Stable Carbocations. CLIV.[1] Halogenated Phenyldifluorocarbenium Ions

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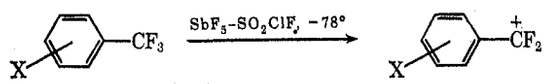
A series of ring halogenated phenyldifluorocarbenium ions was prepared and their structures were studied on the basis of their nmr (^1H and ^{19}F) spectra. The electronic structure and the degree of halogen back-donation in the ions are discussed, based on experimental data of their nmr spectra.

In 1969, Olah and Comisarow reported the first direct observation of alkyl(aryl)halocarbenium ions and haloarylcarbenium ions.[2] The degree of halogen back-donation and the relative stability of halocarbenium ions have been studied by Olah, Mo, and Halpern.[3] As an extension of this work, we have now prepared a series of ring halogenated phenyldifluorocarbenium ions in order to gain better understanding of their electronic structures, based on their nmr spectra, and to study the relationship of fluorine shifts with the degree of halogen back-donation and relative stability of these difluorocarbenium ions.

Results and Discussion

The series of ring halogenated phenyldifluorocarbenium ions (**1a–l**) were prepared by treating halogenated benzotrifluorides (**2a–l**) with SbF_5–SO_2ClF solution at −78°. The nmr (^1H and ^{19}F) chemical



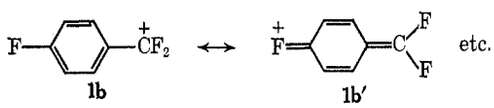
2a–l **1a–l**

a, X = H
b, X = *p*-F
c, X = *p*-Cl
d, X = *p*-Br
e, X = *p*-I
f, X = *o*-F
g, X = *o*-Cl
h, X = *o*-Br
i, X = *m*-F
j, X = *m*-Cl
k, X = *m*-Br
l, X = *p*-Cl and *m*-Br

shifts of ions **1x** (**x** = **a–l**) and their precursor halogenated benzotrifluorides **2x** are summarized in Table I. Representative nmr spectra are shown in Figures 1–4. The parent difluorocarbenium ion (**1a**) has been previously prepared and characterized by nmr spectroscopy.[2] The characteristic, highly deshielded fluorine shift of ion **1a** was considered particularly suitable to study the effect of halogen substitution in the phenyl ring. The stabilization of the ions, *via* halogen back-donation, should be reflected in the $^+CF_2$ fluorine shifts in ions **1b–l**.

In the ^{19}F nmr spectra of all ions **1x**, the $^+CF_2$ group shows a substantially deshielded fluorine shift in the range ϕ −6.45 to −21.0 (deshielded from $CFCl_3$). The CF_3 group of the precursors shows shielded fluorine absorptions ranging from ϕ 62.8 to 66.5. These data are good evidence that ionization of halobenzotrifluorides **2x** to halophenyldifluorocarbenium ions **1x** has occurred. In addition, the aromatic proton absorptions of **1x** are generally 1 ppm deshielded from their precursors.

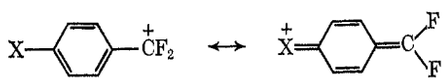
The aromatic fluorine atoms in ions **1b**, **1f**, and **1i** show highly different chemical shifts at ϕ 40.41, 69.24, and 101.00, respectively. The highly deshielded para-fluorine of **1b** indicates substantial fluorine back-donation.[3]



1b **1b′**

Similar fluorine back-donation is also observed in ion **1f**, but is less significant. In the case of ion **1i**, such a resonance effect is not feasible and the slight deshielding of the meta fluorine atom (11.2 ppm) is due solely to the inductive effect of the $^+CF_2$ group.

In *p*-halophenyldifluorocarbenium ions, the fluorine absorption of the $^+CF_2$ group is deshielded in the order **1d** > **1c** > **1b** > **1e** (ϕ −8.64 < −8.61 < −6.77 < −6.45, respectively). If the inductive effect of the halogens would alone be operating in these ions (**1x**, **x** = **b**, **c**, **d**, and **e**), an opposite trend should be observed (**1b** > **1c** > **1d** > **1e**). The possible explanation of these discrepancies may be the greater halogen back-donation in **1b** than in other ions. Recently, we have reported the degree of halogen back-donation of alkylhalocarbenium ions[3] and found it to be in the order F > Cl > Br. Consequently, a similar resonance



effect can lead to charge delocalization which is more extensive for fluorine than for the other halogen atoms. Based on previous data, bromine back-donation was found to be insignificant.[3] Our present data showing the $^+CF_2$ group of **1d** to be more deshielded than that of **1e** suggests that inductive effects are predominantly operating in these ions (**1d** and **1e**).

In contrast, when halogen back-donation is not feasible, as in ions **1i**, **1j**, and **1k**, the $^+CF_2$ fluorine shifts show the opposite trend (ϕ −18.51, −17.90, and −14.70, respectively).

In the case of *o*-halophenyldifluorocarbenium ions (**1f**, **1g**, and **1h**), the two fluorine atoms of the $^+CF_2$ group are nonequivalent and show different chemical shifts (Table I). They also couple to each other with unusually large fluorine–fluorine coupling constants (*e.g.*, 250 Hz in **1g**). The nonequivalence of the two fluorine atoms in the $^+CF_2$ group of ions **1f**, **1g**, and **1h** rises from the partial double bond character of the $C_{Ar}{=}{=}C^+F_2$ bond. Similar observations have been

(1) Part CLIII: G. A. Olah and Y. K. Mo, *J. Org. Chem.*, **38**, 2682 (1973).

(2) G. A. Olah and M. B. Comisarow, *J. Amer. Chem. Soc.*, **91**, 2955 (1969).

(3) G. A. Olah, Y. K. Mo, and Y. Halpern, *ibid.*, **94**, 3551 (1972).

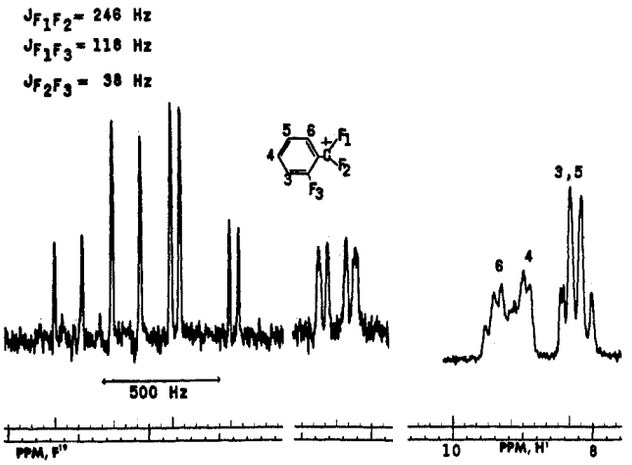


Figure 1.—Nmr (^{1}H and ^{19}F) spectra of ion 1f.

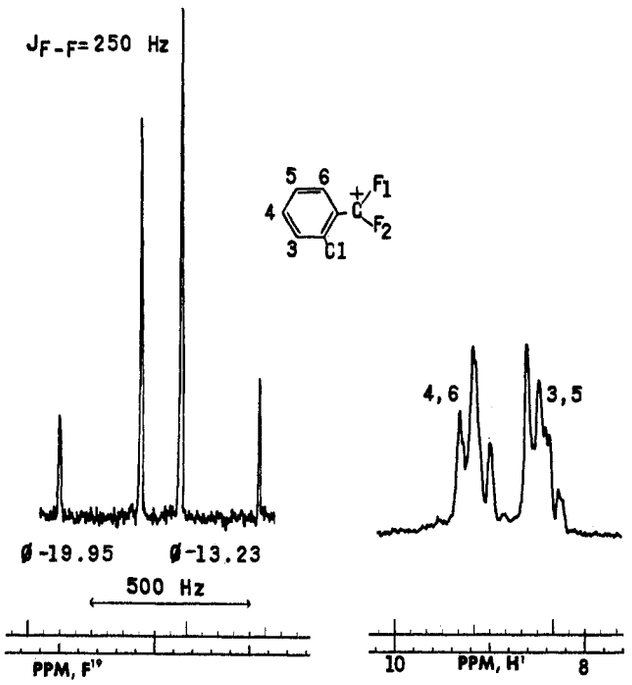
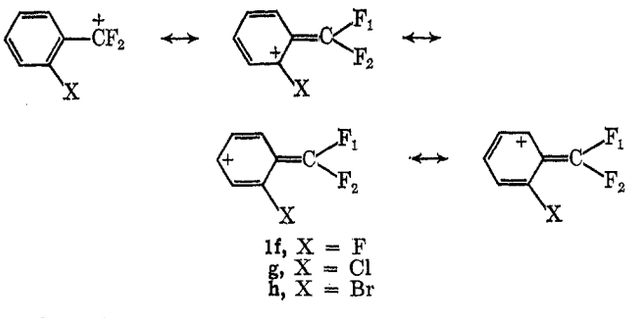


Figure 2.—Nmr (^{1}H and ^{19}F) spectra of ion 1g.



1f, X = F
g, X = Cl
h, X = Br

made in benzyl cations[4] and styryl cations.[5] Since F_2 is closer to the ortho halogen and should exercise a greater inductive deshielding effect, we thus assign the more deshielded fluorine absorption to F_2. Furthermore, F_2–F_3 spin–spin interaction of ion **1f** (118 Hz) is

(4) J. M. Bollinger, M. B. Comisarow, C. A. Cupas, and G. A. Olah, *J. Amer. Chem. Soc.*, **89**, 5687 (1967).

(5) (a) G. A. Olah, R. D. Porter, and D. P. Kelly, *ibid.*, **93**, 464 (1971), (b) G. A. Olah, M. B. Comisarow, E. Namanworth, and B. Ramsey, *ibid.*; **89**, 5259 (1967).

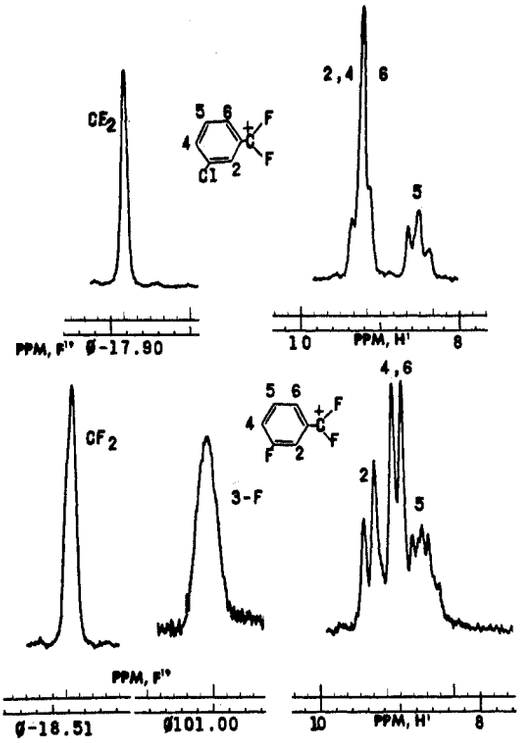


Figure 3.—Nmr (^{1}H and ^{19}F) spectra of ions 1j (upper) and 1i (lower).

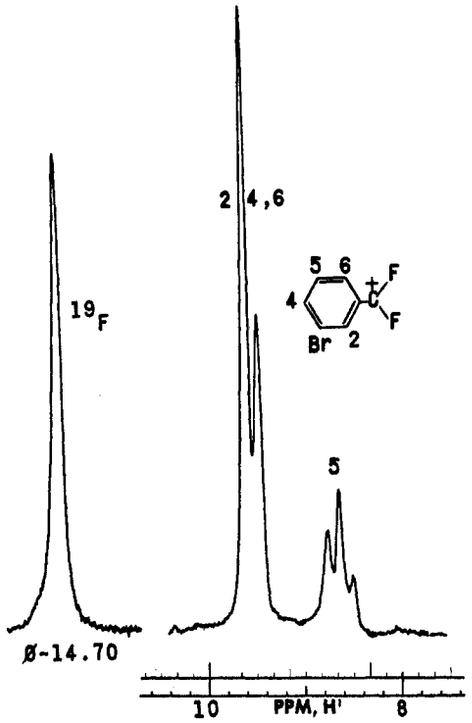


Figure 4.—Nmr (^{1}H and ^{19}F) spectra of ion 1k.

greater than that of F_1–F_3 (38 Hz) (see Figure 1). Our assignments can be based on analogy with the fluorine–fluorine coupling constants ($J_{F_aF_c}$ = 3.6 and $J_{F_bF_d}$ =

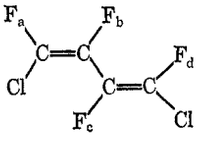


TABLE I

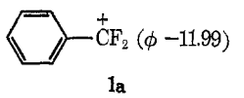
NMR (^{1}H AND ^{19}F) PARAMETERS OF ARYLDIFLUOROCARBENIUM IONS AND THEIR PRECURSORS[a,b]

	Precursor[c] $XC_6H_4CF_3$				Ion $XC_6H_4CF_2^+$			
X	ϕ, CF_3	Ortho	Meta	Para	ϕ, CF_2^+	Ortho	Meta	Para
H	63.63 (s)	7.5 (m)	7.5 (m)	7.5 (m)	−11.99 (q)	8.88 (d d)	8.04 (t d)	8.84 (t d)
					J = 1.0	J_{HH} = 9	J_{HH} = 9	J_{HH} = 9
						J_{FH} = 1		$J_{F\text{-}H}$ = 1
p-F	62.92 (s)	7.5 (m)	7.1 (m)	ϕ 108.52 (m)	−6.77 (d t)	9.00 (d d t)	8.96 (t)	ϕ 40.41 (m)
					J_{FF} = 19.8	J_{HH} = 10	J = 10	J_{FF} = 19.8
					$J_{F\text{-}o\text{-}H}$ = 1	J_{HF} = 4.6		$J_{F\text{-}o\text{-}H}$ = 4.6
						$J_{H\text{-}CF_2}$ = 1.1		$J_{F\text{-}m\text{-}H}$ = 8.4
p-Cl	63.49 (s)	7.6 (d)	7.4 (d)		−8.61 (t)	8.80 (d d)	8.06 (d)	
		J_{HH} = 9	J_{HH} = 9		$J_{F\text{-}o\text{-}H}$ = 1	$J_{F\text{-}o\text{-}H}$ = 1	J_{HH} = 10	
						J_{HH} = 10		
p-Br	63.54 (s)	7.8 (d)	7.5 (d)		−8.78 (d)	8.64 (d d)	8.23 (d)	
		J_{HH} = 10	J_{HH} = 10		$J_{F\text{-}o\text{-}H}$ = 1	$J_{F\text{-}o\text{-}H}$ = 1	J_{HH} = 10	
						J_{HH} = 10		
p-I	66.50 (s)	7.64 (d)	7.26 (d)		−6.45 (t)	8.78 (d)	8.61 (d)	
		J_{HH} = 8	J_{HH} = 8		$J_{F\text{-}o\text{-}H}$ = 1	J_{HH} = 10	J_{HH} = 10	
o-F	62.80 (d)	ϕ 116.13 (m)	7.3 (m)	7.3 (m)	−20.92	ϕ 69.24 (d d)	8.3 (m)	8.9 (m)
	J_{FF} = 11	7.5 (m)	7.5 (m)		J_{FF} = 246	$J_{F\text{-}o\text{-}F}$ = 118,		
					$J_{F\text{-}o\text{-}F}$ = 118	38		
					−13.47 (d d)			
					J_{FF} = 246			
					$J_{F\text{-}o\text{-}F}$ = 38			
o-Cl	63.83 (s)	7.7 (m)	7.7 (m)	7.7 (m)	−19.95 (d)	9.1 (m)	8.5 (m)	9.1 (m)
					J_{FF} = 250			
					−13.23 (d)			
					J_{FF} = 250			
o-Br	63.90 (s)	7.8 (m)	7.5 (m)	7.5 (m)	−17.94 (d)	9.35 (d)	8.4 (m)	8.7 (m)
					−12.13 (d)	J_{HH} = 8	8.7 (m)	
					J_{FF} = 252			
m-F	64.08 (s)	7.4 (m)	ϕ 112.15 (m)	7.4 (m)	−18.51 (s)	9.3 (m)	ϕ 101.0 (s)	9.0 (m)
			7.4 (m)			9.0 (m)	8.7 (m)	
m-Cl	64.00 (s)	7.6 (m)	7.6 (m)	7.6 (m)	−17.90 (s)	9.2 (m)	8.5 (m)	9.1 (m)
m-Br	64.00 (s)	7.9 (s)	7.7 (m)	7.7 (m)	−14.70 (s)	9.6 (m)	8.6 (m)	9.6 (m)
		7.7 (m)						
m-Br-*p*-Cl	64.00 (s)	8.04 (s)	7.70 (s)		−11.73 (s)	9.60 (s)	8.7 (d)	
		7.70 (s)				9.23 (d)	J_{HH} = 10	
						J_{HH} = 10		

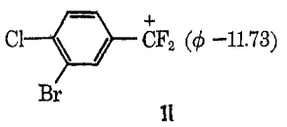
[a] Proton and fluorine chemical shifts are referred to external capillary TMS and $CFCl_3$, respectively. Abbreviation used: s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet. [b] Coupling constants are in hertz. [c] In SO_2ClF solution at −30°.

14.5 Hz) in *cis,trans*-1,4-dichlorotetrafluorobuta-1,3-diene reported by Bladon, Sharp, and Winfield.[6]

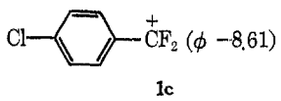
It is of interest to compare the fluorine shifts of the $^+CF_2$ group in ions **1a**, **1c**, **1k**, and **1l**. The $^+CF_2$



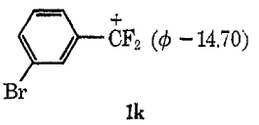
1a



1l



1c



1k

fluorine shift of **1a** is more deshielded than that of **1c**, indicating partial charge delocalization onto the chlorine atom (*via* back-donation). However, the $^+CF_2$ fluorine shift of **1a** is shielded from that of **1k**, showing that mainly the inductive effect is operating in the latter. Similar $^+CF_2$ fluorine shifts are found in both ions **1a** and **1l** because the resonance effect of the chlorine atom cancels out the inductive effect of the bromine atom.

We consider our results of significance, since a more quantitative picture of halogen back-donation could be given in the series of halogenated phenyldifluorocarbenium ions. The present data are not only in good agreement with our previous studies[2,3] but also the general concept of halogen back-donation studied in considerable detail by other methods and considered of significance in both inorganic[7] and organic[8] systems.

Experimental Section

Materials.—All of the halobenzotrifluorides **2x** were commercially available (Columbia Organic Chemicals or PCR Inc.). Antimony pentafluoride (Allied Chemical) was triply distilled before use.

Preparation of Ions and Nmr Studies.—Solutions of the ions

(6) P. Bladon, D. W. A. Sharp, and J. M. Winfield, *Spectrochim. Acta*, **22**, 343 (1966).

(7) (a) H. S. Gutowsky and D. W. McCall, *J. Phys. Chem.*, **57**, 481 (1953); (b) T. P. Onak, H. Landesman, R. E. Williams, and I. Shapiro, paper presented to the Division of Inorganic Chemistry, 135th National Meeting of the American Chemical Society, Boston, Mass., April 1959; (c) F. A. Cotton and G. Wilkinson "Advanced Inorganic Chemistry," Interscience, London, 1966, p 256.

(8) See references quoted in our preceding papers (ref 2–5). For a more comprehensive review see, for example, W. A. Sheppard and C. M. Sharts, "Organic Fluorine Chemistry," W. A. Benjamin, New York, N. Y., 1969, p 18.

in SbF_5–SO_2ClF solution were prepared as described previously.[2] Nmr spectra were obtained on a Varian A-56-60A nmr spectrometer equipped with a variable-temperature probe. Proton and fluorine shifts are referred to external capillary TMS and $CFCl_3$, respectively.

Registry No.—**1a**, 24154-19-6; **1b**, 24154-20-9; **1c**, 24226-22-0; **1d**, 24154-21-0; **1e**, 39982-15-5; **1f**, 39982-16-6; **1g**, 39982-17-7; **1h**, 39982-18-8; **1i**, 39982-16-6; **1j**, 39982-20-2; **1k**, 39982-21-3; **1l**, 39982-22-4; **2a**, 98-08-8; **2b**, 402-44-8; **2c**, 98-56-6; **2d**, 402-43-7; **2e**, 455-13-0; **2f**, 392-85-8; **2g**, 98-15-7; **2h**, 392-83-6; **2i**, 401-80-9; **2j**, 88-16-4; **2k**, 401-78-5; **2l**, 454-78-4.

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Effect of pK on the Rate of Amine-Catalyzed Cleavage of Diacetone Alcohol

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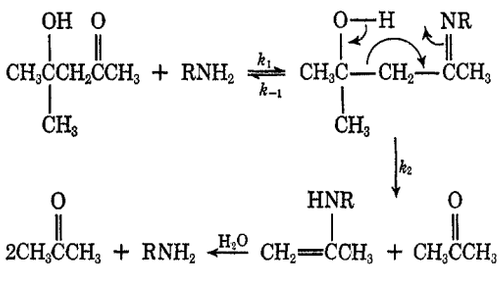
The primary amine catalyzed dealdolization of diacetone alcohol has been investigated with a series of amines whose pK's range from 5.7 to 10.9. Changing the pK of the amine from 10.9 to 5.7 has a small effect on the equilibrium constant for formation of the intermediate ketimine (fourfold decrease) and only a modest effect on the rate of cleavage of ketimine to products (25-fold decrease), indicating a relatively nonpolar transition state. The relevance of these results to the mechanism of aldolase is discussed.

A large class of enzymes, including many aldolases, appears to function *via* the formation of an imine intermediate from a carbonyl group of the substrate and a lysine residue of the enzyme.[1] The replacement of the carbonyl oxygen with the much more basic nitrogen of the enzyme allows facile protonation of the nitrogen and subsequent (or concurrent) acceptance of a pair of electrons from a leaving group to form an enamine. Hydrolysis of the enamine then leads to regeneration of the enzyme. It appears that catalysis by these enzymes is due in large part to a replacement of C=O by C=N.

In an effort to evaluate the contribution of this factor to the rate accelerations caused by these enzymes, much effort has been devoted to catalysis by simple primary amines. A convenient model system for the aldolase enzymes is the primary amine catalyzed dealdolization of diacetone alcohol (Scheme I). This reaction in-

SCHEME I



volves an analogous mechanism to that proposed for the enzymes.[2-4] For catalysis by n-propylamine (pK 10.9) we have shown that the formation of the intermediate ketimine is rapid and reversible followed by slow decomposition to products.[4] In addition we were able to evaluate the individual rate constants k_1, k_{-1}, and k_2. The rate constant for cleavage of imine to products (k_2) is of particular interest since a comparison of this rate to the rate of cleavage of the carbonyl compound itself gives a direct evaluation of the effect of replacing an oxygen by a nitrogen in this system.

The choice of n-propylamine was due to its resemblance to the lysine side chain both in structure and pK. Although the pK of n-propylamine is similar to that normally observed for lysine residues of proteins (p$K \cong 10$), it is not clear that the active site lysine of aldolase has a "normal" pK. In fact, for the related enzyme acetoacetate decarboxylase, the pK of the active site amine group has been found to be about 6.[5] Although the pK of this group in aldolase has not been determined, it is reasonable to suppose that it may be perturbed in a similar manner.

We have now extended our previous work to include a series of primary amines with widely different pK's. Our objectives in this study were threefold: (1) to establish whether there is a change in rate-determining step with changing amine pK; (2) to obtain information concerning the polarity of the transition state for cleavage of the imine; and (3) to determine what, if any, advantage could accrue to an aldolase enzyme if it were to have a lowered active site pK.

Experimental Section

Materials.—Diacetone alcohol and n-propylamine were purified as previously described.[4] Ethanolamine was distilled prior to use. Glycine and glycinamide were reagent grade chemicals used without further purification. 2,2,2-Trifluoroethylamine was prepared by the method of Bissell and Finger.[6]

Kinetic Methods.—For all catalysts except trifluoroethylamine, kinetic measurements were carried out at 260 nm for dealodolization and 235 nm (240 nm for glycinamide) for formation of the imine as described previously.[4] For 2,2,2-trifluoroethylamine, rate constants for conversion of diacetone alcohol

(1) (a) B. L. Horecker, S. Pontremli, C. Ricci, and T. Cheng, *Proc. Nat. Acad. Sci. U. S.*, **47**, 1949 (1961); (b) E. Grazi, P. T. Rowley, T. Cheng, O. Tchol, and B. L. Horecker, *Biochem. Biophys. Res. Commun.*, **9**, 38 (1962); (c) for a general review of the mechanism of action of aldolases see D. E. Morse and B. L. Horecker, *Advan. Enzymol. Relat. Subj., Biochem.*, **31**, 125 (1968).

(2) (a) F. H. Westheimer and H. Cohen, *J. Amer. Chem. Soc.*, **60**, 90 (1938); (b) F. H. Westheimer and W. A. Jones, *ibid.*, **63**, 3283 (1941).

(3) R. W. Hay and K. R. Tate, *Aust. J. Chem.*, **19**, 1651 (1966).

(4) R. M. Pollack and S. Ritterstein, *J. Amer. Chem. Soc.*, **94**, 5064 (1972).

(5) (a) D. E. Schmidt, Jr. and F. H. Westheimer, *Biochemistry*, **10**, 1249 (1971); (b) F. C. Kokesh and F. H. Westheimer, *J. Amer. Chem. Soc.*, **93**, 7270 (1971).

(6) E. Bissell and M. Finger, *J. Org. Chem.*, **24**, 1256 (1959).