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FLUORO OLEFINS. PART V. THE SYNTHESIS AND CYCLIZATION OF POLYFLUORINATED DIKETONES. THE REACTION OF POLYFLUORINATED α,β-UNSATURATED CYCLIC KETONES WITH METHYLENETRIPHENYLPHOSPHORANES*

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SUMMARY

An attempt to prepare terminal polyfluorinated dienes by the reaction of polyfluorinated diketones with difluoromethylenetriphenylphosphorane, generated *in situ* from sodium or lithium chlorodifluoroacetate and triphenylphosphine, was unsuccessful. Polyfluorinated diketones with α-hydrogens underwent a base-catalyzed intramolecular aldol-type condensation in the presence of difluoromethylenetriphenylphosphorane. The resulting α,β-unsaturated cyclic ketones could be more conveniently prepared by the reaction of the polyfluorinated diketone and triethylamine. The 2-cyclopentenones, but not the 2-cyclohexenones, reacted with difluoromethylenetriphenylphosphorane to produce the 3-difluoromethylene cycloalkenes. Both the 2-cyclohexenones and 2-cyclopentenones reacted with methylenetriphenylphosphorane.

INTRODUCTION

In the previous papers of this series, the preparation of various polyhalogenated olefins by the reaction of fluorinated ketones with difluoro-[2] and fluorochloromethylenetriphenylphosphorane[3] was reported. This paper reports the attempted extension of this reaction sequence to include the preparation of polyfluorinated terminal dienes. The cyclization of some new polyfluorinated diketones, and the reaction of various methylene ylids with polyfluorinated 2-cyclopentenones and 2-cyclohexenones are also described.

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* Taken in part from Ref. 1.

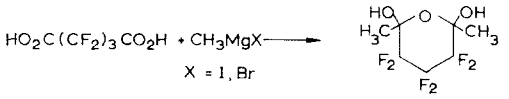
RESULTS

Synthesis of polyfluorinated diketones

The polyfluorinated diketones used in this study were synthesized by the reaction of perfluorodicarboxylic acids and alkylmagnesium halides in a mole ratio of 1 to 6, respectively. The synthesis of 1,2-dibenzoylperfluoroethane (I), 1,3-dibenzoylperfluoropropane (II), and 1,4-dibenzoylperfluorobutane (III) has recently been reported by Yakubovich[4]. Groth[5] prepared 3,3,4,4-tetrafluorohexane-2,5-dione (IV) by the reaction of perfluorosuccinic acid and methylmagnesium bromide. Perfluoroglutaric acid, upon reaction with methylmagnesium bromide, gave an inseparable mixture of products[5].

$$
\begin{array}{lll}
HO_2C(CF_2)_nCO_2H + 6RMgBr \rightarrow & \multicolumn{2}{l}{RCO(CF_2)_nCOR} \\
 & (I); & R = C_6H_5,\ n = 2; \\
 & (II); & R = C_6H_5,\ n = 3; \\
 & (III); & R = C_6H_5,\ n = 4; \\
 & (IV); & R = CH_3,\ \ n = 2.
\end{array}
$$

Smith[6] reported 2,6-dimethylhexafluoropyran-2-6-diol (V) to be the product of the reaction of perfluoroglutaric acid and methylmagnesium iodide. We have found that (V) was also produced from methylmagnesium bromide and perfluoroglutaric acid.



(V)

Thus, it appeared that dialkyl diketones could not be prepared from perfluoroglutaric acid and alkylmagnesium halides. Unexpectedly, the reaction of ethylmagnesium bromide and perfluoroglutaric acid produced 4,4,5,5,6,6-hexafluorononane-3,7-dione (VI) in a 70% yield. Substitution of ethylmagnesium iodide for ethylmagnesium bromide gave only a 10% yield of (VI). The diketones could be prepared from perfluorosuccinic acid in equal yields from the alkylmagnesium bromide or iodide. The physical properties of the polyfluorinated diketones prepared for use in this study are summarized in Table 1. The di-2,4-dinitrophenylhydrazone derivatives of previously unreported polyfluorinated diketones are listed in Table 2.

Wittig reaction on polyfluorinated diketones

The polyfluorinated diketones were reacted with difluoromethylenetriphenylphosphorane, generated *in situ* from lithium chlorodifluoroacetate and triphenylphosphine. The lithium salt was chosen since its use has been demonstrated as minimizing the isomerization of the terminal olefin to the internal olefin[2]. A mole

TABLE 1

PHYSICAL PROPERTIES OF POLYFLUORINATED DIKETONES, $RCO(CF_2)_nCOR$

Compound	R	*n*	% Yield [a]	B.p. (mmHg)	n_D^{20}	$\nu(C{=}O)$, μ	C, % Calcd.	C, % Found	H, % Calcd.	H, % Found	Ref.
(I)	C_6H_5	2	60	m.p. 64–64.5	.....	5.90	61.94	61.96	3.25	3.43	4
(II)	C_6H_5	3	60	m.p. 49.5–50	.....	5.84	56.59	56.37	2.80	2.78	4
(IV)	CH_3	2	56	42(50)	.....	5.68	38.71	38.77	3.23	3.52	5
(VII)	C_2H_5	2	61	71(17)	1.3712	5.70	44.85	45.08	4.67	4.71	b
(VI)	C_2H_5	3	70	83–83.5(11)	1.3647	5.68	40.90	40.84	3.74	3.89	b
(VIII)	C_2H_5	4	47	98(19)	1.3614	5.67	38.22	38.23	3.18	3.11	b
(IX)	n-C_3H_7	2	60	67(5.5)	1.3831	5.68	49.59	49.39	5.78	5.71	b
(X)	n-C_3H_7	3	67	55–56(0.9)	1.3771	5.67	45.20	45.24	4.79	4.87	b

[a] Isolated yield based on diacid.

[b] New compounds.

TABLE 2

DI-2,4-DINITROPHENYLHYDRAZONES OF POLYFLUORINATED DIKETONES, $\mathrm{RC(=NNHR')(CF_2)_nC(=NNHR')R}$ WITH $\mathrm{R'=2,4\text{-}(O_2N)_2C_6H_3}$ (nc)

R	*n*	M.p.	C, % Calcd.	C, % Found	H, % Calcd.	H, % Found	N, % Calcd.	N, % Found
C_2H_5	2	202.5–203.0	41.81	42.02	3.13	3.26	19.51	19.59
C_2H_5	3	177.0–177.5	40.36	40.51	2.88	2.85	17.94	17.81
C_2H_5	4	191–192	39.16	38.75	2.67	2.57	16.61	16.25
n-C_3H_7	2	190.0–190.5	43.85	43.88	3.65	3.76	18.60	18.57
n-C_3H_7	3	118–119	42.33	42.52	3.37	3.55	17.17	17.25

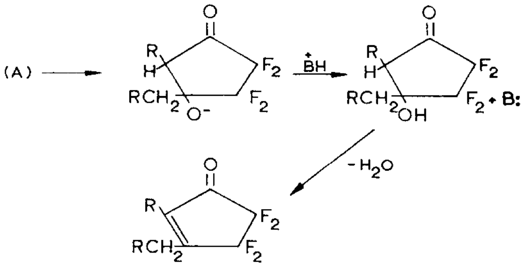
ratio of 1 to 4 to 4, diketone to phosphine to salt, was employed since the largest consumption of diketone (I) was observed with this ratio.

The reaction of polyfluorinated diketones which contained no α-hydrogens with alkali metal salts of chlorodifluoroacetic acid and triphenylphosphine was found inapplicable to the synthesis of the desired terminal dienes. For example, the reaction of (I) or (II) with triphenylphosphine and the lithium salt in dimethylformamide (DMF), or the sodium salt in diglyme, produced a small amount of two products in addition to unreacted (I) or (II). Fractional distillation, preparative GLPC and alumina column chromatography failed to separate these two products from the reaction mixture.

This reaction sequence was then applied to the dialkyl diketones. The α-hydrogen of these diketones was found to react with either the solvent, or the ylid in a solvent which was inert to the diketone. An α,β-unsaturated cyclic ketone was thus the product of the reaction.

$$\mathrm{RCH_2CO(CF_2)_2COCH_2R + B{:} \rightarrow R\overset{-}{C}HCO(CF_2)_2COCH_2R + \overset{+}{B}H}$$

(A)



Addition of lithium chlorodifluoroacetate to a solution of diketone (VII) and triphenylphosphine in dry DMF produced a 14% yield of 2-methyl-3-ethyl-tetrafluoro-2-cyclopentenone (XII). Upon heating (VII) in DMF alone, (XII) was also formed. It will be shown later, that the dimethylamine produced in the decomposition of DMF was responsible for this observation. Unfortunately, the best solvent (DMF) for preparation of difluoromethylenetriphenylphosphorane could not therefore be used.

Similar results were obtained when the ylid was generated from sodium chlorodifluoroacetate and triphenylphosphine in dry diglyme. Thus, when 5,5,6,6-tetrafluorodecane-4,7-dione (IX) or 5,5,6,6,7,7-hexafluoroundecane-4,8-dione (X) was heated with the sodium salt and the phosphine in dry diglyme, low yields of the cyclic products, 2-ethyl-3-n-propyltetrafluoro-2-cyclopentenone (XIII) and 2-ethyl-3-n-propylhexafluoro-2-cyclohexenone (XV), were produced. Heating (IX) or (X) with diglyme and triphenylphosphine did not produce any (XIII) or (XV). Apparently, difluoromethylenetriphenylphosphorane in diglyme reacted preferentially as a base to remove an α-hydrogen from the diketone.

A few other examples of a Wittig reaction in which the ylid reacted as a base have also been reported. Mesityl oxide was formed in the reaction of acetone with Wittig reagents[7]. Small amounts of 2-cyclopentylidenecyclopentanone were isolated from the reaction of carbomethoxymethylenetriphenylphosphorane and cyclopentanone[8]. Easily enolizable ketones, such as cyclopentanone and cyclohexanone also underwent α-hydrogen abstraction in the presence of strongly basic phosphoranes[9].

Cyclization of polyfluorinated diketones

The polyfluorinated diketones (VI), (VII), (IX), and (X) reacted with catalytic amounts of a base, such as dimethylamine or triethylamine, to form excellent yields of the aldol-type products, (XIV), (XII), (XIII), and (XV), respectively. Table 3 summarizes the physical properties of the α,β-unsaturated cyclic ketones, while Table 4 lists the 2,4-dinitrophenylhydrazone derivatives of these cyclic ketones.

Since DMF has been reported to decompose to dimethylamine[10] ($pK_a = 10.61$[11]), it was suspected that this amine was the basic catalyst for the cyclizations observed in DMF. Indeed, the addition of a trace amount of triethylamine ($pK_a = 10.64$[12]) to (VII) resulted in an exothermic reaction. A 67% yield of (XII) was produced, and beads of water were formed in the reaction mixture. Similar results were obtained by heating a solution of (VII) in DMF.

In order to cyclize 3,3,4,4-tetrafluorohexane-2,5-dione (IV), it was necessary to resort to the strongly basic hybride ion which irreversibly removed an α-hydrogen from the diketone. Upon reaction of (IV) with sodium hydride in ether, a 43% yield of (XI) and a 50% yield of black tar was formed. This tar was the only evidence of dimerization or telomerization noted in these cyclization reactions. The failure of the weak base, triethylamine, to effect cyclization of (IV) was due to the lower reactivity of the methyl group as compared to the ethyl and n-propyl groups. Hunsdieker[13] has observed that similar hydrocarbon diketones, with a methyl group on one end, and a larger alkyl group on the other end, afforded exclusively the aldol product with an intact methyl group.

TABLE 3

PHYSICAL PROPERTIES OF POLYFLUORINATED CYCLIC α,β-UNSATURATED KETONES, $\underline{\ulcorner CR'=CRCO(CF_2)_n \urcorner}$ (nc)

Compound	R	R′	*n*	B.p. (mmHg)	n_D^{20}	ν(C=O); ν(C=C) μ	C, % Calcd.	C, % Found	H, % Calcd.	H, % Found
(XI)	H	CH_3	2	90(92)	1.3915	5.63; 6.11	42.85	42.97	2.38	2.03
(XII)	CH_3	C_2H_5	2	66(17)	1.4109	5.68; 6.06	48.97	49.08	4.08	3.61
(XIII)	C_2H_5	n-C_3H_7	2	122–123(78)	1.4188	5.69; 6.10	53.57	53.52	5.35	5.40
(XIV)	CH_3	C_2H_5	3	53(20)	1.3988	5.78; 6.11	43.90	44.23	3.25	3.18
(XV)	C_2H_5	n-C_3H_7	3	52(28)	1.4054	5.79; 6.15	48.17	48.23	4.37	4.03

TABLE 4

2,4-DINITROPHENYLHYDRAZONES OF POLYFLUORINATED CYCLIC α,β-UNSATURATED KETONES, $\underline{\text{CR}'{=}\text{CRC}({=}\text{NNHR}^2)(\text{CF}_2)_n}$ WITH $R^2 = 2,4\text{-}(O_2N)_2C_6H_3$ (nc)

R	R′	n	M.p.	C, %		H, %		N, %	
				Calcd.	Found	Caldc.	Found	Calcd.	Found
H	CH_3	2	137–138	41.37	41.72	2.29	2.38	16.09	16.04
CH_3	C_2H_5	2[a]	144–145	44.68	44.57	3.19	3.16	14.89	14.81
C_2H_5	n-C_3H_7	2[a]	93–94	47.52	47.48	3.96	3.99	13.86	13.71
CH_3	C_2H_5	3[a]	130–131	42.25	41.86	2.81	2.77	13.14	12.92

[a] Elemental analyses are the average of three runs.

An attempt to extend this cyclization scheme to include the preparation of the seven-membered ring system was not successful. The addition of 4,4,5,5,6,6,7,7-octafluorodecane-3,8-dione (VIII) to triethylamine in DMF produced a deep wine-red solution. However, only (VIII) in a 95% yield was recovered from the solution. Upon treatment of (VIII) with sodium hydride in ether, the evolution of hydrogen occurred. After hydrolysis of the reaction mixture, a 98% recovery of (VIII) was obtained. This observation indicated that the carbanion did form, but did not cyclize or dimerize.

In addition to satisfactory elemental analyses, structure proof was accomplished by spectral data. The infrared spectra of these compounds exhibited a strong carbonyl absorption (*ca.* 5.7 μ), and a weak olefinic absorption (*ca.* 6.01 μ). These absorptions were in agreement with those reported for similar α,β-unsaturated cyclic ketones[14]. The ultraviolet spectra, summarized in Table 5, showed extinction coefficients indicative of conjugated systems. The proton NMR showed the loss of a methylene group from the parent diketone. For example, (XII) displayed the methyl group adjacent to the carbonyl as a triplet (1.92 δ, $J = 3.5$ cps, 3H), and the ethyl group as a triplet (1.27 δ, $J = 7.5$ cps, 3H), and a quartet (2.61 δ, $J = 7.5$ cps, 2H). The methyl group was probably coupled to the

TABLE 5

ULTRAVIOLET DATA FOR CYCLIC α,β-UNSATURATED KETONES, $\underline{\text{CR}' = \text{CRCO}(\text{CF}_2)_n}$

Compound	R	R′	n	$\lambda_{\text{max.}}$, mμ	ε, C_6H_{12}
(XI)	H	CH_3	2	210	15 400
(XII)	CH_3	C_2H_5	2	226	18 000
(XIII)	C_2H_5	n-C_3H_7	2	227	18 200
(XIV)	CH_3	C_2H_5	3	235	16 000
(XV)	C_2H_5	n-C_3H_7	3	238	15 000

fluorines in the four position. This type of coupling was further evidenced by the appearance of the methyl group in 3-difluoromethylene-2-methyl-1-ethyltetrafluorocyclopentene (XVI) as a quartet. Here, the methyl group was coupled to the fluorines in the five position as well as the adjacent vinylic fluorine. Proton NMR data for the cyclic α,β-unsaturated ketones are given in Table 6.

TABLE 6

PROTON NMR DATA FOR POLYFLUORINATED CYCLIC α,β-UNSATURATED KETONES, $\underline{\text{—CR}'\text{=CRCO(CF}_2)_n\text{—}}$

Compound	n	R	m[a]	δ[b]	J[c]	R′	m[a]	δ[b]	J[c]
(XI)	2	H	o	6.52	1.3	CH_3	q	2.28	1.6
(XII)	2	CH_3	t	1.92	3.5	C_2H_5	t	1.27	7.5
							q	2.61	7.5
(XIII)	2	C_2H_5	ot	1.09		n-C_3H_7	ot	1.09	
							sx	1.67	7.5
			m	2.48			m	2.48	
(XIV)	3	CH_3	t	2.08	3.5	C_2H_5	t	1.27	7.5
							q	2.68	7.5
(XV)	3	C_2H_5	t	1.07	7.5	n-C_3H_7	t	1.07	7.5
							m	1.64	
			m	2.57			m	2.57	

[a] Multiplicity; t, triplet; ot, two overlapping triplets; q, quartet; o, octet; sx, sextet; m, multiplet.
[b] Reported in δ values downfield from internal standard of TMS.
[c] Coupling constants in cps.

Wittig reaction on cyclic α,β-unsaturated ketones

Upon reaction with difluoromethylenetriphenylphosphorane, generated *in situ* from lithium chlorodifluoroacetate and triphenylphosphine, the cyclopentenones, (XII) and (XIII), produced low yields of the exocyclic difluoromethylene olefins (XVI) and (XVII), respectively. When sodium chlorodifluoroacetate and triphenylphosphine were used, no (XVI) or (XVII) was formed. Slagel[15] has also recently reported that better yields of olefin were obtained when lithium not sodium chlorodifluoroacetate was used.

Treatment of (XIII) with dichloromethylenetriphenylphosphorane, generated by the method of Speziale and Ratts[16], failed to produce any exocyclic dichloromethylene olefin. Heating (XIII) with sodium trichloroacetate and triphenylphosphine in dry monoglyme, also did not produce any exocyclic dichloromethylene olefin.

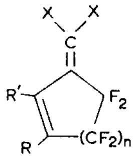
In a similar manner, the cyclohexenones, (XIV) and (XV), did not produce any corresponding exocyclic dihalomethylene olefin upon reaction with difluoro-, fluorochloro-[3], or dichloro-methylenetriphenylphosphorane.

Both (XII) and (XIV) reacted with methylenetriphenylphosphorane, generated from methyl-lithium and methyltriphenylphosphonium bromide in ether, to form a 23% yield of (XVIII), and a 17% yield of (XIX), respectively. Apparently, fluorine substitution in the ring did not aid the reaction. Antonucci[17] reported the synthesis of 3-methylene-2-methyl-cyclohexenone in a 24% yield by the reaction of 2-methyl-2-cyclohexenone with methylenetriphenylphosphorane.

The physical properties of the olefins are listed in Table 7. All the olefins were isolated by preparative GLPC; all yields are thus isolated yields. These olefins were unstable, upon storing in sealed glass ampules (XVI) and (XVIII) eliminated hydrofluoric acid and deposited a solid. Olefins (XVII) and (XIX) turned to a glass which eventually solidified. Samples of the olefins could be stored for a short time in nitrogen-flushed, sealed glass ampules stored at Dry Ice temperature. Due to their instability, satisfactory elemental analyses could not be obtained for all of the olefins.

TABLE 7

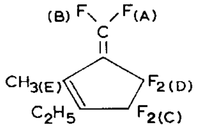
PHYSICAL PROPERTIES OF 3-EXOMETHYLENECYCLOALKENES,



Compound	R	R′	X	*n*	Yield	n_D^{20}	$\nu(C{=}CX_2), \nu(C{=}C)$ μ	$\lambda_{max.}(\varepsilon)$ mμ
XVI	C_2H_5	CH_3	F	1	15%	1.4033	5.71, 6.06	223 (20 300)
XVIII	C_2H_5	CH_3	H	1	23%	1.4289	6.07, 6.10	229 (25 000)
XVII	*n*-C_3H_7	C_2H_5	F	1	27%[a]	1.4133	5.70, 6.12	224 (19 700)
XIX	C_2H_5	CH_3	H	2	17%[b]	1.4156	6.08, 6.17	231 (19 700)

[a] Calcd. for $C_{11}H_{12}F_6$: C, 51.56; H, 4.65. Found: C, 51.12; H, 4.30.
[b] Calcd. for $C_{10}H_{10}F_6$: C, 49.18; H, 4.09. Found: C, 48.33; H, 3.93.

The most useful criteria for establishing the structure of the exocyclic difluoromethylene olefins were the proton and fluorine NMR spectra. For example, the fluorine NMR spectrum of (XVI) showed two different vinylic fluorines. Fluorine (A) appeared as a doublet (J(AB) = 27.5 cps) of triplets centered at 80.1 ϕ (1F). The order of magnitude of this coupling agreed with the reported[18] coupling constant for olefinic geminal fluorines (J(FF) = 27–87 cps). The triplets at 80.0



(XVI)

and 81.2 ϕ each had J(AD) = 11.5 cps. Similar coupling has been observed for *cis*- and *trans*-2-phenylheptafluoro-2-butenes[19]. Vinylic fluorine (B) appeared as a doublet at 83.2 ϕ (J(AB) = 27.5 cps, 1F). The fine structure on this doublet indicated that (B) was coupled to methyl protons (E), J(BE) = 3 cps. Ring fluorines (C) appeared as a singlet at 112.7 ϕ (2F). The fine structure on this singlet indicated that fluorines (C) were also coupled to protons (E), J(EC) = 3 cps. Ring fluorines (D) appeared as a doublet centered at 115.8 ϕ (J(AD) = 11.5 cps, 2F). The doublet and singlet due to the ring fluorines indicated that (C) and (D) did couple, but J(CD) $<$ 1 cps. The lack of coupling between two sets of fluorine atoms on neighboring carbons has also been observed in fluorocyclobutanes[20]. The proton NMR spectrum displayed the methyl protons (E) as a quartet at 1.86 δ (J(EC) = 3 cps, J(EB) = 3 cps, 3H); the ethyl protons as a quartet at 2.74 δ (J(HH) = 7.5 cps, 2H) and a triplet at 1.10 δ (J(HH) = 7.5 cps, 3H).

The fluorine NMR spectrum of (XVII) displayed fluorine (A) as a doublet (J(AB) = 26.5 cps) of triplets (J(AD) = 12 cps) centered at 80.1 ϕ; fluorine (B) as a doublet at 82.9 ϕ (J(AB) = 26.5 cps); fluorines (C) as a singlet at 112.3 ϕ, and fluorines (D) as a doublet centered at 115.5 ϕ (J(AD) = 12 cps). The proton NMR spectrum displayed a multiplet at 0.93 δ (6H); a sextet at 1.52 δ (J(HH) = 7.5 cps, 2H), and a multiplet at 2.22 δ (4H).

The proton NMR spectrum of olefin (XVIII) displayed the vinyl protons as a doublet (J(HH) = 9 cps) of triplets; the vinyl hydrogen adjacent to the ring fluorines as a triplet at 5.46 δ (J(HF) = 3 cps, 1H), and the other vinyl proton as a poorly resolved triplet at 5.61 δ (J(HF) = 2 cps, 1H). The methyl group appeared as a triplet at 2.00 δ (J(HF) = 3.5 cps, 3H), while the ethyl group appeared as a triplet at 1.26 δ (J(HH) = 7.5 cps, 3H) and a quartet at 2.46 δ (J(HH) = 7.5 cps, 2H).

Olefin (XIX) displayed the vinyl protons as a doublet centered at 5.91 δ (J(HH) = 9.5 cps, 2H). The methyl protons appeared as a triplet at 2.03 δ (J(HF) = 3.5 cps, 3H). The ethyl group appeared as a triplet at 1.16 δ (J(HH) = 7.5 cps, 3H), and a quartet at 2.41 δ (J(HH) = 7.5 cps, 2H).

EXPERIMENTAL

All melting points are corrected. Boiling points are uncorrected. Infrared spectra were recorded on a Perkin–Elmer Model 21 spectrophotometer using a neat film calibrated *vs.* a 0.07 mm polystyrene film. Ultraviolet spectra were recorded on a Beckman DK-2A recording spectrophotometer with cyclohexane as the solvent. The proton NMR spectra were recorded on a Varian A60 or HA-100 spectrometer, and are reported in δ values downfield from an internal standard of TMS. The fluorine NMR spectra were recorded on an HA-100 spectrometer tuned to 94.1 Mcps, and are reported in ϕ values upfield from an internal standard of $CFCl_3$. GLPC analyses were carried out on an F and M Model 700 dual programmed gas chromatograph with helium as the carrier gas. Quantitative analyses were determined from the relative peak areas using external standards. Preparative GLPC separations were carried out with a Varian Aerograph Model 700 using helium as the carrier gas. Column A was a 3 m × 6 mm o.d. copper column packed with 10% w/w Carbowax 20M supported on 80–100 mesh Chromosorb ST 142. Column B was a 1.8 m × 6 mm o.d. stainless steel column packed with 20% w/w Silicon Rubber SE 30 supported on 60–80 mesh WAWDMCS 700. Column C was a 3 m × 1.2 cm o.d. stainless steel column packed with 30% w/w Carbowax 20M supported on 80–100 mesh Gas Chrom P. Column D was a 6 m × 1 cm o.d. aluminium column packed with 30% w/w Silicon Rubber SE 30 supported on 45–60 mesh Chromosorb W. Column E was a 3 m × 1.2 cm o.d. stainless steel column packed with 30% w/w Fluorosilicon QF1 supported on 80–100 mesh Gas Chrom P. Diglyme (Ansul Ether 141) was purified by pre-drying over calcium hydride and distilled from lithium aluminium hydride under reduced pressure. DMF was purified by pre-drying over calcium hydride, followed by distillation from barium oxide under reduced pressure. Triphenylphosphine was obtained from Carlisle Chem. Co. and was used directly. Sodium and lithium chlorodifluoroacetate were prepared as previously[2] reported. *However, the lithium salt must be nearly dry before final oven-drying. When the wet salt was placed in the oven, the salt partially decarboxylated.*

Perfluoroglutaric acid

Perfluoroglutaric acid was prepared by addition of 36 ml (2.00 mole) water to 276 g (1.00 mole) perfluoroglutaryl dichloride (Hooker Chemical Co.). The reaction mixture was allowed to stand 36 h. During this period, the reaction mixture was agitated periodically to break up the solid formed. The solid was dried under vacuum, first with a rotary evaporator, then in a vacuum dessicator ove rphosphorus pentoxide to give the acid, 228 g (95%), m.p. 84–87°; reported[21] m.p. 78–88°.

Perfluorosuccinic acid

The method of Rapp[22] was used to prepare 1,2-dichlorotetrafluorocyclobutene which was then oxidized to perfluorosuccinic acid by a modification of the procedure of Burdon[23].

A 3 l, three-necked, round-bottomed flask equipped with a mechanical stirrer, addition funnel, and Friedrich condenser was charged with 632 g (4.00 mole) potassium permanganate, 1 l water, and 60 ml conc. sulfuric acid. The pot contents were vigorously stirred, and 356 g (1.83 mole) 1,2-dichlorotetrafluorocyclobutene was added over a period of 23 h. Slight heating by means of a steam bath was necessary to initiate the exothermic reaction which produced chlorine as a byproduct. The excess permanganate was decolorized with sulfur dioxide. The reaction mixture was extracted with two 200 ml portions of ether, acidified with 50 ml conc. sulfuric acid, and again extracted with ether. This process was continued until no more solid remained after the ether was removed *in vacuo*. The solid was dried in a vacuum dessicator over phosphorus pentoxide for 2 d to give 257 g (74%) perfluorosuccinic acid, m.p. 118–120°; reported[24] m.p. 120°.

Perfluoroadipic acid

Perfluoroadipic acid was prepared in a manner similar to that described for perfluorosuccinic acid, by a modification of the procedure of McBee[25].

General method for the synthesis of polyfluorinated diketones

The polyfluorinated diketones used in this study were prepared by a modification of the procedure of Groth[5]. A typical procedure for (VI) is given below.

Ethylmagnesium bromide was prepared from 65.5 g (0.60 mole) ethyl bromide and 19.0 g (0.642 g at.) magnesium in 200 ml anhydrous ether. The Grignard reagent was filtered into a 1 l, three-necked, round-bottomed flask equipped with a mechanical stirrer, a reflux condenser surmounted by a drying tube, and an addition funnel which contained 24.0 g (0.10 mole) perfluoroglutaric acid in 60 ml anhydrous ether. The acid was added drop-wise at a rate sufficient to sustain vigorous reflux of the reaction mixture. After the addition of the acid was completed, the reaction mixture was allowed to stir until it cooled (*ca.* 0.5 h), and was then hydrolyzed by pouring into 700 g cracked ice which contained 150 ml conc. hydrochloric acid. The ether layer was separated, and the aqueous layer was extracted with four 100 ml portions of ether. The combined ether extracts were washed with four 100 ml portions of saturated sodium bicarbonate solution, three 100 ml portions of water, and dried over anhydrous magnesium sulfate. The drying agent was removed, and the ether was distilled at atmospheric pressure. Fractional distillation of the residue gave 18.4 g (70%) of (VI), b.p. 83–83.5°/11 mmHg. GLPC analysis on column B showed only one peak.

General method for the reaction of polyfluorinated diketones with difluoromethylenetriphenylphosphorane

A typical procedure for the reaction of (X) with sodium chlorodifluoroacetate and triphenylphosphine is given below.

The apparatus consisted of a 1 l, three-necked, round-bottomed flask equipped with a gas inlet tube for nitrogen, a pressure-equalized addition funnel, and a reflux condenser in series with a Dry Ice, isopropyl alcohol trap and a gas bubbler. Stirring was provided by a magnetic stirrer.

A solution of 105 g (0.40 mole) triphenylphosphine and 29.2 g (0.10 mole) of (X) in 110 ml dry diglyme was heated to a bath temperature of 140–145°. A solution of 76.1 g (0.50 mole) sodium chlorodifluoroacetate in 120 ml dry diglyme was added drop-wise over a period of 1 h. The evolution of carbon dioxide ceased 0.25 h after the addition of the salt was completed. After steam distillation of the reaction mixture, the organic layer was separated, washed with water and dried over anhydrous magnesium sulfate. The organic layer was subjected to preparative GLPC on column E. A low yield of (XV) was obtained.

General method for the cyclization of polyfluorinated diketones

Method I

A solution of 16.9 g (0.079 mole) of (VII) and 4 drops of triethylamine in 20 ml ether was stirred at room temperature for 24 h. The solution was then washed with dil. hydrochloric acid, water and dried over anhydrous magnesium sulfate. After removal of the ether at atmospheric pressure, the residue was fractionated to give 12.2 g (79%) of (XII), b.p. 66°/17 mmHg. GLPC analysis on columns A and B showed only one peak.

Method II

A suspension of 2.39 g (0.096 mole) sodium hydride in 500 ml anhydrous ether was prepared. To this suspension, 17.9 g (0.096 mole) of (IV) was added drop-wise over a 0.5 h period. The reaction mixture was allowed to stir at room temperature for an additional 12 h, then 15 ml conc. hydrochloric acid was slowly added and stirring was continued for another 12 h. The ether layer was separated and dried over anhydrous magnesium sulfate. After the drying agent was removed, the ether was distilled at atmospheric pressure. The residue was fractionated to give 7.0 g (43%) of (XI), b.p. 90°/92 mmHg, and 10 g of a tarry black residue. GLPC analysis on column B showed that (XI) was only 90% pure. A sample of (XI) which showed only one peak on column B was obtained by preparative GLPC on column D.

General method for the reaction of cyclic α,β-unsaturated ketones with ylids

Method I

The apparatus was similar to that described for the reaction of (X) with difluoromethylenetriphenylphosphorane, except that the addition funnel was replaced by a stopper.

A mixture of 5.6 g (0.025 mole) of (XIII), 6.9 g (0.050 mole) lithium chlorodifluoroacetate, and 13.1 g (0.050 mole) triphenylphosphine in 80 ml dry DMF was heated at a bath temperature of 90°. Carbon dioxide was evolved smoothly for 20 min. The reaction mixture was then flash-distilled, and the flash-distillate was poured into 500 ml of water. The organic layer was separated and subjected to preparative GLPC on column C. There was obtained 1.8 g (27%) of (XVII).

Method II

An ether solution of methyl-lithium (8.1 ml, calculated to contain 0.014 mole methyl-lithium) was added to 5.25 g (0.015 mole) methyltriphenylphosphonium bromide in 60 ml dry ether at 0°. The reaction mixture was stirred for 2.5 h, then 2.46 g (0.010 mole) of (XIV) in 5 ml dry ether was added. The reaction mixture was then heated to reflux for 12 h. After the ether was removed, the residue was flash-distilled. Preparative GLPC of the flash-distillate on column D afforded 0.4 g (17%) of (XIX).

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