Table IV along with values of the free energy of formation for some of the olefins. It is generally found that the thermodynamically more stable isomer reacts at about the same rate or more rapidly than its partner. The rate and stability differences are such that the more stable isomer is reacting with a lower activation energy in all cases. This implies that the free-energy relationships which exist for the isomerization of the olefins under kinetically controlled conditions have the shape of Figure 4. The transition states thus appear to reflect the ground-state stability of the olefin. This model implies that in the transition state for the proton elimination process extensive C–H bond breaking and formation of the double bond has taken place. These considerations appear to hold whether Saytzeff or Hofmann elimination is occurring. Unfortunately, the authors do not know of accurate thermodynamic data for the trimethylpentenes but the ratio of the 1 to 2 olefin found in the solvolysis and exchange studies, if it is assumed to approximate equilibrium, bears this out.

The relative reactivity of the five heptenes generally reflects the ability of alkyl groups to increase the nucleophilicity of a double bond. Thus, in the series 2,4-dimethyl-1-pentene, 2,3-dimethyl-1-pentene, and 2,3,-3-trimethylbutene, there is a progressive replacement of allylic hydrogens in isobutylene by one, two, and three alkyl groups which results in a continual increase in reactivity.

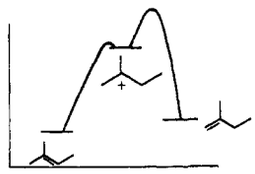

Figure 4.—Free-energy relationships during olefin isomerization.

In summary olefins have been found to undergo a slow stepwise exchange process in 73% sulfuric acid. The intermediate carbonium ions show a progressively decreasing tendency to form acid-soluble compounds as their size is increased. Proton elimination from the ion yields Saytzeff and Hofmann products approaching those distributions found in classical solvolysis studies, but with a somewhat sharper distinction of the onset of steric factors. The relative reactivity of pairs of isomers generally shows the more stable isomer to be about as reactive as or more reactive than its partner and implies that the transition state leading to the ions has much olefinic character.

**Registry No.**—Sulfuric acid, 7664-93-9; $HTSO_4$, 16878-40-3.

# The Chemistry of Nitrogen Radicals. VIII. The Free-Radical Addition of Monoalkyl-N-chloramines to Substituted Olefins

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The addition of monoalkyl-N-chloramines RNHCl in a sulfuric acid–acetic acid medium to olefins substituted in the vinylic or allylic position is described. Yields of the resulting substituted β-chloramines were 40–70%.

We have recently described the free-radical addition of N-chlorodialkylamines in strongly acidic media to olefinic hydrocarbons[1] and to a variety of vinyl and allyl compounds.[2] In Table I are summarized the results obtained when N-chloro*mono*alkylamines R-NHCl were used in this type of reaction (eq 1). Most

$$\mathrm{RNHCl} + \mathrm{CH_2{=}C}\begin{matrix}\mathrm{R}\\ \diagdown\\ \diagup\\ \mathrm{X}\end{matrix} \xrightarrow[\substack{\mathrm{HOAc},\\ h\nu,\ 30^\circ}]{\mathrm{H_2SO_4}} \mathrm{RNHCH_2C}\begin{matrix}\mathrm{R}\\ |\\ \mathrm{Cl}\\ |\\ \mathrm{X}\end{matrix} \quad (1)$$

X = Cl, F, $CH_2Cl$, $CH_2CN$: 50–70%
X = Br, $CH{=}CH_2$, $Si(CH_3)_3$, OR: no adduct

of the olefins substituted with a vinylic or allylic halogen atom gave the expected products, although in yields averaging about 20% lower[3] than were realized in the case of the dialkylchloramines. Since the adducts are secondary amines, the potential now exists to carry out further reactions at the nitrogen, such as acylation and alkylation. These results further extend the generality of the chloramine–olefin addition reaction as a synthetically important route to derivatives of β-chloramines.

In sharp contrast to the results in Table I, several olefins which gave good to excellent yields of adducts with dialkylchloramines now gave no adducts with monoalkylchloramines. Thus, chloramine decomposition within 30–50 min was observed in reactions of butadiene, trimethylvinylsilane, vinyl bromide, allyl ethyl ether, or allyl 2,4-dichlorophenyl ether, but no isolable adducts were formed. Allyl ethyl ether and *t*-butylchloramine were also irradiated in 70% (vol.) $H_2SO_4$ in water, since this solvent had previously[2] been suitable for preparing the adduct of N-chloropiperidine and allyl ethyl ether in 64% yield; again, however, no adduct of the monoalkylchloramine was isolated. Only a small amount (~15%) of a crude product, probably the adduct, was obtained from allylbenzene, but the adduct could not be purified. Finally, none of the anticipated 2:1 adduct was obtained when **10**, the 1:1 adduct of isopropylchloramine and 2-chloropropene, was converted into its N-chloro derivative and treated under standard conditions with 2-chloropropene; instead, 50% of the original compound **10** was recovered.

Evidence for the fate of allyl 2,4-dichlorophenyl ether was sought by working up this reaction mixture

(1) R. S. Neale, *J. Org. Chem.*, **32**, 3263 (1967).
(2) R. S. Neale and N. L. Marcus, *ibid.*, **32**, 3273 (1967).
(3) Perhaps coincidentally, the yield was also significantly lower when N-bromovaleramide instead of the N-alkyl analog N-*t*-butyl-N-bromovaleramide was rearranged in a radical chain reaction to the 4-bromo isomer: R. S. Neale, N. L. Marcus, and R. G. Schepers, *J. Amer. Chem. Soc.*, **88**, 3051 (1966).

TABLE I

ADDITION OF MONOALKYLMONOCHLORAMINES TO OLEFINS IN ACETIC ACID[a]

| Chloramine | | | Olefin | | *M*, $H_2SO_4$ | Time, min | Adduct | | |
|---|---|---|---|---|---|---|---|---|---|
| Structure | Mol[b] | Prepn[c] | Structure | Mol | | | Structure | % yield[d] | No. |
| *t*-$C_4H_9NHCl$ | 0.10 | 1 | $CH_2{=}C{=}CH_2$ | 0.13[e] | 4 | 45 | *t*-$C_4H_9NHCH_2C(Cl){=}CH_2$ | 41 | 1 |
| *t*-$C_4H_9NHCl$ | 0.11 | 1 | $CH_3C(Cl){=}CH_2$ | 0.11 | 4 | 25 | *t*-$C_4H_9NHCH_2CCl_2CH_3$ | 66 | 2 |
| | 0.12 | 2 | | 0.12 | 4 | 20 | | 68 | |
| *t*-$C_4H_9NHCl$ | 0.12 | 1 | $CH_2{=}CHCH_2Cl$ | 0.12 | 4 | 65 | *t*-$C_4H_9NHCH_2CHClCH_2Cl$ | 58[f] | 3 |
| | 0.12 | 2 | | 0.12 | 4 | 70 | | 70 | |
| *t*-$C_4H_9NHCl$ | 0.12 | 2 | $CH_2{=}CHCl$ | 0.14[e] | 4 | 75 | *t*-$C_4H_9NHCH_2CHCl_2$ | 59 | 4 |
| *t*-$C_4H_9NHCl$ | 0.12 | 2 | $CH_2{=}CHF$ | 0.13[e] | 4 | 60 | *t*-$C_4H_9NHCH_2CHClF$ | 61 | 5 |
| *t*-$C_4H_9NHCl$ | 0.12 | 2 | $CH_2{=}CHCH_2CN$ | 0.12 | 4 | 40 | *t*-$C_4H_9NHCH_2CH{=}CHCN$ | 56[g] | 6 |
| Cyclo-$C_6H_{11}NHCl$ | 0.09 | 1 | $CH_3C(Cl){=}CH_2$ | 0.10 | 4 | 15 | Cyclo-$C_6H_{11}NHCH_2CCl_2CH_3$ | 60 | 7 |
| Cyclo-$C_6H_{11}NHCl$ | 0.09 | 1 | $CH_2{=}CHCH_2Cl$ | 0.10 | 4 | 55 | Cyclo-$C_6H_{11}NHCH_2CHClCH_2Cl$ | 52[h] | 8 |
| *i*-$C_3H_7NHCl$ | 0.10 | 1 | $CH_2{=}CHCH_2Cl$ | 0.10 | 4 | 35 | *i*-$C_3H_7NHCH_2CHClCH_2Cl$ | 36 | 9 |
| | 0.09 | 1 | | 0.10 | 6 | 30 | | 49 | |
| | 0.12 | 2 | | 0.12 | 4 | 40 | | 56 | |
| *i*-$C_3H_7NHCl$ | 0.10 | 1 | $CH_3C(Cl){=}CH_2$ | 0.10 | 4 | 10 | *i*-$C_3H_7NHCH_2CCl_2CH_3$ | 30[i] | 10 |
| | 0.10 | 2 | | 0.10 | 4 | 15 | | 72 | |
| *i*-$C_3H_7NHCl$ | 0.12 | 2 | $CH_2{=}CHCl$ | 0.15[e] | 4 | 50 | *i*-$C_3H_7NHCH_2CHCl_2$ | 40 | 11 |
| | 0.07 | 2 | | 0.11[e] | 6 | 25 | | 58 | |

[a] Vicor vessel, 30°, 100-W external Hanovia uv lamp, $N_2$. [b] By iodometric titration of reaction mixture before introduction of olefin. [c] Method 1, amine added to 5% aqueous NaOCl; method 2, NaOCl solution added to aqueous amine. [d] Distilled, free base. [e] As weight loss of gas from cylinder. [f] 68% as the hydrochloride. [g] Yield of *t*-$C_4H_9NH(CH_2)_3CN$ (**12**) after reduction of **6** (mixture with nonconjugated isomer) with $H_2$/Pd. [h] 66% as the picrate. [i] As the picrate.

for neutral as well as basic products. Unfortunately, only traces of neutral and basic products were found, and 50% of allyl 2,4-dichlorophenyl ether was recovered.

The structures of adducts **1–11** were assigned on the basis of elemental analyses of their hydrochloride or picrate derivatives and the nmr spectra of the free bases, which showed the expected characteristics relative to the products from the previous dialkylchloramine reactions. In only one case was the product isolation anything but routine. The adduct **6** from allyl cyanide and *t*-butylchloramine lost hydrogen chloride on work-up to give a mixture of two products containing a conjugated and a nonconjugated cyano group; however, this mixture was unstable toward distillation, undoubtedly because of a facile cyanoalkylation by one adduct molecule of the amino group of the next. The known, saturated analog **12** was therefore prepared by hydrogenation of crude **6**. One may recall that the analogous 4-dialkylaminocrotononitrile obtained previously[2] was conveniently stable, since cyanoalkylation of a tertiary amino group does not readily occur.

Finally, it is clear from Table I that one must prepare a monoalkylmonochloramine in a way that avoids the formation of the dichloramine, *i.e.*, by maintaining the amine in excess relative to the chlorinating agent which is slowly added *to* the amine solution. This was especially important in the synthesis of adducts **9**, **10**, and **11** from isopropylchloramine, but less important in the case of *t*-butylchloramine or cyclohexylchloramine, since the latter two compounds separated from solution as they formed. Since the presence of the dichloramines appears to be detrimental to the desired addition reactions, the lowered yields observed in even the best examples above, relative to corresponding results with dialkylchloramines, may reflect a certain amount of disproportionation of the monoalkylchloramines in the reaction medium, a process that has been noted before.[4,5] Because very strong acid inhibits this disproportionation,[4] two additions were carried out in a stronger than usual acid medium; the adducts were indeed formed in higher yield when the ratio of sulfuric acid to isopropylchloramine was increased from 8 to 12 (to give **9**) or from 8 to 17 (to give **11**).

## Experimental Section

All the reactions were carried out in the apparatus and according to the procedures previously described[1,2] and as additionally specified below. The physical properties of the adducts and elemental analyses of hydrochloride or picrate derivatives are listed in Table II. The infrared spectra of the adducts all contained a sharp, weak NH band at 3330–3280 $cm^{-1}$; broad, strong absorption in the region 800–650 $cm^{-1}$ obscured any definition of the several distinct bands previously observed[2] in similar, tertiary amine adducts, although the spectra of all three adducts from allyl chloride (**3**, **8**, and **9**) did contain a distinctly strong, broad band at 670 $cm^{-1}$. The nmr spectra of all the adducts were entirely as anticipated from the spectra of the tertiary amine adducts,[2] including the spectrum from $\tau$ 3 to 8 of the fluoro compound **5** which was practically identical with that reported[2] for diethyl-2-chloro-2-fluoroethylamine (less the N-ethyl absorption). The spectrum of 4-*t*-butylaminobutyronitrile (**12**) consisted of a nine-peak pattern at $\tau$ 7.25–7.70 (4 H, $NCH_2$ and $CH_2CN$), a less well-defined multiplet at 8.10–8.65 (2 H, $CCH_2C$), the *t*-butyl singlet at 8.95 (9 H), and the broad NH peak at 9.1.

All the distillations were carried out using an externally heated 60 cm × 6 mm column packed with an 18 gauge tantalum wire spiral and capillary air bleed agitation of the pot contents under a very low reflux ratio (1:1 up to 5:1 max) in a minimum volume head.

Although we did not attempt to prepare the materials in pure form, all three of the monochloramines used in the present work have been described previously[6] and were prepared in aqueous hypochlorite solution. As noted above, one can avoid the extensive and detrimental formation of N,N-dichloramines by adding the hypochlorite solution to the amine (method 2 in

(4) R. S. Neale and M. R. Walsh, *J. Amer. Chem. Soc.*, **87**, 1255 (1965).
(5) J. Jander and C. Lafrenz, *Angew. Chem. Intern. Ed. Engl.*, **5**, 598 (1966).
(6) V. L. Heasley, P. Kovacic, and R. M. Lange, *J. Org. Chem.*, **31**, 3050 (1966); G. Allinger, U. S. Patent 2,495,085 [*Chem. Abstr.*, **45**, 177 (1951)] and U. S. Patent 2,459,759 [*Chem. Abstr.*, **43**, 3033 (1949)].

TABLE II

PHYSICAL CONSTANTS OF PRODUCTS AND ANALYSES OF NEW COMPOUNDS

| Compd and derivative | Registry no. | Empirical formula | Bp (mm) or mp, °C | $n^{23}D$ | Carbon, % Calcd | Carbon, % Found | Hydrogen, % Calcd | Hydrogen, % Found | Chlorine, % Calcd | Chlorine, % Found | Nitrogen, % Calcd | Nitrogen, % Found |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1[a] | 17026-97-0 | | 52 (15) | 1.4438 | | | | | | | | |
| 2 | 17026-98-1 | | 73 (35) | 1.4463 | | | | | | | | |
| 2·HCl | 17026-99-2 | $C_7H_{16}Cl_3N$ | 200 dec | | 38.12 | 38.31 | 7.31 | 7.09 | 48.22 | 48.15 | 6.35 | 6.22 |
| 2·picrate | 17027-00-8 | $C_{13}H_{18}Cl_2N_4O_7$ | 187–189 | | 37.79 | 37.91 | 4.38 | 4.44 | | | 13.56 | 13.28 |
| 3 | 17027-01-9 | | 40–41 (1) | 1.4570 | | | | | | | | |
| 3·HCl | 17027-02-0 | $C_7H_{16}Cl_3N$ | 185–186 | | 38.12 | 37.93 | 7.31 | 7.35 | 48.22 | 47.89 | 6.35 | 6.25 |
| 3·picrate | 17027-03-1 | $C_{13}H_{18}Cl_2N_4O_7$ | 171–172.5 | | 37.79 | 37.86 | 4.38 | 4.33 | 17.16 | 16.96 | 13.56 | 13.31 |
| 4 | 17027-04-2 | | 82 (35) | 1.4500 | | | | | | | | |
| 4·HCl | 17027-05-3 | $C_6H_{14}Cl_3N$ | 215–220 dec | | 34.89 | 34.81 | 6.83 | 6.84 | 51.50 | 50.87 | 6.78 | 6.89 |
| 4·picrate | 17027-06-4 | $C_{12}H_{16}Cl_2N_4O_7$ | 188–189 | | 36.10 | 36.25 | 4.04 | 4.07 | | | 14.04 | 14.11 |
| 5 | 17027-07-5 | | 62 (42) | 1.4157 | | | | | | | | |
| 5·HCl[b] | 17027-08-6 | $C_6H_{14}Cl_2FN$ | 204–205.5 dec | | 37.91 | 37.68 | 7.42 | 7.60 | 37.30 | 37.22 | 7.37 | 7.26 |
| 5·picrate | 17027-09-7 | $C_{12}H_{16}ClFN_4O_7$ | 160–161 | | 37.66 | 38.04 | 4.21 | 4.38 | 9.26 | 9.70 | 14.64 | 14.76 |
| 6[c] | 17027-10-0 | | 65–66 (2) | 1.4414 | | | | | | | | |
| 7 | 17027-11-1 | | 72 (1) | 1.4830 | | | | | | | | |
| 7·HCl | 17027-12-2 | $C_9H_{18}Cl_3N$ | 195–200 dec | | 43.83 | 44.03 | 7.36 | 7.33 | 43.13 | 43.57 | 5.68 | 5.43 |
| 8 | 17027-13-3 | | 70–71 (0.3) | 1.4912 | | | | | | | | |
| 8·HCl | 17027-14-4 | $C_9H_{18}Cl_3N$ | 195.5–196 | | 43.83 | 43.56 | 7.36 | 7.07 | 43.13 | 43.30 | 5.68 | 5.59 |
| 8·picrate | 17027-15-5 | $C_{15}H_{20}Cl_2N_4O_7$ | 169–170 | | 41.01 | 40.88 | 4.59 | 4.63 | 16.14 | 15.99 | 12.76 | 12.49 |
| 9 | 17027-16-6 | | 100 (42) | 1.4581 | | | | | | | | |
| 9·HCl | 17027-17-7 | $C_6H_{14}Cl_3N$ | 153.5–155.5 | | 34.89 | 34.73 | 6.83 | 6.78 | 51.50 | 51.36 | 6.78 | 6.81 |
| 9·picrate | 17027-18-8 | $C_{12}H_{16}Cl_2N_4O_7$ | 127–129 | | 36.10 | 35.98 | 4.04 | 4.23 | 18.00 | 17.66 | 14.04 | 14.28 |
| 10 | 17027-19-9 | | 70 (24) | 1.4456 | | | | | | | | |
| 10·HCl | 17027-20-2 | $C_6H_{14}Cl_3N$ | 164–166 | | 34.89 | 35.03 | 6.83 | 6.85 | 51.50 | 51.36 | 6.78 | 6.41 |
| 10·picrate | 17027-21-3 | $C_{12}H_{16}Cl_2N_4O_7$ | 165–168 | | 36.10 | 36.14 | 4.04 | 4.22 | 18.00 | 18.25 | 14.04 | 13.90 |
| 11 | 17027-22-4 | | 67–68 (24) | 1.4502 | | | | | | | | |
| 11·HCl | 17027-23-5 | $C_5H_{12}Cl_3N$ | 175–177 | | 31.19 | 31.21 | 6.28 | 6.25 | 55.25 | 55.62 | 7.28 | 7.31 |
| 11·picrate | 17047-83-5 | $C_{11}H_{14}Cl_2N_4O_7$ | 135–136 | | 34.30 | 34.32 | 3.66 | 3.70 | 18.41 | 18.59 | 14.54 | 14.57 |
| 12[d] | 17027-24-6 | | 66 (1) | 1.4314 | | | | | | | | |

[a] Lit. bp 61–62° (26 mm), $n^{25}D$ 1.4431 [A. T. Bottini, B. J. King, and R. E. Olson, *J. Org. Chem.*, **28**, 3241 (1963)]. [b] Calcd for Fl: 9.99. Found: 10.28. [c] Undetermined purity. [d] Lit. bp 102–105° (19 mm) [British Patent 948,897 to Parke, Davis and Co.; *Chem. Abstr.*, **60**, 10690 (1964)].

Table I). Both this and the opposite order of addition (method 1) are illustrated in the following examples. Direct evidence of dichloramine formation was obtained in the case when *t*-butylamine was added *to* a hypochlorite solution. The uv spectrum of a solution of the product in pentane (but not of a product from method 2) showed characteristic dichloramine absorption[4] at 303 and 305 mμ (double maximum) in addition to the monochloramine band[4] at 258 mμ; the *t*-butylamine absorption at 290 mμ was not evident in either solution.

**Cyclohexyl-2,2-dichloropropylamine (7).**—To 140 ml of 5% sodium hypochlorite solution (0.095 mol) was added 0.1 mol of cyclohexylamine at a rate to maintain the temperature of the well-stirred solution at 9° with an ice bath (method 1). The order of addition was not critical, since cyclohexylchloramine separated from the aqueous solution as it formed. After 30 min, the chloramine was extracted into pentane, dried over $Na_2SO_4$, and chilled. The ice-cold solution was extracted into 44 ml of cold concentrated $H_2SO_4$ in two portions. The acid was then filtered under suction through a medium fritted-glass funnel. The reaction solution was prepared by adding the resulting sulfuric acid solution to 144 ml of glacial acetic acid; iodometric titration of an aliquot showed 0.09 mol of electropositive chlorine was present. The reaction with 2-chloropropene was then carried out as described previously.[2] Crude **7** was isolated in the usual manner from the partially neutralized solution and purified by distillation, which proceeded without decomposition of the adduct.

***t*-Butyl-2-chloro-2-propenylamine (1).**—A solution containing 0.10 mol of *t*-butylchloramine was prepared as described in the preceding example and a reaction was carried out with allene. The olefin was admitted to the reaction solution through a coarse fritted gas dispersion tube, and no reaction occurred until irradiation was begun. The crude adduct was obtained only on complete basification of the diluted reaction mixture. Apparently, a significant amount of an unstable isomer of **1** was also produced, since distillation reduced the 74% crude yield to 41% of purified **1**. A hydrochloride of the crude product was obtained after one recrystallization from acetone in 58% yield based on the chloramine, but the 150–157° melting range was low compared with the reported[7] range of 153–160°. No attempt was made to isolate whatever unstable products were present.

**Reaction between *t*-Butylchloramine and Allyl Cyanide.**—An acidic solution of *t*-butylchloramine was prepared by method 2, *i.e.*, by adding 0.18 mol of 5% NaOCl to 0.2 mol of *t*-butylamine in 50 ml of water at 10° with vigorous stirring and then preparing the sulfuric acid–acetic acid solution as usual. This gave 0.12 mol of titratable chlorine. The reaction with 0.12 mol of allyl cyanide was carried out and worked up in the usual manner to afford 16 g of a crude, basic product (**6**) that separated only on complete basification of the diluted reaction mixture. This product was presumed to contain both the conjugated and nonconjugated olefinic nitriles which would form on dehydrochlorination of the initial 1:1 adduct, since no chlorine was present in the product, both conjugated and nonconjugated nitrile and olefin stretching bands were present in the ir spectrum of crude **6**, and distillation of **6** produced a nonvolatile tar in 80% yield. The distillate (20% yield) [bp 65–66° (2 mm), $n^{23}D$ 1.4414] had the same spectral properties as crude **6** and decomposed on standing.

Hydrogenation of crude **6** was then carried out[8] in nearly quantitative yield to give 4-*t*-butylaminobutyrontrile (**12**) in 56% yield based on the chloramine. To 2.0 g (0.0145 mol) of **6** in 40 ml of ethanol was added 0.2 g of 5% palladium on charcoal and hydrogenation at 25° and ~1 atm was allowed to proceed until the uptake of hydrogen ceased (0.015 mol). Work-up and distillation gave **12**, which appeared homogeneous from its glpc and nmr spectra.

***t*-Butyl-2,3-dichloropropylamine (3).**—The chloramine was prepared according to method 2 from the addition over 30 min of 0.18 mol of 5% NaOCl solution to 0.20 mol of *t*-butylamine in 50 ml of water at −10°. The addition to allyl chloride and subsequent work-up were carried out as usual and crude **3** was

(7) A. T. Bottini and R. E. Olsen, *J. Amer. Chem. Soc.*, **84**, 195 (1962).

(8) R. L. Augustine, "Catalytic Hydrogenation," Marcel Dekker, Inc., New York, N. Y., 1965, p 60.

obtained from the completely basified aqueous solution in 73% yield. Distillation afforded pure **3** without difficulty.

**Isopropyl-2,2-dichloroethylamine (11).**—The best preparation of **11** resulted from maintaining a very high acid/chloramine ratio as follows. A solution containing 0.07 mol of isopropylchloramine in 64 ml of concentrated $H_2SO_4$ and 124 ml of glacial acetic acid (6 *M* $H_2SO_4$) was purged at 25° with nitrogen for 15 min as usual and then treated under irradiation with gaseous vinyl chloride to completion of the reaction. The mixture was poured over 200 g of ice, diluted with 700 ml of water, extracted with pentane (no neutral products isolated), and fully basified with 295 ml of 12 *N* NaOH. The 6.6 g of crude **11** (61%) was extracted into a total of 350 ml ether and subsequently purified by an unusually efficient distillation.

**Attempted Addition of N-Chlorinated 10 to 2-Chloropropene.**—The crude N-chloro derivative of adduct **10** was prepared by stirring 0.05 mol of **10** and 0.05 mol of *t*-butylhypochlorite in 200 ml of ether for 60 min at room temperature. Ether was removed from N-chloro **10**, the residue was dissolved in 22 ml of concentrated $H_2SO_4$, and this was added to 75 ml of glacial acetic acid in the Vicor flask. Irradiation in the presence of a total 0.10 mol of 2-chloropropene for 15 min destroyed the active chlorine, but normal work-up gave 50% of **10** as the only isolable product.

# Kinetics and Mechanisms of Hydrolysis of 5-Halouracils[1]

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The determined log *k*–pH profiles for the hydrolyses of the 5-fluoro-, 5-chloro-, 5-bromo-, and 5-iodouracil and their heats of activation at several pH values are similar. The ease of hydrolysis increases with the stated sequence. The observed major products of the strongly alkaline hydrolysis of 5-iodouracil are uracil and barbituric acid, whereas only the barbituric acid product is observed for 5-bromouracil. The rates of production of these products are dependent on hydroxyl ion attack on the halouracil monoanion or the kinetically equivalent solvent attack on the dianion. A certain fraction of the halouracil produces a nonchromophoric product. Possible barbituric acid formation from 5-chlorouracil and 5-fluorouracil cannot be observed because of the relatively large rates of barbituric acid degradation under equivalent conditions. The greater portion of the hydrolysis in phosphate and borate buffer pH regions is a consequence of hydroxyl ion attack on the undissociated halouracil or the kinetically equivalent solvent attack on the monoanion and results in nonchromophoric products and no barbituric acid. Isobarbituric acid is obtained from 5-bromouracil degraded in oxygen-free bicarbonate buffer. It is not observable as a product in buffers under ambient conditions. Isobarbituric acid has a high degree of stability when air is excluded from the solution. The observed general base-catalyzed hydrolysis in buffer solutions can be explained by phosphate dianion attack on the undissociated halouracil and its monoanion and the kinetic dependencies have been determined. A small borate buffer catalysis exists in the cases of iodouracil and bromouracil. The rate of alkaline hydrolysis of bromouracil is the same as the rate of bromide ion production and proves that there is no appreciable storage in a reactive adduct that leads to products. 5-Methyluracil and uracil are highly stable under equivalent alkaline conditions and definitely implicate the need of a halogen substituent for facile hydrolysis of substituted uracils.

The alkaline solvolysis of 5-halouracils has not been delineated. Insight into the mechanism of action in biological systems and the need for synthetic routes for derived compounds such as glycosides demand fundamental physical organic and kinetic studies of the solvolytic transformations of these compounds.

Isobarbituric acid has been claimed as a product of the solvolysis of 5-bromouracil in the alkaline pH region.[2] It was isolated under specific conditions with $NaHCO_3$ as the reacting species. It was claimed that isobarbituric acid could not be obtained from the 5-halouracils in the presence of stronger bases because of the great instability of isobarbituric acid in alkali.[2]

We have systematically investigated the solvolysis of 5-fluoro, 5-chloro-, 5-bromo-, 5-iodo-, 5-methyl-, 5-hydroxy- (isobarbituric acid), and 6-hydroxyuracil (barbituric acid) in the entire pH region, in order to establish the log *k*–pH profiles for such solvolyses and to determine the routes and mechanisms of reaction as functions of the ionic state of the reacting species. We have obtained definite information that the major product of strong alkaline solvolysis of 5-halouracils is not isobarbituric acid but barbituric acid and that the routes of degradation are pH dependent.

## Results

**Spectral Changes and Product Identification.**—The 5-halouracils are reasonably stable in acid.[3] Iodouracil is unstable in the presence of acid-degraded deoxyribose.[4,5] 5-Fluorouracil (FU) and 5-chlorouracil (CU) lose their ultraviolet absorbance at all wavelengths without any observed change in the chromophoric absorption band at all alkaline pH values greater than 5.6. Typical spectra as a function of time are given for CU in 0.22 *M* NaOH in Figure 1. Typical first-order plots for the loss of the spectral absorbance of CU and FU at various pH values are given for FU in Figure 2. The apparent first-order rate constants were calculated from the slopes of the plots of logarithms of absorbance *vs.* time and are listed in Table I.

The 5-bromouracil (BU) spectral changes for pH values below *ca.* 9.5 follow a similar pattern. The absorbance values at the $\lambda_{max}$ disappear by apparent first-order processes without any observed changes in the chromophoric absorption band.

At pH values above 10, however, an initial increase in absorbance appears at 257 mμ and this new maximum can be distinguished from that assigned to the BU

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