Pyrolysis of 2-Azido-2′,4′,6′-trimethoxybiphenyl (XII).—A solution of azide XII (4.2 g., 0.0148 mole) in diphenyl ether (20 ml.) was added dropwise to hot (190–200°) stirred diphenyl ether (40 ml.) maintained in a nitrogen atmosphere. Nitrogen evolution was essentially instantaneous and ceased shortly after the final addition; however, heating was continued 10 more minutes. The cooled, darkly colored reaction solution was chromatographed on a column of 120 g. of Merck alumina. The diphenyl ether was eluted with petroleum ether, the product with chloroform. The crude, dark, oily product was transferred to a sublimation apparatus and heated to 100–120° (0.1 mm.) for 24 hours. The sublimate (110 mg., 3%) proved to be somewhat impure 2-amino-2′,4′,6′-trimethoxybiphenyl (XIII), as determined by m.p. and infrared spectrum.

Pyrolysis of *o*-Azidocumene (XIX).—A solution of 4.56 g. (0.0283 mole) of XIX in 20 ml. of diphenyl ether was added dropwise to 40 ml. of hot (200°) stirred diphenyl ether maintained in a nitrogen atmosphere. Gas evolution was instantaneous and the reaction darkened considerably. Heating was stopped when gas evolution ceased (~10 min.). The cooled reaction solution was chromatographed on 400 g. of Merck acid-washed alumina; the diphenyl ether was eluted with petroleum ether, the product with isopropyl alcohol–chloroform. The crude, dark-colored, ill-smelling product was subjected to a short path distillation (0.1 mm.). The almost colorless distillate (2.8 g.) was further separated by means of vapor phase chromatography[18] into three fractions (in the ratio 1:2.5:1.25): dihydroskatole (XX), *o*-aminocumene (XXI) and diphenyl ether. The diphenyl ether and *o*-aminocumene were identified by comparison of their respective infrared spectra with those of authentic samples. The identity of the dihydroskatole was established by preparing a picrate, m.p. 147–148° (lit.[19] m.p. 149–150°).

Anal. Calcd. for $C_{15}H_{16}O_7N_4$: C, 49.73; H, 3.90. Found: C, 49.77; H, 3.88.

Pyrolysis of *o*-Azidophenylcyclohexane (XXII).—To 50 ml. of hot (200–210°) stirred diphenyl ether maintained in an atmosphere of nitrogen was added dropwise a solution of 3.43 g. (0.0171 mole) of azide XXII in 10 ml. of diphenyl ether. Gas evolution was smooth and rapid and ceased shortly after the final addition. Heating was continued an additional 5 minutes and the reaction solution then cooled. The reddish-colored solution was chromatographed on 120 g. of Merck acid-washed alumina. Petroleum ether eluted the diphenyl ether, and isopropyl alcohol–benzene eluted the crude crystalline product (2.79 g., 95%). This material when subjected to sublimation (80° (0.1 mm.)) gave 2.55 g. (86%) of yellowish crystalline material which after several recrystallizations from hexane yielded 217 mg. of *trans*-hexahydrocarbazole (XXIV), m.p. 126–128° (lit.[20] m.p. 127°) and λ_{max}^{EtOH} 287 mμ (lit.[20] value 286.5 mμ). The residue from the hexane mother liquors when recrystallized several times from ethanol yielded 115 mg. of *cis*-hexahydrocarbazole (XXIII), m.p. 97–98° (lit.[20] m.p. 99°) and λ_{max}^{EtOH} 293 mμ (lit.[21] value 293 mμ). The *cis* and *trans* compounds had sufficiently different infrared spectra in carbon tetrachloride to have allowed an analysis of their relative proportions in the original reaction product. Four separate bands in each spectrum were used for the analysis. It was estimated that the pyrolysis gave 45–50% *cis*- and 40–45% *trans*-hexahydrocarbazole.

Dehydrogenation of Hexahydrocarbazole (XXIV).—Crude sublimed hexahydrocarbazole (100 mg.) obtained from the above reaction was heated at 200° for 17 hours in diphenyl ether (3 ml.) in the presence of 38 mg. of 10% palladized carbon while sweeping the mixture with nitrogen. The cooled reaction mixture was chromatographed on 8 g. of Woelm neutral alumina (activity grade 1). After the diphenyl ether had been eluted with petroleum ether, 102 mg. of crude carbazole (m.p. 210–220°, ultraviolet spectrum in ethanol essentially identical with that of an authentic sample) was eluted with benzene. One recrystallization from alcohol gave 65 mg. of carbazole of m.p. 246–247° (lit.[22] value m.p. 245°).

(18) A. Beckman GC-2 gas chromatograph having a 40″ column packed with Ucon Polar on Fluoropak was used. A temperature of 140° and pressure of 40 p.s.i. gave good separation.

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(20) J. Gurney, W. H. Perkin, Jr., and S. G. P. Plant, *J. Chem. Soc.*, 2676 (1927).

(21) T. Masamune, *J. Am. Chem. Soc.*, **79**, 4418 (1957).

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[CONTRIBUTION FROM THE DEPARTMENT OF PHYSIOLOGICAL CHEMISTRY, THE JOHNS HOPKINS UNIVERSITY SCHOOL OF MEDICINE, BALTIMORE 5, MD.]

A Kinetic Study of the Reaction of a "Meso-ionic" Compound (Dehydrodithizone) with Haloacetates

BY J. OGILVIE, V. K. MIYAMOTO AND THOMAS C. BRUICE[1]

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"Meso-ionic" compounds which possess very low pK'_a values but high polarizability would be expected to be excellent nucleophiles toward the sp³ carbon but very poor nucleophiles toward the ester sp² carbon atom. This assumption has been shown to be valid in studies on the rates of nucleophilic displacement of halogen from α-haloacetates and *p*-nitrophenol from *p*-nitrophenyl acetate by the "meso-ionic" compound dehydrodithizone (I).

Introduction

The ability of a nucleophile to enter into an SN2 displacement at the sp³ carbon is a function of both pK'_a and polarizability as expressed by the equation of Edwards.[2] Nucleophilicity toward

$$\log \frac{k_r}{k_{H_2O}} = \alpha(E_0 + 2.60) + \beta(pK'_a + 1.74) \quad (1)$$

the ester sp² carbon may be correlated by the Brönsted equation[3]

$$\log k_r = \alpha' pK_a + C \quad (2)$$

where

$$C \neq \alpha(E_0 + 2.60) + \beta 1.74$$

"Meso-ionic" compounds possessing very low pK'_a values, such as dehydrodithizone (I), should, therefore, be very effective nucleophiles in those displacements in which $\alpha >> \beta$. In this category is found the SN2 displacement of halogen from α-haloacetates. We describe, herein, the kinetics of the reaction of I with α-iodo-, α-bromo- and α-chloroacetic acids and anions, as well as with bromoacetamide.

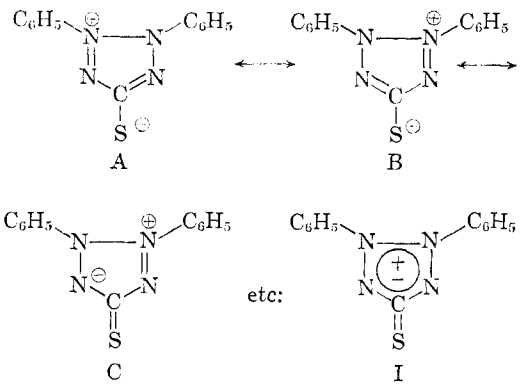
Results

The reagent I (red color, λ_{max} 250 mμ, $\epsilon \cong 24{,}000$) reacts as a sulfur nucleophile to yield colorless

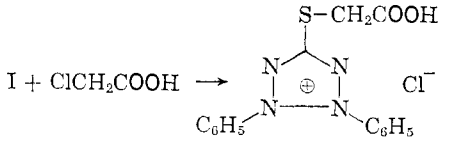
(1) Inquiries concerning this article addressed to this author should be sent to The Department of Chemistry, Cornell University, Ithaca, N. Y.

(2) J. O. Edwards, *J. Am. Chem. Soc.*, **78**, 1540 (1954); **78**, 1819 (1956).

(3) T. C. Bruice and R. Lapinski, *ibid.*, **80**, 2265 (1958).



tetrazolium salts (ϵ at 250 mμ $\cong$ 7,000) allowing the simple spectrophotometric determination of rate



constants. The reaction of I with haloacetic acids was followed at 250 mμ in aqueous solution (2% EtOH, v./v.) at μ = 0.05 to 0.125 M (with KCl) and T = 30.0 ± 0.1°. The observed rates for chloroacetic acid were found to be insensitive to ionic strength changes in this range. To simplify the kinetics the haloacetate was present in large excess over I (10^2 – 10^3 ×) and served as both reactant and buffer. Under these conditions the disappearance of I was found to follow first-order kinetics (at constant pH).

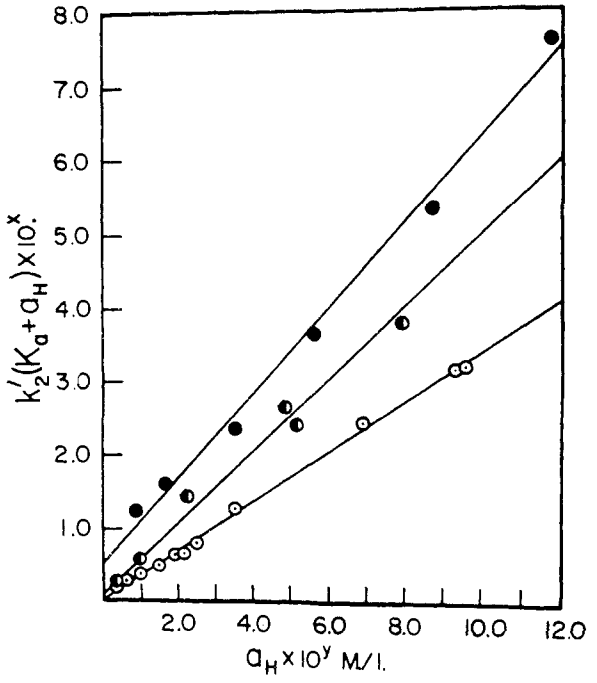


Fig. 1.—Plots of $k_2'(K_a + a_H)$ *vs.* a_H for the reactions of α-chloroacetic acid (–◐–◐–, x = 4, y = 3), α-bromoacetic acid (–⊙–⊙–, x = 2, y = 3), and α-iodoacetic acid (–●–●–, x = 3, y = 4) with dehydrodithizone (solvent H_2O; μ = 0.125–0.05 M).

$$-dI/dt = k_1(I) \quad (4)$$
$$k_2' = k_1/A_T$$

where k'_2 is the pseudo-second-order rate constant at any given pH and A_T represents the total concentration of haloacetic acid (HA) and anion (A) present in the reaction mixture.

The pK_a' of I has been determined to be −1.57[4] so that in aqueous solution above pH 0.5 one does not need to take into account the state of ionization of the nucleophile. The values of k'_2 determined at pH values between 2 and 4 were found to be pH dependent, in accord with the expected differences in the rates of the reaction of A and AH with I.

$$-dI/dt = k_A(A)(I) + k_{HA}(AH)(I) \quad (5)$$
$$= k_A(A_T)\left(\frac{K'_a}{K'_a + a_H}\right) + k_{HA}A_T\left(\frac{a_H}{K'_a + a_H}\right)$$

and

$$k'_2 = \frac{k_A K'_a + k_{HA}a_H}{K'_a + a_H} \quad (6)$$

where K'_a represents the dissociation constant of the haloacetic acid, a_H the hydrogen ion activity determined by the glass electrode and k_A and k_{HA} are the true second-order rate constants for the reaction of I with A and HA, respectively. From 6 it follows that a plot of $k'_2(K_a' + a_H)$ *vs.* a_H should be linear with a slope equal to k_{HA} and intercept at a_H = 0 of $k_A K_a'$. In Fig. 1 plots of eq. 5 are presented for the three haloacetates investigated. The values of k_A and k_{HA} calculated from Fig. 1 are presented in Table I. In Table II are recorded the calculated second-order rate constants for the reaction of I with α-bromoacetamide. No perceptible reaction occurred between I and p-nitrophenyl acetate in water at 30°.

TABLE I

RATE CONSTANTS (30°) FOR THE REACTION OF HALOACETATE (k_A) AND HALOACETIC ACID (k_{HA}) WITH DEHYDRODITHIZONE (SOLVENT H_2O; μ = 0.125 – 0.05 M)

Substrate	K'_a[a]	k_{HA}, l. mole^{-1}	k_A, min.$^{-1}$	k_{HA}/k_A
$ClCH_2COOH$	1.316×10^{-3}	0.050	0.0057	8.77
$BrCH_2COOH$	1.213×10^{-3}	3.39	.37	9.16
ICH_2COOH	6.436×10^{-4}	5.84	.81	7.21

[a] K_a' values employed are those of D. J. G. Ives and J. H. Pryor, *J. Chem. Soc.*, 2104 (1955), corrected to 30° as described by these authors.

TABLE II

SECOND-ORDER RATE CONSTANTS FOR THE REACTION OF I WITH α-BROMOACETAMIDE AT VARYING pH (30°; μ = 0.05 M; SOLVENT WATER)

pH	2.62	2.95	3.40	3.89	4.50
k_2, l. mole^{-1} min.$^{-1}$	1.52	1.50	1.59	1.63	1.47
			Av.	1.54 ± 0.05	

Discussion

Dehydrodithizone (I) can be characterized as a nucleophile *via* the Edwards eq. 1 employing the α- and β-constants previously provided[2] (eq. 7) from the experimental data on α-iodoacetate anion.[5,6] The value of *En* and *H* so determined for

(4) J. Ogilvie and A. H. Corwin, *J. Am. Chem. Soc.*, **83**, in press.

(5) H. J. Backer and W. H. van Mels, *Rec. trav. chim.*, **49**, 177 (1930).

(6) C. Wagner, *Z. physik. Chem.*, **A115**, 121 (1925).

$$\log (k/k_{H_2O}) = 2.59En - 0.052H \quad (7)$$

I are given in Table III along with chosen literature constants[2] for comparative purposes.

TABLE III

COMPARISON OF THE NUCLEOPHILIC CONSTANT (En) AND ACIDITY (H) FUNCTION OF DEHYDRODITHIZONE TO A SELECTED GROUP OF NUCLEOPHILES

Nucleophile	En	H	Nucleophile	En	H
$S^=$	3.08	14.66	$(NH_2)_2C{=}S$	2.18	0.80
$SO_3^=$	2.57	9.00	CN^-	2.02	10.88
$S_2O_3^=$	2.52	3.60	SCN^-	1.83	(1.00)
	2.34	0.17	$SO_4^=$	0.59	3.74

It may be noted that of those nucleophiles which are particularly effective toward the sp^3 carbon, I possesses the lowest value of H. The high values of both En and H possessed by some of the other nucleophiles such as $S^=$ and $SO_3^=$ provide these bases with the ability to undergo displacement reactions at the sp^3 and sp^2 carbon atoms. This should not be expected of I on the basis of its very low H value. Experimentally, this is found to be the case, and I, unlike these other bases with large En values, is incapable of displacing p-nitrophenol from p-nitrophenyl acetate.

The somewhat higher value of En for I as compared to thiourea and thiocyanate (which also possess the N–C–S configuration) may be attributed to a greater polarizability of the molecule, which might result from its "meso-ionic" structure.

Aside from the apparent increased polarizability of I, it does not, as a "meso-ionic" compound, appear to be unusual in its sensitivity to electronic effects, nor in its sensitivity to the nature of leaving groups. Thus, the rate ratios k_A/k_{AH} and $k_I:k_{Br}:k_{Cl}$ compare with those previously listed for other nucleophiles possessing high En values.[5,6]

Experimental

Materials.—Dehydrodithizone was that of another study.[4] Bromoacetamide was prepared by the method of Papendick.[7] The haloacetates were obtained commercially and recrystallized to constant m.p. from petroleum ether.

Apparatus.—The determination of pH values was carried out with a model 22 Radiometer pH meter. All spectrophotometric measurements were made with a model PMQ II Zeiss spectrophotometer fitted with a special hollow brass cuvette holder thermostated at 30 ± 0.01° by a Haake constant temperature circulating bath.

Kinetics.—For iodoacetic and chloroacetic acids the substrate was employed as buffer. For bromoacetamide and bromoacetic acid 0.01 M tartrate buffer was employed. All reactions were followed at ionic strengths (calculated) of 0.125–0.05 M provided by KCl. The disappearance of dehydrodithizone was followed at 250 mμ (λ_{max}). Specific procedures for the kinetic experiments and method of calculation of observed rate constants have been given previously.[8]

Acknowledgments.—We should like to thank Mr. S. A. Mendoza for performing a portion of the experimental work reported herein. This work was supported by grants to J. O. from The National Heart Institute and to T. C. B. from The National Science Foundation and The National Institutes of Arthritic and Metabolic Diseases.

(7) A. Papendick, *Ber.*, **25**, 1160 (1892).

(8) T. C. Bruice and M. F. Mayahi, *J. Am. Chem. Soc.*, **82**, 3067 (1960).

[CONTRIBUTION FROM THE RESEARCH AND DEVELOPMENT DEPARTMENT, PENNSALT CHEMICAL CORP., PHILADELPHIA 18, PA.]

Addition of Iodine Halides to Fluorinated Olefins. I. The Direction of Addition of Iodine Monochloride to Perhaloölefins and Some Related Reactions

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Contrary to prior reports, the addition of iodine monochloride to chlorotrifluoroethylene is bidirectional and both isomers $CF_2ClCFClI$ (I) and $CFCl_2CF_2I$ (II) are formed. The isomer ratio was shown to be temperature dependent with higher temperatures favoring isomer II. If the reaction is carried out at 0° or lower, nearly pure I can be obtained. In the presence of iron, however, the isomer mixture consisted of about 65% of II even at 0°. Pure II was isolated in quantity from isomer mixtures by the selective reaction of I at 50° with chlorosulfonic acid. In the presence of aluminum chloride third possible $C_2Cl_2F_3I$ isomer, the rearranged CF_3CCl_2I, was produced in 100% isomeric purity in low yield. The addition of iodine monochloride to 1,1-dichlorodifluoroethylene gave the isomer CF_2ClCCl_2I exclusively at −10°, but at higher temperatures or in the presence of iron, the isomer CCl_3CF_2I also was produced. The formation of relatively large amounts of the chlorination product CF_2ClCCl_3 was favored under the latter conditions. At 98° the addition of iodine monochloride to perfluoropropene gave an isomer composition of 91.5% CF_3CFICF_2Cl and 8.5% $CF_3CFClCF_2I$. The direction of the thermal addition of fluorocarbon iodides to some fluorinated olefins has been determined. The great utility of vapor–liquid partition chromatography in both the analysis and separation of the addition compounds is described and characteristic elution time ratios for a series of isomeric fluoroiodides are presented.

This is the first paper in a series dealing with the addition of iodine halides to fluorinated olefins and is concerned primarily with the direction of addition of iodine monochloride to various perhaloölefins.

The Addition of Iodine Monochloride to Chlorotrifluoroethylene.—The addition of iodine monochloride to chlorotrifluoroethylene has been reported to give $CF_2ClCFClI$ (I) as the exclusive ICl adduct.[1,2] We now wish to report that this addition is in fact bidirectional under the various conditions reported[1,2] and that at the reaction temperatures previously used, *i.e.*, room temperature to 50°, the adduct actually consists of at least 20–30% of the isomer $CFCl_2CF_2I$ (II).[3]

(1) R. N. Haszeldine, *J. Chem. Soc.*, 4423 (1952).

(2) J. T. Barr, J. D. Gibson and R. H. Lafferty, *J. Am. Chem. Soc.*, **73**, 1352 (1951), did not investigate the structure of the adduct but assigned the structure $CF_2ClCFClI$ by analogy to other addition reactions of the olefin $CF_2{=}CFCl$.

(3) Professor R. N. Haszeldine, University of Manchester, has recently informed us that he has independently discovered that the ad-