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CYCLOCONDENSATION OF F-2-METHYL-2-PENTENE WITH ACTIVATED METHYLENE COMPOUNDS USING 'FREEZE-DRIED' POTASSIUM FLUORIDE

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SUMMARY

The reactions of F-2-methyl-2-pentene with activated methylene compounds such as acetylacetone, ethyl acetoacetate, benzoylacetonitrile, and benzoylmethyl perfluoroalkyl ketones in the presence of potassium fluoride were carried out. Each reaction proceeded smoothly in acetonitrile at room temperature by using 'freeze-dried' potassium fluoride as a condensing agent. Acetylacetone and ethyl acetoacetate gave both divinyl ether and pyran compounds, whereas other activated methylene compounds afforded only pyrans in good yields.

INTRODUCTION

In our continuous systematic studies on the nucleophilic reactions of perfluoroolefins, we have reported reactions of these compounds with various nucleophiles except those with C-nucleophiles. In particular, perfluoroolefins such as F-propene and its dimers or trimers were found to be useful reagents for synthesis of fluorinated heterocyclic compounds [1 - 9]. For example, F-propene [1], F-2-methyl-2-pentene and F-2,4-dimethyl-3-heptene [6, 8, 9] reacted easily with ortho-N, O- (or S-) difunctional benzenes affording five- to nine-membered benzoheterocycles.

On the other hand, the idea that a hydrogen-bonding with a fluoride ion enhances the nucleophilicity of protic organic molecules has been demonstrated recently by the formation of various products of C-, N-, and S-alkylations under mild neutral conditions [10 - 19]. Especially, as a result of the discovery that potassium fluoride is activated by the advent of crown ether [20], studies on these and related systems, e.g., potassium fluoride-polyethyleneglycol [21], tetraalkylammonium fluorides [22, 23], have contributed to the wide application of fluoride ion in organic syntheses.

In our recent studies, we also have revealed that 'freeze-dried' potassium fluoride is efficient as a nonhygroscopic source of the catalytic reagent [24, 25]. This type of potassium fluoride has also been found to be very useful for the reactions between $\underline{F}$-2-methyl-2-pentene and activated methylene compounds, leading mainly to fluorinated pyrans, and we now wish to report in detail.

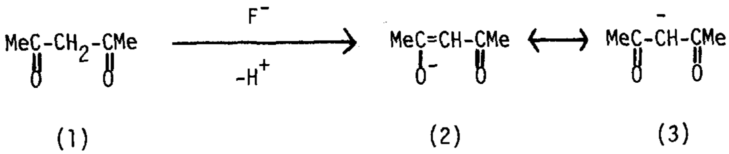
RESULTS AND DISCUSSION

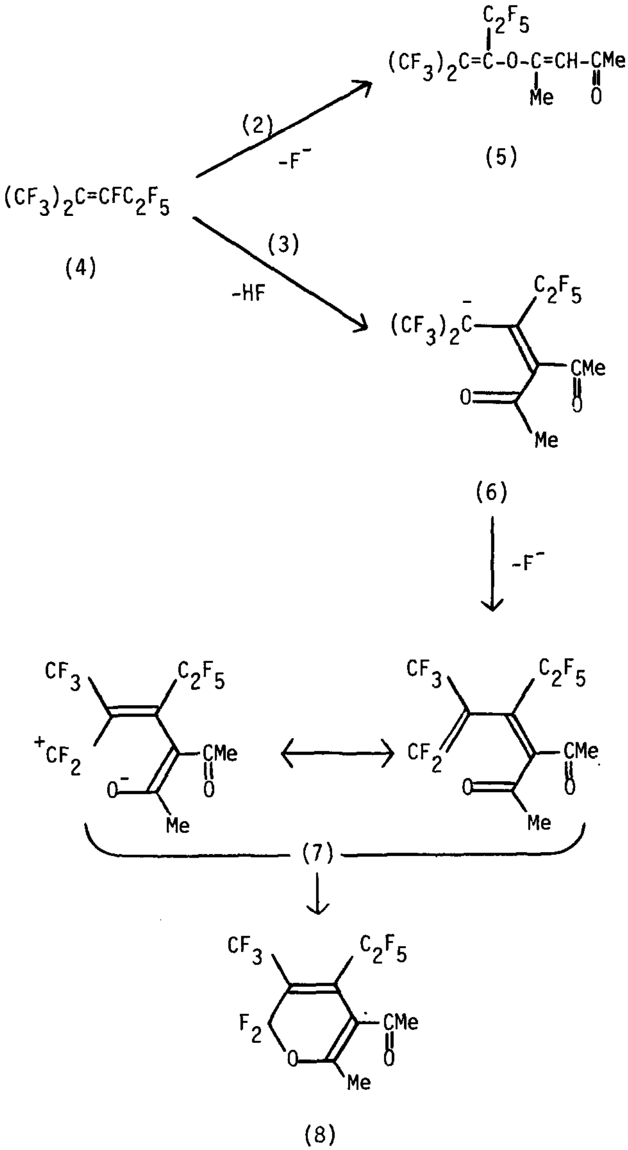
Reaction of $\underline{F}$-2-methyl-2-pentene with acetylacetone

In our research on the reactions of $\underline{F}$-2-methyl-2-pentene (4), a dimer of hexafluoropropene, with activated methylene compounds in the presence of potassium fluoride, acetylacetone (1) was first examined as the nucleophile. The reaction was carried out in acetonitrile at room temperature, using various kinds of potassium fluoride, freeze-dried KF [24], calcine-dried KF[13], KF-Al_2O_3, CsF-Al_2O_3, and KF-Zeolite [18]. In each case, two products, a divinyl ether (5) and a pyran (8), were found in the reaction mixture. These resulted from the condensation of the perfluoroalkene (4) with an enolate ion (2) or with a carbanion (3), respectively.

The structures of these two products were established by various spectral data. The ^{19}F nmr for the divinyl ether (5) showed resonances at δ -20.2, -16.3, 4.7 and 34.5 ppm (upfield from ext. CF_3CO_2H) in the ratios 3 : 3 : 3 : 2. The signal at δ -20.2 due to one of the CF_3 groups attached to the double bond appeared as overlapping triplets of quartets of quartets split by all other fluorines in the molecule ($J_{C\underline{F}_3-C\underline{F}_3}$ 9.2 Hz, $J_{C\underline{F}_3-C\underline{F}_2CF_3}$ 18.8 Hz, $J_{C\underline{F}_3-CF_2C\underline{F}_3}$ 3.8 Hz). The ^1H nmr spectrum contained three signals at δ 2.24 (=C-C$\underline{H}_3$), 2.40 (COC$\underline{H}_3$) and 5.58 (=C$\underline{H}$).

The ^{19}F nmr spectrum for the pyran (8) showed resonances at δ -29.8, -21.3, -0.4 and 22.1 ppm in the ratios 2 : 3 : 3 : 2. The signal due to C$\underline{F}_3$-C= at δ -21.3 was split both by C$\underline{F}_2$ (22.1) and C$\underline{F}_3$ (-4.0) of the pentafluoroethyl group ($J_{C\underline{F}_3-C\underline{F}_2CF_3}$ 16.8 Hz, $J_{C\underline{F}_3-CF_2C\underline{F}_3}$ 7.9 Hz).


MeC-CH2-CMe
F-
-H+
MeC=CH-CMe
MeC-CH-CMe
(1)
(2)
(3)


(CF3)2C=CFC2F5
(4)
(2)
-F-
(CF3)2C=C(C2F5)-O-C(Me)=CH-CMe
(5)
(3)
-HF
(CF3)2C
C2F5
CMe
Me
(6)
-F-
CF3
C2F5
+CF2
CMe
Me
CF2
(7)
CF3
C2F5
F2
CMe
Me
(8)

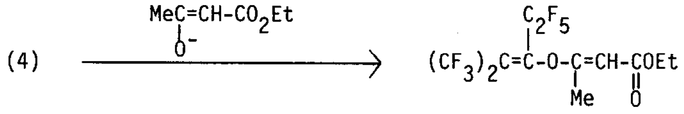
The ^1H nmr signals appeared at δ 2.26 due to $=C-C\underline{H}_3$ and at 2.44 due to $CO-C\underline{H}_3$ appropriately.

The reaction pathway is apparently as shown above. Although the formation of a pyran-ring may seem strange, it is explicable from the mechanistic point of view. The first step should be initiated by the nucleophilic attack of the carbanion (3) formed from (1) by the aid of a fluoride ion. Resultant carbanion (6) would release a fluoride ion giving a terminal alkene (7), stabilized by the conjugate effect, finally affording the cyclized pyran compound (8).

It was noteworthy that the rate of the reaction was highly dependent on the type of potassium fluoride used. Thus the yields of (5) and (8) after 24 h's reaction at room temperature using various types of KF were as follows: 51 and 39% for freeze-dried KF, 33 and 25% for calcine-dried KF, 36 and 14% for $KF-Al_2O_3$, 38 and 25% for $CsF-Al_2O_3$, and 38 and 14% for KF-Zeolite (F-9). Consequently, freeze-dried potassium fluoride gave the best result and it was proved that this type of KF worked very effectively as in the case of the common alkylation of protic compounds [24].

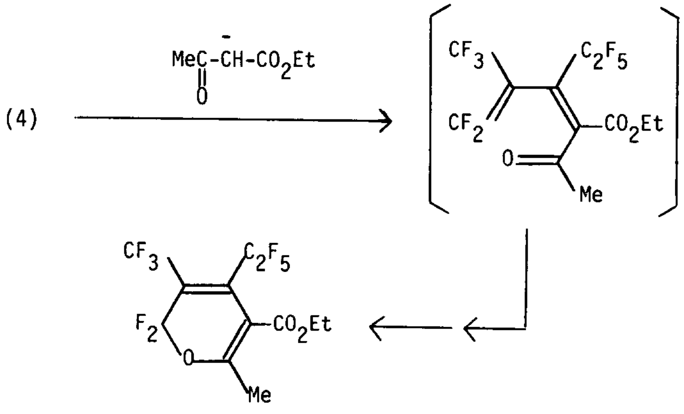
Reaction with ethyl acetoacetate

Instead of acetylacetone in the above reaction, ethyl acetoacetate was used under similar conditions. The reaction proceeded smoothly at room temperature, and by using freeze-dried potassium fluoride as the condensing agent, a divinyl ether (9) and a pyran (10) were obtained in yields of 48 and 42% respectively. When other types of KF were used, the yields of these products were much lower. The structures were similarly established by the ^{19}F and ^1H nmr spectra (Tables 1 and 2)



$$(4) \xrightarrow{\underset{O^-}{MeC}=CH-CO_2Et} (CF_3)_2C=\overset{C_2F_5}{C}-O-\underset{Me}{C}=CH-\underset{O}{\overset{\|}{C}}OEt$$

(9)



(10)

Reactions with benzoylacetonitrile

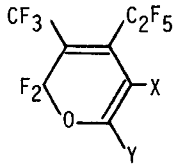
In contrast with the reactions with acetylacetone or ethyl acetoacetate, giving a divinyl ether and a pyran mentioned above, the perfluoroalkene (4) reacted with benzoylacetonitrile affording only a pyran compound (12). Thus by the reaction in the presence of freeze-dried KF, a pyran compound (12) was obtained in a yield of 89% and no formation of a divinyl ether was observed. This should be ascribed to the higher stability of the carbanion (11) rather than the enolate anion, owing to the adjacent strong electron-withdrawing CN group.

When calcine-dried KF or KF-Al_2O_3 was used, the yield of (12) was 29 and 66% respectively.

The structure of (12) was supported by various spectral data. The IR spectrum showed characteristic absorption bands due to CN and C=C bonds at 2230 and 1630 cm^{-1} respectively, and the ^1H nmr spectrum revealed only one signal due to aromatic protons at δ 7.20 - 8.20. In the ^{19}F nmr spectrum five signals appeared at δ -29.5 (CF_2, q), -22.3 (CF_3, t, t, q), 1.2 ($C\underline{F}_3CF_2$, q) and 26.6 ($CF_3C\underline{F}_2$, q) in the ratios 2 : 3 : 3 : 2. The signal at δ -22.3 due to =C-CF_3 was an overlapping triplets of triplets of quartets split by the all other fluorine nuclei in the molecule ($J_{CF_3\text{-}OCF_2}$ 11.4 Hz, $J_{CF_3\text{-}C\underline{F}_2CF_3}$ 18.1 Hz, $J_{CF_3\text{-}CF_2C\underline{F}_3}$ 9.1 Hz). The molecular ion, M^+ 405, and other appropriate fragment peaks, such as m/e 336 (M^+ -CF_3), 286 ($C_{13}H_5NOF_5$), 105 (C_6H_5CO), appeared in the mass spectrum.

TABLE 1

2,2-Difluoro-4-(F-ethyl)-3-(F-methyl)-5-(X)-6-(Y)-2H-pyrans,



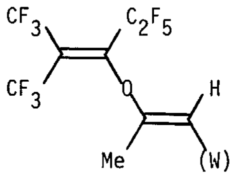
Compd.	X	Y	Yield	B.p.(°C/mmHg)	^{19}F Chemical shifts[a)]			Anal (%)					
								C		H		N	
			(%)	[M.p.(°C)]	2-F_2	3-CF_3	4-CF_2CF_3	Found	Calcd	Found	Calcd	Found	Calcd
(8) (nc)	C(O)Me	Me	39[b)]	82-84/20	-29.8	-21.3	22.1, -0.4	37.09	36.68	1.66	1.68	—	—
(10) (nc)	C(O)OEt	Me	42[b)]	70-72/23	-25.0	-19.8	19.4, -3.6	36.64	36.94	1.95	2.07	—	—
(12) (nc)	CN	Ph	89	[89]	-29.5	-22.3	26.6, 1.2	44.62	44.46	1.38	1.24	3.41	3.46
(14a) (nc)	C(O)CF_3	Ph	82	89-90/4	-26.3	-20.2	20.2, -0.8	40.40	40.36	1.06	1.06	—	—
(14b) (nc)	C(O)C_2F_5	Ph	68	96-98/3	-21.3	-18.8	37.5, 2.5	38.80	38.91	0.96	1.02	—	—

a) Chemical shifts are given in δ ppm upfield from ext. CF_3CO_2H in $CDCl_3$.

b) A divinyl ether (Table 2) was obtained as a side-product.

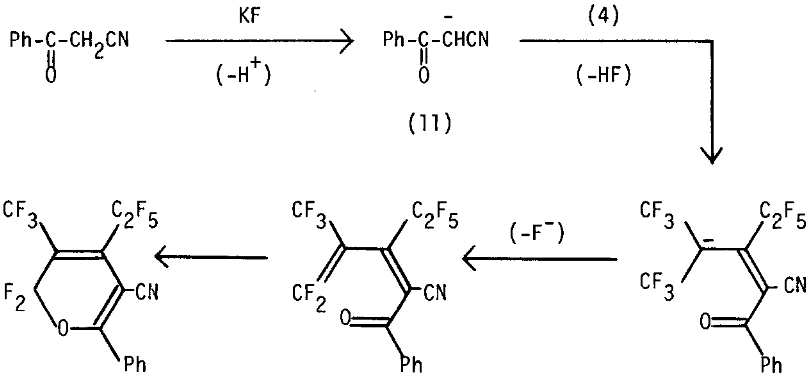
TABLE 2

($\underline{F}$-2-Methyl-2-pentene-3-yl) 1-methyl-2-(W)-vinyl ether,



Compd.	W	Yield (%)	B.p. (°C/mmHg)	^{19}F Chemical shifts[a)]		Anal (%)			
						C		H	
				$(C\underline{F}_3)_2F$	$C\underline{F}_2C\underline{F}_3$	Found	Calcd	Found	Calcd
(5) (nc)	C(O)Me	51	59-60/20	-20.2, -16.3	34.5, 4.7	35.16	34.75	1.87	1.86
(9) (nc)	C(O)OEt	48	58/23	-20.0, -16.3	34.4, 4.1	35.42	35.14	2.18	2.21

a) Similar to the foot-note a) of Table 1.

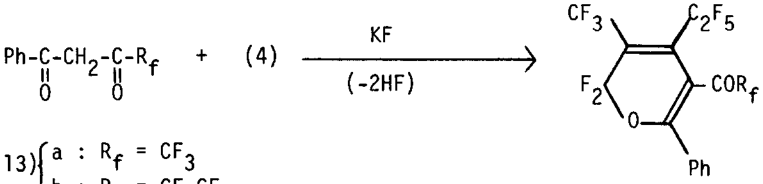


(11)

(12)

Reactions with benzoylmethyl (F-alkyl) ketones

When benzoylmethyl (F-methyl) ketone (13a) was used as a nucleophile in the above reaction, a similar pyrane compound (14a) was obtained as a sole product. The yields by using freeze-dried KF, calcine-dried KF, or $KF-Al_2O_3$ were 82, 36, and 52% respectively.



(13) a : $R_f = CF_3$
b : $R_f = CF_2CF_3$

(14) a : $R_f = CF_3$
b : $R_f = CF_2CF_3$

The structure of (14a) was also established by spectral data. The ^{19}F nmr spectrum contained resonances at δ -26.3, -20.2, -11.2, -0.8 and 20.0 in the ratios 2 : 3 : 3 : 3 : 2. The resonance at δ -26.3 in multiplets was assigned to the CF_2O group. The resonance of the CF_3 group on carbon-carbon double bond at δ -20.2 was split by all fluorine nuclei in the CF_2CF_3 group ($J_{CF_3-\underline{CF_2}CF_3}$ 16.7 Hz, $J_{CF_3-CF_2\underline{CF_3}}$ 8.5 Hz).

The molecular ion, M^+ 476, and other appropriate fragment peaks appeared in the mass spectrum.

Benzoylmethyl (F-ethyl) ketone (13b) and (4) also reacted under the same conditions giving a similar product, (14b).

EXPERIMENTAL

(F-2-Methyl-2-pentene-3-yl) 2-acetyl-1-methylvinyl ether (5) (nc) and 5-acetyl-4-(F-ethyl)-2,2-difluoro-3-(F-methyl)-2H-pyran (8) (nc)

Into a mixture of F-2-methyl-2-pentene (4) (9.00 g, 30 mmol), "freeze-dried" potassium fluoride [24] (3.54 g, 60 mmol) and acetonitrile (40 ml), acetylacetone (2.0 g, 20 mmol) was added. After 24 h or stirring at room temperature (20 °C), the reaction mixture was poured into water. An oily material was extracted with diethyl ether and the ethereal solution was dried over magnesium sulfate. After removal of the solvent, the residual oil was subjected to distillation in vacuo, giving a divinyl ether (5), b.p. 59 - 60 °C/ 20 mmHg, and a pyran (8), b.p. 82 - 84 °C/ 20 mmHg, in 51 and 39% yields, respectively.

Ethyl acetoacetate was used instead of acetylacetone in the above reaction, affording similar products, (9) and (10) (Table 1 and 2).

5-Cyano-4-(F-ethyl)-2,2-difluoro-3-(F-methyl)-6-phenyl-2H-pyran (12) (nc)

A mixture of F-2-methyl-2-pentene (4) (4.50 g, 15 mmol), benzoylacetonitrile (1.45 g, 10 mmol), freeze-dried KF (1.77 g, 30 mmol) and acetonitrile (20 ml) was stirred at room temperature for 24 h. After removing a solid material by filtration, the reaction mixture was poured into water, and an oily material was extracted with diethyl ether. The ethereal solution was dried ($MgSO_4$) and the solvent was evaporated. Remained crude product was recrystallized from hexane, yielding a pyran compound (12), m.p. 89 °C, in 89% yield.

4-(F-Ethyl)-2,2-difluoro-3-(F-methyl)-6-phenyl-4-(F-acetyl)-2H-pyran (14a) (nc)

Benzoylmethyl (F-methyl) ketone (2.16 g, 10 mmol), F-2-methyl-2-pentene (4) (4.50 g, 15 mmol), freeze-dried KF (1.77 g) and acetonitrile (20 ml) were made to react similarly and the reaction mixture was worked up as usual. Distillation gave a pyran (14a) in 82% yield.

When benzoylmethyl (F-ethyl) ketone (2.66 g, 10 mmol) was used instead of (F-methyl) ketone in the above reaction, a similar pyran (14b) was obtained in 68% yield.

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