Gmbh). 2-Polyfluoroacylcycloalkanones (1,2),[21] (3,6),[11] (4),[22] (5)[23] were prepared by a Claisen-type condensation of cyclopentanone or cyclohexanone and alkylpolyfluoroacylates in the presence of lithium hydride in dried benzene.[11]

*1-[*N*-(*p*-tolyl)-amino]-2-(2,2,3,3-tetrafluoropropanoyl)cyclohexene (39)*

According to ref.[11] By a condensation of (3) (10.0 g, 44 mmol) and *p*-toluidine (5.4 g, 50 mmol) in toluene (150 mL) was obtained (39) (10.5 g, 76%) as yellow crystals, m.p. 75–76°C (hexane) (Found: C, 61.1; H, 5.6; F, 23.9; N, 4.4%. Calc. for $C_{16}H_{17}F_4NO$: C, 61.0; H, 5.4; F, 24.1; N, 4.4%). ^{1}H NMR δ 1.56–1.68, m, 4H, CH_2; 2.35, s, CH_3; 2.40–2.77, m, 4H, CH_2; 6.32, tt, $^2J_{HF}$ = 53.1 Hz, $^3J_{HF}$ = 5.9 Hz, CF_2H; 6.95–7.22, m, C_6H_4; 13.33, s, NH.

Synthesis of Compounds (14–31,33,35,36,40) (General Procedure)

To a mixture of 1,3-diketone or (39) (5 mmol) and aldehyde (5 mmol) in propan-2-ol (15 mL) were added BF_3·OEt_2 (3 drops). The mixture was refluxed (see Table 1) then cooled and diluted with water (100 mL).

Workup Procedures

a) (15,17,20,26,27,33): The mixture was extracted with $CHCl_3$ (3 × 10 mL), the combined extracts were dried ($MgSO_4$) and evaporated to give a solid residue which was recrystallized to afford products as yellow crystals (Table 1).

b) (14,16,18,19,21,23,28,31,35): The precipitate was dried and recrystallized to afford crystals (14) (yellow-brown), (16) (orange), (18,31) (violet), (19,23,28) (red-violet), (21,35) (yellow) (Table 1).

Table 9. MS data (EI) of compounds (16,18,20,22,31–38)

Comp.	*m/z* (%)
(16)	268 (M^+, 70), 199 ([M–CF_3]$^+$, 100), 171 ([M–CF_3CO]$^+$, 6), 77 ($C_6H_5^+$, 6) and other fragments
(18)	325 (M^+, 100), 256 ([M–CF_3]$^+$, 49), 228 ([M–CF_3CO]$^+$, 4), 184 ([M–CF_3CO–$N(CH_3)_2$]$^+$, 3) and other fragments
(20)	312 (M^+, 100), 243 ([M–CF_3]$^+$, 85) and other fragments
(22)	316 (M^+, 6), 281 ([M–Cl]$^+$, 100), 247 ([M–CF_3]$^+$, 13), 69 (CF_3^+, 5) and other fragments
(31)	475 (M^+, 100), 256 ([M–C_4F_9]$^+$, 88) and other fragments
(32)	280 (M^+, 52), 211 ([M–CF_3]$^+$, 100), 183 ([M–CF_3CO]$^+$, 49) and other fragments
(33)	284 (M^+, 100), 267 ([M–OH]$^+$, 20), 215 ([M–CF_3]$^+$, 50), 187 ([M–CF_3CO]$^+$, 10), 69 (CF_3^+, 9) and other fragments
(34)	266 (M^+, 100), 197 ([M–CF_3]$^+$, 96) and other fragments
(35)	294 (M^+, 100), 225 ([M–CF_3]$^+$, 40), 77 ($C_6H_5^+$, 15) and other fragments
(36)	308 (M^+, 100), 239 ([M–CF_3]$^+$, 28), 77 ($C_6H_5^+$, 20) and other fragments
(37)	235 (M^+, 60), 220 ([M–CH_3]$^+$, 10), 166 ([M–CF_3]$^+$, 100), 44 ($(CH_3)_2N^+$, 18) and other fragments
(38)	249 (M^+, 80), 234 ([M–Me]$^+$, 27), 180 ([M–CF_3]$^+$, 100), 69 (CF_3^+, 13), 44 ($(CH_3)_2N^+$, 26) and other fragments

c) (22,24,25,29,30,36,40): The mixture was extracted with $CHCl_3$ (3 × 10 mL). The combined extracts were dried ($MgSO_4$) and evaporated to give a residue which was purified by column chromatography (eluent: $CHCl_3$) and recrystallized to afford crystals (22,24,25,29,36) (yellow), (40) (red) and (30) as a yellow oil (Table 1).

*4-Trifluoroacetyl-2,3-dihydro-1*H*-xanthene (32)*

To a mixture of (2) (1.5 g, 7.7 mmol) and salicylaldehyde (0.9 g, 7.7 mmol) in propan-2-ol (15 mL) were added BF_3·OEt_2 (3 drops). The mixture was refluxed for 10 h, then cooled, diluted with water (100 mL) and extracted with $CHCl_3$ (3 × 10 mL). The combined extracts were dried ($MgSO_4$) and evaporated to give a residue which was distilled and recrystallized to afford (32) (0.65 g, 30%) as yellow crystals (Table 1). ^{19}F NMR δ –75.44, s.

*3-Trifluoroacetyl-1,2-dihydrocyclopenta-[*b*]-chromene (34)*

A mixture of (33) (0.2 g, 0.7 mmol) and conc. H_2SO_4 (10 mL) was heated to 160°C for 1 h. The cooled mixture was diluted with cold water (70 mL) and extracted with $CHCl_3$ (3 × 10 mL). The combined extracts were dried ($MgSO_4$) and evaporated to give a residue which was purified by column chromatography (eluent: $CHCl_3$) and recrystallized to afford (34) (0.04 g, 21%) as yellow crystals. ^{19}F NMR δ –77.69, s.

Synthesis of Compounds (37,38) (General procedure)

A mixture of (1) or (2) (10 mmol) and DMF–DMA (1.3 g, 11 mmol) was refluxed in dry toluene (8 mL) for 2 h. The solvent was evaporated to give a solid residue that was recrystallized to afford (37,38) as yellow needles (Table 1).

X-Ray Analysis of Compounds (21) and (32)

Yellow prisms of (21), suitable for X-ray diffraction investigation, were obtained from a 1:1 hexane/$CHCl_3$ solution. Yellow prisms of (32) were obtained from a 1:1 hexane/acetone solution. Data was collected at 173(2) K on a Siemens P4 diffractometer with low temperature device LT2 and graphite-monochromated Mo–Kα radiation (λ = 71.073 pm). Details of crystal data, measurement of intensities, and data processing are summarized in Table 2. The structures were solved by direct methods, and full-matrix least-squares refinement was performed with the SHELX-97 (Sheldrick, 1997) program system. All non-hydrogen atoms were refined anisotropically. H(2), H(2a) atoms for (21) were refined isotropically. The positions of the remaining hydrogen atoms were calculated using a riding model. The weighting schemes

were $w^{-1} = \sigma^2(F_o)^2 + (0.0556P)^2 + 1.0987P$ (21) and $w^{-1} = \sigma^2(F_o)^2 + (0.0689P)^2 + 0.1701P$ (32) with $P = (F_o^2 + 2F_c^2)/3$. Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre as supplementary publications, CCDC 157925 (21) and CCDC 157926 (32). Copies of the data can be obtained on application to the director, CCDC; 12 Union Road, Cambridge CB2 1EZ, UK (e-mail: deposit@ccdc.cam.ac.uk).

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