TABLE I

EPOXIDATION OF ETHYL ALKYLIDENEACETOACETATES

Ethyl alkylideneaceto-acetate	Epoxy compd.	B.p., °C. (mm.)	Yield, %	Formula	Calcd., %		Found, %	
					C	H	C	H
Ethylidene[a]	IIa	123–125 (23)	47	$C_8H_{12}O_4$	55.80	7.03	55.14	6.93
Propylidene	IIb	127–130 (20)	60	$C_9H_{14}O_4$	58.05	7.58	57.69	7.36
Butylidene[b]	IIc	140–143 (20)	65	$C_{10}H_{16}O_4$	59.98	8.05	59.58	8.04
n-Heptylidene[c]	IId	151–152 (6)	70	$C_{13}H_{22}O_4$	64.44	9.15	64.46	9.00

[a] See ref. 3. [b] A. C. Cope and C. M. Hofmann, *J. Am. Chem. Soc.*, **63**, 3456 (1941). [c] J. M. L. Stephen, I. M. Tonkin, and J. Walker, *J. Chem. Soc.*, 1034 (1947).

TABLE II

PREPARATION OF α-DIKETONES FROM EPOXY ESTERS (II)

α-Diketone	B.p., °C.	Yield, %	Formula	Calcd., %		Found, %	
				C	H	C	H
IVa[a]	112–113[b]	41	$C_5H_8O_2$	59.98	8.05	59.70	7.98
IVb	127–128[c]	62	$C_6H_{10}O_2$	63.13	8.83	62.77	8.75
IVc[d]	150–151[e]	52	$C_7H_{12}O_2$	65.59	9.44	64.99	9.62
IVd	104–107[f] (20 mm.)	53	$C_{10}H_{18}O_2$	70.54	10.66	69.83	10.16

[a] Dioxime m.p. 172°, lit. m.p. 172–173° [I. M. Heilbron, E. R. H. Jones, P. Smith, and B. C. L. Weedon, *J. Chem. Soc.*, 54 (1946)]. *Anal.* Calcd. for $C_5H_{10}N_2O_2$: C, 46.14; H, 7.75; N, 21.53. Found: C, 46.31; H, 7.70; N, 21.67. [b] Lit.[a] b.p. 110–112°. [c] Lit.[a] b.p. 128–130°. [d] Dioxime m.p. 173°, lit. m.p. 173° [H. J. Cavell and S. Sugden, *J. Chem. Soc.*, 621 (1935)]. *Anal.* Calcd. for $C_7H_{14}N_2O_2$: C, 53.14; H, 8.92; N, 17.71. Found: C, 53.04; H, 8.73; N, 17.80. [e] Lit.[6] b.p. 46° (13 mm.). [f] Lit[5c] b.p. 66–68° (2 mm.).

was kept at 180–200° in an oil bath, decarboxylation took place and the product was the expected α-diketone. The yield of 2,3-heptanedione (IVc), b.p. 150–151°, was 52% based on IIc. The epoxy acid also gave a considerable amount of viscous oil distilling at 170–175° (6 mm.) with slight decomposition as a by-product of decarboxylation. The substance was reflected in the analytical figure but no further details were investigated.

Anal. Calcd. for $C_7H_{12}O_2$: C, 65.59; H, 9.44. Found: C, 65.86; H, 8.93.

The compounds and yields obtained by this method are summarized in Tables I and II.

Experimental

General Procedure. Epoxidation.—To ethyl alkylideneacetoacetate (0.01 mole) in ethanol (15 ml.) were added 30% hydrogen peroxide (15 ml.) and sodium tungstate dihydrate (0.7 g.). The mixture was kept for 1 hr. at 70–80° on a water bath. After removal of ethanol, the oily layer was separated from the aqueous layer. The aqueous layer was shaken with ether. The ethereal extract was combined with the oil and then dried over anhydrous sodium sulfate. After removal of ether, the residue was distilled under reduced pressure to give epoxy ester (II).

Hydrolysis.—A mixture of the epoxy ester (II) and a 1 *N* sodium hydroxide (mole equiv.) solution was allowed to saponify overnight at low temperatures (10–15°). The alkaline solution was shaken with ether and then acidified with dilute hydrochloric acid. The aqueous solution was extracted with ether. The ethereal solution was dried for several hours over anhydrous sodium sulfate. Removal of the solvent left the impure epoxy acid (III) as a viscous oil which decomposed on attempted distillation. The yields of crude epoxy acids were 75–80%. The acids were used without further purification for the following reaction.

Decarboxylation—The epoxy acid (III) was placed in a Claisen flask and heated at atmospheric pressure in an oil bath at 180–200° until the decarboxylation had ceased. The product was distilled directly from the reaction flask. Redistillation gave α-diketone (IV) as a yellow oil.

Ethyl Propylideneacetoacetate.—The titled compound was prepared by Knoevenagel's[3] method from propionaldehyde and ethyl acetoacetate. The yield was 65%, b.p. 116–118° (20 mm.).

Anal. Calcd. for $C_9H_{14}O_3$: C, 63.51; H, 8.29. Found: C, 63.30; H, 8.01.

Acknowledgment.—The authors wish to express their sincere thanks to Dr. Taro Hayashi and Dr. Tatsuo Takeshima for their kind advice.

Fluoro Ketones. II. Reaction of Amides with Fluoroacetones[1]

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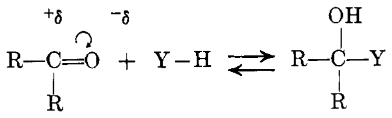
The fluoroacetones are highly reactive compounds which have been shown to undergo a number of interesting reactions. Moreover, their commercial availability[2] makes them even more attractive for chemical synthesis. The facility of the fluoro ketones to react



$$\underset{R}{\underset{|}{R-\overset{+\delta}{C}{=}\overset{-\delta}{O}}} + Y-H \rightleftharpoons R-\underset{R}{\underset{|}{\overset{OH}{\overset{|}{C}}}}-Y \qquad (1)$$

with nucleophilic agents can be attributed to the strong electropositive nature of the carbonyl carbon. A comparison of the reactivity of a series of fluoroacetones illustrates the powerful I effect of the α-fluorine atoms, *i.e.*, the greater the number of α-fluorine atoms, the greater the electrophilicity of the ketone. This effect is also manifested in the position of the equilibrium of eq. 1. In contrast to acetone, the position of equilibrium for hexafluoroacetone lies far to the right. We have observed the reversibility of this reaction in our

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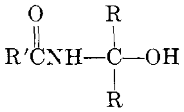
(1) For paper I of this series, see B. Farah and S. Horensky, *J. Org. Chem.*, **28**, 2494 (1963).

(2) General Chemical Division, Allied Chemical Corp., Morris Township, N. J.

TABLE I

AMIDE–FLUOROACETONE ADDUCTS

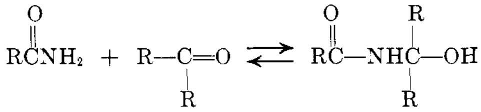


$$\mathrm{R'\overset{\overset{O}{\|}}{C}NH{-}\underset{R}{\overset{R}{\overset{|}{C}}}{-}OH}$$

Compd. III	R′	R	Yield, %	M.p., °C.	Calcd., % C	Calcd., % H	Calcd., % F	Found, % C	Found, % H	Found, % F
a	CH_3	CF_3	70	90–92 dec.	26.7	2.22		26.9	2.49	
b	CH_3	CF_2Cl	50	83–84 dec.	23.3	1.44		22.9	2.23	
c	C_2H_5	CF_2Cl	38	47–49	25.0	2.43		25.5	2.64	
d	$(CH_3)_2CHO$	CF_3	67	64–66	31.2	3.35		31.0	3.45	
e	$(CH_3)_2CHO$	CF_2Cl	60	53–55	27.8	2.98		27.4	3.00	
f	NH_2	CF_3	97	110 dec.	21.2	1.77		21.2	1.88	
g	NH_2	CF_2Cl	100	114–115 dec.	18.5	1.54		18.9	2.02	
h	NH_2	CF_2Cl; $CFCl_2$	70	100–101 dec.			20.6			20.3
i	NH_2	$CFCl_2$	79	106 dec.	16.4	1.4		16.4	1.80	
j	$NH_2C(O)NH$	CF_2Cl	57	130–131 dec.	20.1	1.7		20.1	2.0	
k	$(CH_3)_2N$	CF_3	50	139–140 dec.	28.4	3.14		28.1	2.90	

laboratories,[3] in the case of the formation of hemiketals. Although these reactions are reversible, isolation of hydrates,[4] hemiketals,[4a,5] amine adducts,[4a,5b,6] and cyanohydrins,[7] has been effected, albeit usually with appreciable decomposition.

Thus, it is surprising to find that the reaction of fluoro ketones with amides has not been reported. We have found that a wide variety of primary amides (I) react readily with fluoroacetones (II) to give good yields of the adducts (III) as shown in eq. 2. The



$$\mathrm{R\overset{\overset{O}{\|}}{C}NH_2 + R{-}\underset{R}{\underset{|}{C}}{=}O \rightleftarrows R\overset{\overset{O}{\|}}{C}{-}NH\underset{R}{\overset{R}{\overset{|}{C}}}{-}OH} \qquad (2)$$

I II III

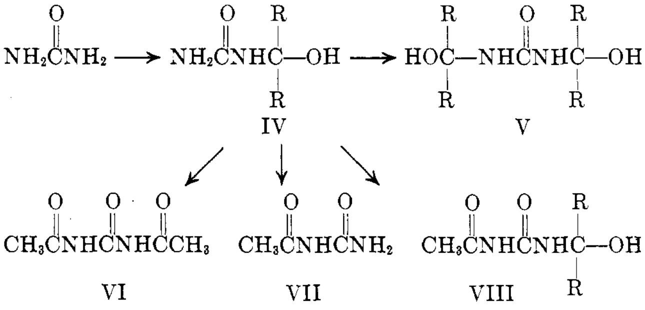
yields and physical properties of the amide–fluoroacetone adducts (III) are given in Table I.

Primary amides (I) undergo this reaction in a very facile manner in isopropyl ether or tetrahydrofuran; however, secondary amides (*e.g.*, N-methylbenzamide) do not. Thioamides and sulfonamides also failed to give the desired products. This reaction was successfully extended to the carbamates; however, longer reaction times were necessary with acetonitrile as the solvent of choice. Recently, a carbamate derivative has been reported by Hoover,[8] *et al.*, which had been prepared from the tetrafluorodichloroacetone–hydrocyanic acid adduct and aniline.

Primary ureas also were found to react with the fluoroacetones to give 1:1 adducts, and the yields and physical properties of these derivatives are given in Table I. Only ureas with primary amidic groups gave the adducts. A 50% yield was obtained from II (R = CF_3) and 1,1-dimethylurea, whereas 1,3-dimethyl- and 1,1,3-trimethylurea gave only starting materials.

The infrared and n.m.r. spectra confirmed the structures of these adducts and indicated internal hydrogen bonding. The infrared spectrum of IIIg exhibited the characteristic bands[9]: amide bands at 5.95 and 6.45 μ, intense C–F bands in the 8.0-μ region, broad absorption in the 2.9–3.2-μ range, with discernible bands for OH at 2.90 μ, NH at 3.05 and 3.2 μ. No solvent shifts for the NH and OH vibrational frequencies were observed for IIIg, in the 0.01 to 4.0 *M* range with both tetrahydrofuran and acetonitrile as solvents.[10] Thus, little if any intermolecular proton exchange occurs. The F^{19} n.m.r. spectra for IIIa and IIIg gave sharp singlets at $\delta_{CFCl_3} = +83.8$ and 83.7 p.p.m., respectively, which is in good agreement with chemical shifts observed for similar compounds.[11]

Chemical evidence can also be cited to substantiate the strong hydrogen bonding in the case of urea adducts (IIIf–i).



IV V VI VII VIII

Employing a large excess of fluoroacetone under forcing conditions failed to give the 2:1 adduct, V. However, IV was smoothly converted to its pyridine salt which did react with another mole of fluoroacetone to give the pyridine salt of V. Acidification then gave the free 1:2 adduct V. Thus, removal of the proton

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(3) P. Lombardo, unpublished results.

(4) (a) C. Woolf, Abstracts of Papers, 137th National Meeting of the American Chemical Society, New York, N. Y., Sept., 1957, p. 23M; (b) A. L. Henne, J. W. Shepard, and E. J. Young, *J. Am. Chem. Soc.*, **72**, 3577 (1950); (c) A. T. Morse, P. B. A. Ayscough, and L. C. Leitch, *Can. J. Chem.*, **33**, 453 (1955).

(5) (a) I. L. Knunyants and Yu. A. Cherburkov, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 678 (1960); (b) H. E. Simmons and D. W. Wiley, *J. Am. Chem. Soc.*, **82**, 2288 (1960); (c) I. L. Knunyants, C. Ch'ing-yun, and N. P. Gambaryan, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 686 (1960).

(6) R. G. Koshyanovskii, *Proc. Acad. Sci. USSR, Chem. Sec.*, **137**, 379 (1961).

(7) I. L. Knunyants, Y. M. Rokhlin, N. P. Gambaryan, Y. A. Cherburkov, and C. Tsin-Yun, *Khim. Nauka i Promy.*, **4**, 802 (1959).

(8) F. W. Hoover, H. B. Stevenson, and H. S. Rothrock, *J. Org. Chem.*, **28**, 1825 (1963).

(9) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1958.

(10) A Beckman IR-8 spectrophotometer with 0.025-mm. NaCl liquid cells was used. We are indebted to Mrs. Nancy Bolan for these results. One of the referees suggested that a single bridge complex with the solvent may be involved. Although this cannot be definitely ruled out, it seems unlikely in view of our failure to observe shifts of any of the bands on changing solvents. Unfortunately, the adduct either reacted with or was insoluble in most organic solvents.

(11) Hexafluoroacetone and its hydrates exhibit sharp F^{19} singlets at $\delta_{CFCl_3} = 84.6 \pm 0.2$ p.p.m.: Dr. B. Stewart, private communication.

by pyridine, freed the amido function for nucleophilic attack on another molecule of fluoroacetone.

Acetylation of IV under acidic conditions gave VI, VII, or VIII.

Acetic anhydride with a few drops of concentrated sulfuric acid gave only VI, diacetylurea, while monoacetyl urea VII was obtained with acetic anhydride and catalytic amounts of either methane- or *p*-toluene sulfonic acid. Compounds VI and VII were probably formed *via* the acetylation of urea which was presumably generated by the acid-catalyzed hydrolysis of IV. These compounds were identified by a comparison of their infrared spectra with those of authentic samples and mixture melting points.

When IV was heated with acetyl chloride at reflux for 1 hr. a 33% yield of a monoacetylated derivative VIII was obtained. This was shown to be the N-acetyl derivative of IV by the presence of the hydroxyl group (2.95) and absence of the primary amide moiety (3.05 μ) in its infrared spectrum. Furthermore, treatment of VIII with amines gave the corresponding amine salts. Its proton n.m.r. spectrum was also consistent with the assigned structure and its F^{19} n.m.r. spectrum showed a sharp singlet[11] at $\delta_{CFCl_3} = 83.8$ p.p.m.

All attempts to prepare the acetates of the amide and carbamate adducts (IIIa–i) employing acid and basic conditions resulted in failure. Either the adducts were recovered unchanged or were hydrolyzed to the amides and fluoroacetone hydrates.

Experimental

The F^{19} and H' n.m.r. spectra were obtained with a Varian high-resolution spectrophotometer Model V-4302B. The spectra were calibrated in parts per million displacements from the external primary standards trichlorofluoromethane and tetramethylsilane.

Amide–Fluoroacetone Adducts.—To a stirred solution of 0.2 mole of acetamide in 150 ml. of tetrahydrofuran at room temperature was introduced 0.24 mole of fluoroacetone. The rate of addition was controlled so that the temperature of the reaction mixture did not exceed 50°. After the addition was complete, the mixture was stirred for an additional 30 min. and allowed to cool to room temperature. Removal of the solvent at reduced pressure gave the crude product which was distilled or recrystallized.

Carbamate–Fluoroacetone Adducts.—To a solution of 0.1 mole of carbamate in 40 ml. of acetonitrile nitrile was added 0.11 mole of the fluoroacetone. This was kept in a stoppered pressure bottle with occasional shaking for 5 days. After removal of the solvent under reduced pressure, the crude product was recrystallized from toluene.

Urea–Fluoroacetone (1:1) Adducts.—The fluoroacetone (0.2 mole) was added to 0.2 mole of the urea in tetrahydrofuran at 40° over a 30 min. period with stirring. The reaction mixture was stirred at 40° for an additional 30 min. and was allowed to cool to room temperature. After evaporating the solution to one-third volume, it was chilled to −60° and filtered to give the solid product.

Pyridine Salt of Urea–Fluoroacetone (1:2) Adduct.—To a solution of 2.4 g. (0.03 mole) of pyridine in 40 ml. of tetrahydrofuran was added 7.8 g. (0.03 mole) of IV ($R = CF_2Cl$) followed by 6.0 g. (0.03 mole) of *sym*-dichlorotetrafluoroacetone. The reaction mixture was stirred at room temperature for 2 days. Removal of solvent under reduced pressure gave 14.0 g. of a crude solid which was triturated with hexane leaving 13.0 g. (80%) of a white solid, m.p. 91–95°. Recrystallization from a cold ether–hexane mixture raised the melting point to 96–97°.

Anal. Calcd. for $C_{12}H_9Cl_4F_8N_3O_3$: C, 26.8; H, 1.7; N, 7.8. Found: C, 26.7; H, 1.8; N, 7.5.

Urea–Fluoroacetone (1:2) Adducts.—The pyridine salt of V, 0.5 g. (0.01 mole), was stirred with 10 ml. of 1:1 hydrochloric acid for 30 min. The solid was filtered and was dissolved in methylene chloride, washed with water, and dried over anhydrous magnesium sulfate. Removal of the solvent under reduced pressure gave 0.2 g. (50%) of a white solid, m.p. 90–91°.

Anal. Calcd. for $C_7H_4Cl_4F_8N_2O_3$: N, 6.1. Found: N, 6.3.

Acetylation of the Urea–Hexafluoroacetone 1:1 Adduct. A.—A mixture of 5.7 g. (0.025 mole) of IV, 5.1 g. (0.05 mole) of acetic anhydride, and 2 drops of concentrated H_2SO_4 was heated on a steam bath for 2 hr. The mixture was chilled in a Dry Ice–acetone bath and filtered. The solid was dissolved in methylene chloride, washed with water, and dried; the solvent was removed under reduced pressure. A yield of 1.0 g. (39%) of a white solid, m.p. 150–152° (lit.[12] m.p. 154–155°), was obtained. This was identical in every way with the authentic sample of N,N′-diacetylurea.

B.—A mixture of 2.3 g. (0.01 mole) of IV, 5.1 g. (0.05 mole) of acetic anhydride, and 1 drop of methane sulfonic acid[13] was heated on a steam bath for 5 min. This was worked up in the same manner as A to give a white solid, 0.3 g. (35%), m.p. 217–219° (lit.[12] m.p. 216–217°). This was identical with the authentic sample of N-acetylurea.

C.—A mixture of 18 g. (0.08 mole) of IV and 39 g. (0.5 mole) of acetyl chloride was refluxed for 1 hr. Chilling the mixture and filtration of the solid gave 7.0 g. (33%) of a white solid, m.p. 92–94° identified as N-acetyl N′-2 hydroxyhexafluoroisopropylurea (VIII).

Anal. Calcd. for $C_6H_6F_6N_2O_3$: C, 26.9; H, 2.2. Found: C, 26.8; H, 2.4.

Acknowledgment.—We are indebted to Dr. B. B. Stewart for the n.m.r. spectra, to Mrs. N. Bolan for the infrared spectra, and to Dr. C. Woolf for some helpful discussion.

[12] E. A. Werner, *J. Chem. Soc.*, **109**, 1120 (1916); R. W. Stoughton, *J. Org. Chem.*, **2**, 514 (1937).

[13] When *p*-toluene sulfonic acid was used as a catalyst, the yield was 25%.

Formation of 2-Propyl-5-methyl- and 2-Propyl-4-methyl-Δ^2-oxazolines from the Thermal Decomposition of Phosphoric Amides Derived from 1-Amino-2-propyl and 2-Amino-1-propyl Butyrates

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Tris[1-(2-methyl)aziridinyl]phosphine oxide (I) undergoes imine opening, addition reaction with carboxylic acids to form phosphoric amide derivatives of esters of aminopropanols, which accounts for the utility of I as a cross-linking agent for carboxyl-containing polymers.[1] It has been observed,[2] however, that these cross links are sometimes susceptible to thermal degradation. In an effort to determine a possible mode of cross-link scission, I was treated with butyric acid at reflux temperature in a toluene solution and the thermal decomposition of the phosphoric amide product (II) was investigated (eq. 1).

The reaction of carboxylic acids with three-membered imine rings has been reported to be an SN2 reaction,

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[1] (a) Interchemical Corporation, "MAPO" New Product Bulletin; (b) P. S. Hudson and C. C. Bice, U. S. Patent 3,087,844 (1963).

[2] B. M. Wall and G. Thompson, unpublished results.