The existence of such a process in competition with intermolecular reactions or cleavage of the intermediate alkoxy radical would be of interest, since Corey[4] has suggested that the intramolecular nature of the N-chloramine reaction may arise from a positive charge on the intermediate radical which is here lacking.[5] Also, since preferential attack through a quasi-six membered transition state ($n = 2$ in reaction 1) would be anticipated,[5] the reaction should provide a convenient synthesis of δ-chloroalcohols and accordingly a variety of substituted tetrahydrofurans.

We find that a number of long chain t-hypochlorites indeed undergo photodecomposition in CCl_4 or $C_2Cl_4F_2$ to give the expected δ-chloroalcohols as indicated in Table I. The reaction evidently involves long chains, since the solutions are stable in the dark, but the color of the hypochlorite disappears rapidly at $0°$ on illumination with an incandescent lamp. Products were separated by gas–liquid chromatography and the chloroalcohols identified by infrared spectra and conversion to the corresponding tetrahydrofurans by alcoholic potassium hydroxide, then analysis or comparison with known samples.

TABLE I

PHOTODECOMPOSITION OF HYPOCHLORITES $RC(CH_3)_2OCl$
(AT $0°$ IN CCl_4 UNLESS INDICATED)

| R–	Concn. (molar)	Products (% yield)[a]
1 CH₃–	2.6	CH₃Cl, acetone (97)
2 C₂H₅–	1.5	C₂H₅Cl, acetone (96)
3 n-C₃H₇	1.8	C₃H₇Cl, acetone (59)
		Cl(CH₂)₃C(CH₃)₂OH (17)
	1.8 (40°)	C₃H₇Cl, acetone (63)
		Cl(CH₂)₃C(CH₃)₂OH (16)
	1.8 (80°)	C₃H₇Cl, acetone (68)
		Cl(CH₂)₃C(CH₃)₂OH (15)
4 (CH₃)₂CHCH₂–	1.6	i-C₄H₉Cl, acetone (43)
		ClCH₂CH(CH₃)CH₂C(CH₃)₂OH (29)
	1.6 (40°)	i-C₄H₉Cl, acetone (48)
		ClCH₂CH(CH₃)CH₂C(CH₃)₂OH (27)
	1.6 (80°)	i-C₄H₉Cl, acetone (55)
		ClCH₂CH(CH₃)CH₂C(CH₃)₂OH (26)
5 n-C₄H₉–	1.7	n-C₄H₉Cl, acetone (13)
		CH₃CHClCH₂CH₂C(CH₃)₂OH (80)
	0.8 (C₂Cl₄F₂)	n-C₄H₉Cl, acetone (15)
		CH₃CHClCH₂CH₂C(CH₃)₂OH (76)
	3.2 (C₂Cl₄F₂)	n-C₄H₉Cl, acetone (13)
		CH₃CHClCH₂CH₂C(CH₃)₂OH (77)
	6.7 (C₂Cl₄F₂)	n-C₄H₉Cl, acetone (14)
		CH₃CHClCH₂CH₂C(CH₃)₂OH (79)

[a] Major products only, yields ±5% of indicated values.

The intramolecular nature of the hydrogen abstraction step in the rearrangement was demonstrated for compound 5 by examining the competition with the unimolecular decomposition of the intermediate alkoxy radical as a function of concentration. No significant variation of yields with concentration was found and it is notable that the intramolecular reaction remains the major path even in 6.7 M solution.

(5) The possibility of such a reaction in the steroid series has been suggested by D. H. R. Barton, J. M. Beaton, L. E. Geller and M. M. Pechet, *J. Am. Chem. Soc.*, **82**, 2640 (1960), and, we understand, recently observed, D. H. R. Barton, *ibid.*, **83**, 2213 (1961).

Cleavage of the intermediate alkoxy radical to yield acetone and alkyl chloride

$$RC(CH_3)_2O\cdot \longrightarrow R\cdot + CH_3COCH_3 \quad (3)$$
$$R\cdot + RC(CH_3)_2OCl \longrightarrow RCl + RC(CH_3)_2O\cdot \quad (4)$$
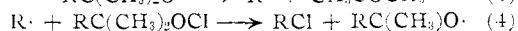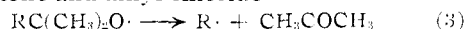
is the most serious side-reaction,[6] and varies with hypochlorite structure in a predictable manner. With $R < C_3$ it is essentially the sole reaction in keeping with our failure to detect any β or γ-chloroalcohols from longer chain hypochlorites. In hypochlorites containing δ-hydrogen, more cleavage occurs when intramolecular attack must be on primary hydrogen than when it is on a secondary hydrogen. Assuming the rates of cleavage of alkoxy radicals from 3, 4 and 5 are the same we may calculate relative reactivities per H for the abstraction process as 0.028, 0.036 and 1.0, respectively, at $0°$, a greater difference than would be predicted from the relative reactivities of primary and secondary hydrogens in intermolecular *tert*-butyl hypochlorite chlorinations (1:17 at $0°$).[7]

Since the amount of cleavage increases with temperature, our yields of chloroalcohols presumably could be improved at lower temperatures. For hypochlorite[4] the variation in product ratio with temperature indicates $E_{cleavage} - E_{abstraction} = 0.8$ kcal., together with a slightly larger PZ factor for the cleavage. Actually the difference in PZ factors is surprisingly small considering that intramolecular hydrogen abstraction requires a sharply defined cyclic transition-state.

We have detected no ϵ-chloroalcohol from hypochlorite.[5] Here its formation would require attack on a primary H, and we are currently examining more favorable cases.

We also have examined the products from the photodecomposition of the primary and secondary hypochlorites from 1-pentanol and 2-hexanol. Valeraldehyde and 2-hexanone are major products, and chlorine appears to be liberated during the reaction (presumably from HCl and ROCl) so that the process loses its intramolecular character. Higher boiling products are formed as well, and their structure is being studied, as well as the possibility of favoring the intramolecular reaction by changes of reaction conditions.

(6) Reaction (3) is considerably more rapid when R = a higher alkyl group than when R = CH₃, cf. P. Gray and A. Williams, *Chem. Revs.*, **59**, 239 (1959).

(7) Our earlier value at 40°? has been redetermined as 12.1:1³ proportional adjustment of the old value at 0° gives 17:1.

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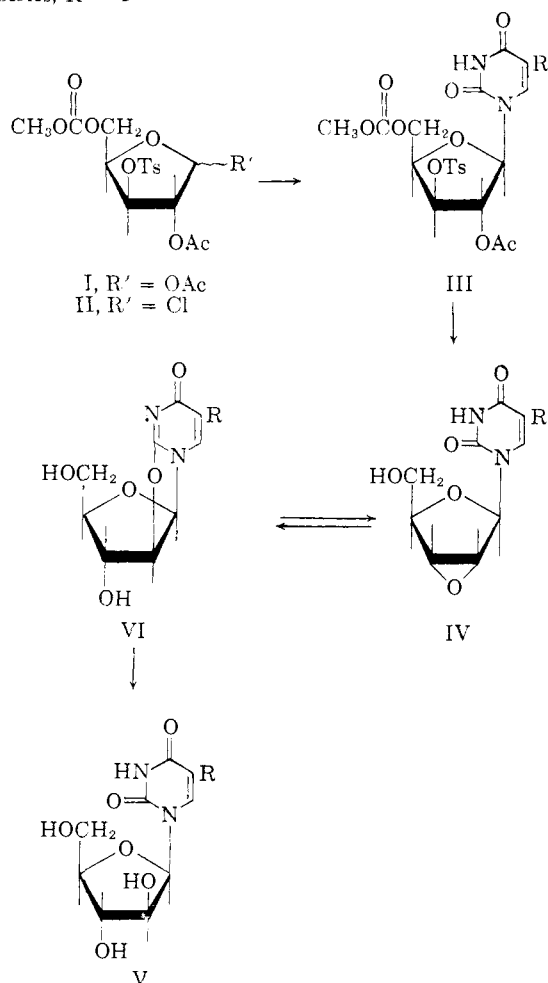POTENTIAL ANTICANCER AGENTS.[1] LXI. A NOVEL SYNTHESIS OF "SPONGO" NUCLEOSIDES

Sir:

Interest in nucleosides derived from β-D-arabinofuranose that can undergo anabolism by enzymes

(1) This work was carried out under the auspices of the Cancer Chemotherapy National Service Center, National Cancer Institute, National Institutes of Health, Public Health Service, Contract No. SA-43-ph-1892. The opinions expressed in this paper are those of the authors and are not necessarily those of the Cancer Chemotherapy National Service Center. For the preceding paper in this series, see L. O. Ross, E. M. Acton, W. A. Skinner, L. Goodman and B. R. Baker, *J. Am. Chem. Soc.*, **83**, in press (1961).

utilizing 2'-deoxynucleosides without cleavage to the base has been expressed previously[2] and has resulted in the synthesis of 9-(β-D-arabinofuranosyl)-adenine.[2] Pyrimidine β-arabinofuranosides such as 1-(β-D-arabinofuranosyl)-thymine (spongothymidine) (Vb)[3] and 1-(β-D-arabinofuranosyl)-uracil (spongouridine) (Va)[4] can be synthesized in about 10% yield from the corresponding pyrimidine ribofuranosides. This route is most practical with naturally occurring ribosides such as uridine. However, when the intermediate ribonucleoside must be synthesized,[5] this route becomes more laborious. A more direct—though less obvious—route to those "spongo" nucleosides now has been found, which makes this type of nucleoside more readily available for biological evaluation and is illustrated in I → V. This approach to the

a series, R = H
b series, R = CH₃
c series, R = F

I, R' = OAc
II, R' = Cl

III

VI   IV

V

spongonucleosides (V) from the readily available 3-tosyl-D-xylose derivative (I) is based on these observations: (1) Compound II can be coupled with purines and serves as a direct route to 2',3'-anhydronucleosides such as IV where the base is a purine.[6] (2) Ring opening of the cyclonucleoside can give a product which arises from either IVa or VIa, depending on reagent used, thus suggesting that IVa and VIa are readily interconvertible.[7] (3) Cyclonucleosides such as VIb, on treatment with acid, cleanly form the spongonucleosides (V).[3]

Therefore, coupling of II with a uracil derivative could be expected to lead directly to the cyclonucleoside VI, via IV, when the intermediate blocked nucleoside (III) is treated with base.

Condensation of II[6] with dithyminylmercury[5] in hot toluene gave the blocked nucleoside IIIb, which was treated directly with methanolic sodium methoxide to give the crude cyclonucleoside VIb with λ_{max} at 257 mμ and R_{Ad} 0.76.[8] Purification of the product was effected with an ion exchange column of Dowex 2 (OH) and was accompanied by the simultaneous hydrolysis of the cyclonucleoside VIb to spongothymidine (Vb) with λ_{max} at 268 mμ and R_{Ad} 0.95.[8] Thus, elution of the column with 1% aqueous acetic acid gave 11% (from I) of Vb, m.p. 248–249°, $[\alpha]^{20}D$ +90° (0.5% in water), $\lambda_{max}^{pH\ 1}$ 268 mμ (ε 9590), $\lambda_{max}^{pH\ 7}$ 268 mμ (ε 9530), $\lambda_{max}^{pH\ 13}$ 270 mμ (ε 7870) (Found for $C_{10}H_{14}N_2O_6\cdot0.25H_2O$: C, 46.1; H, 5.92, N, 10.5). Compound Vb slowly consumed 1 mole equivalent of periodate over a period of 48 hours.[9]

Condensation of II with monomercuri-5-fluorouracil[10] in a similar fashion gave, after treatment with methanolic sodium methoxide and purification by a Dowex 2 (OH) column, a 16% yield (from monomercuri-5-fluorouracil) of Vc, m.p. 187–188°; $[\alpha]^{23}D$ +107.2° (0.5% in water); $\lambda_{max}^{pH\ 1}$ 270 mμ (ε 9080), $\lambda_{max}^{pH\ 7}$ 270 mμ (ε 8670), $\lambda_{max}^{pH\ 13}$ 272 mμ (ε 7590), (Found for $C_9H_{11}FN_2O_6$: C, 41.1; H, 4.32; F, 7.34; N, 10.1).

The identity of the sugar portion of Vc with that of spongothymidine (Vb) was confirmed further by n.m.r. spectroscopy; the spectra of these compounds were identical with respect to the fine structure, chemical shifts and relative intensities of the peaks which can be assigned to the sugar portion of the nucleosides V.[11] The spectra of Vc had peaks with δ values (in p.p.m.) of 4.56, 4.47, 4.39, 4.27, 4.19, 4.09, 4.04, 4.00 and 3.94 compared with the corresponding δ values for Vb of 4.52, 4.46, 4.37, 4.27, 4.20, 4.12, 4.05, 4.02 and 3.97, respectively, using tetramethylsilane as an external standard.

(2) W. W. Lee, A. Benitez, L. Goodman and B. R. Baker, J. Am. Chem. Soc., 82, 2648 (1960).

(3) J. J. Fox, N. Yung and A. Bendich, ibid., 79, 2775 (1957).

(4) D. M. Brown, A. Todd and S. Varadarajan, J. Chem. Soc., 2388 (1956).

(5) J. J. Fox, N. Yung, J. Davoll and G. B. Brown, J. Am. Chem. Soc., 78, 2117 (1956).

(6) C. D. Anderson, L. Goodman and B. R. Baker, ibid., 81, 3967 (1959).

(7) D. M. Brown, D. B. Parihar, A. Todd and S. Varadarajan, J. Chem. Soc., 3028 (1958).

(8) Paper chromatograms were run in water-saturated butyl alcohol by the descending procedure on Whatman No. 1 paper. Adenine was used as a standard and spot locations were expressed as R_{Ad} units with adenine at 1.00.

(9) The slow uptake of periodate is strongly indicative of a trans-glycol configuration.³ Fox, et al., report m.p. 238–242°, $[\alpha]^{24}D$ +93° (water), for spongothymidine³ in contrast to m.p. 156°, $[\alpha]^{31}D$ −2° (water), for xylofuranosylthymine,⁵ the alternative nucleoside with a trans-glycol stereochemistry.

(10) M. Hoffer, R. Duschinsky, J. J. Fox and N. Yung, J. Am. Chem. Soc., 81, 4112 (1959).

(11) See R. U. Lemieux and M. Hoffer, Can. J. Chem., 39, 110 (1961), for a discussion on the use of n.m.r. spectroscopy for the determination of conformation of the sugar moiety of nucleosides with emphasis on the identification of α and β anomers, based on differences in fine structure.

The generality of this method for preparing other β-arabinosides for biological evaluation is currently under investigation.[12]

(12) The synthesis of 1-β-D-arabinofuranosyl-5-fluorouracil (Vc) by another route was announced by J. J. Fox, N. Yung, I. Wempen, R. Duschinsky and L. Kaplan, Abstr. Intl. Union Pure and Applied Chemistry (Symposium on Natural Products), Australia, August 1960, p. 66. Their synthesis begins with 5-fluorouridine (prepared from 5-fluorouracil) which is converted *via* a 2,2′-anhydronucleoside intermediate to Vc in 26% yield based upon 5-fluorouracil (personal communication from Fox and Yung).

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RECEIVED FEBRUARY 9, 1961

SYNTHESIS OF PHENYLCHLOROTRISPHOSPHONITRILE

Sir:

We wish to report the direct preparation and positive identification of phenylchlorotrisphosphonitrile, [Ph(Cl)PN]₃. Although previous workers have studied the synthesis of the $[Ph(Cl)PN]_n$ system, none has reported isolation of the trimer. Thus Bode and Bach[1] treated PhPCl₄ with ammonium chloride and could isolate only a partially hydrolyzed derivative for which analysis indicated the formula $N_3P_3Ph_3Cl(OH)_2$. Shaw and Stratton[2] repeated the reaction and isolated [Ph(Cl)PN]₄ in two isomeric forms. Herring,[3] using the novel procedure of treating NaN₃ with PhPCl₂, isolated a mixture of phenylchlorophosphonitriles with an average molecular weight of 5000. Recently, Tesi[4] reported synthesis of [Me(Cl)PN]₃ by treatment of $N_3P_3Cl_3(NMe_2)_3$ with MeMgBr to give $N_3P_3Me_3(NMe_2)_3$ which was converted to [Me(Cl)PN]₃ by treatment with HCl. Although this procedure gives an [R(Cl)PN]₃ compound, it is not a direct synthesis.

In our preparation PhPCl₄ was made by chlorination of PhPCl₂ (Victor Chemical Works) in carbon tetrachloride then recrystallization from the same solvent under dry nitrogen. A solution of 121 g. (0.484 mole) of PhPCl₄ in 250 ml. of dried and redistilled *s*-tetrachloroethane was added over a period of 28 hr. to a slurry of 197 g. (3.71 moles) of NH₄Cl in 50 ml. of dry xylene. Reflux was then maintained for an additional 24 hours; unreacted ammonium chloride was filtered off, washed with dry benzene, and the washes were combined with the filtrate. Concentration of the solution gave a gummy solid (I) and solution (II) which could not be separated effectively by filtration. However, addition of petroleum ether converted (I) to a solid which was filtered off and recrystallized from acetonitrile to give 8 g. of crude trimer, m.p. 135–150° (A). Solution (II) was distilled to dryness to give a hard gum which was crystallized fractionally from acetonitrile to give an additional 12 g. of crude trimer, m.p. 130–150° (B). The infrared curves of A and B were similar, showing strong absorptions in the 1200 cm.⁻¹ region, typical of the trimeric phosphonitrile ring. A was frac-

(1) H. Bode and H. Bach, *Ber.*, **75**, 215 (1942).
(2) R. A. Shaw and C. Stratton, *Chem. & Ind.*, **52** (1959).
(3) D. L. Herring, *Chem. & Ind.*, 717 (1960).
(4) G. Tesi, *Proc. Chem. Soc.*, 404 (1960).

tionally recrystallized three times from acetonitrile to give 3 g. of material, the analytical sample, m.p. 161–163° (Fisher–Johns block, uncorrected). *Anal.*[5] Calcd. for C_6H_5ClPN: P, 19.66; N, 8.90; C, 45.74; H, 3.20; Cl, 22.51; mol. wt. calcd. for $(C_6H_5(Cl)PN)_3$, 473. Found: P, 19.63; N, 9.01; C, 45.67; H, 3.44; Cl, 22.38; mol. wt.,[6] 445, 448. The principal P–N ring infrared absorptions are at 1180 cm.⁻¹ (s) and 1210 cm.⁻¹ (s), with no discernible absorptions at the reported values[2] for the tetramer. Infrared analysis indicated that the remainder of the reaction product contained additional trimer and also tetramer. Although recovery of trimer from this residue is difficult, procedures for its accomplishment are being investigated.

Using a different procedure, the tetramer recently has been prepared in this laboratory in better than 60% yield and this work will be reported shortly. Both trimer and tetramer now are being studied with respect to alkylation, arylation, and other substitution reactions.

We wish to thank the Armstrong Cork Company, Lancaster, Penna., for generous support of this work.

(5) Schwartzkopf Microchemical Laboratories.
(6) Ebulliometric measurement in benzene. We are indebted to Dr. Ralph Griffith, Sinclair Research Laboratories, for this measurement.

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STEREOCHEMISTRY OF SUBSTITUTION TO ASYMMETRIC SILICON

Sir:

Since the removal of the barrier to synthesis of optically active organosilicon compounds having reactive groups bonded to asymmetric silicon, and the discovery of many stereospecific reactions at silicon,[1,2,3] one of the major remaining tasks has been stereochemical correlation of configuration for a few key compounds containing the α-naphthylphenylmethylsilyl group (α-NpPhMeSi-, designated R₃Si*-below), in order that the stereochemistry of many reactions of these compounds might become known.

One of the most widely used methods for correlating configurations of optically active compounds having *similar* structures is the Fredga method based on *differences* in phase behavior.[4] This method as applied by K. Mislow has provided many fruitful results in recent years, and the pertinent case observed in the present work is his "case 2"[5] in which pure optical isomers of two dif-

(1) L. H. Sommer and C. L. Frye, *J. Am. Chem. Soc.*, **81**, 1013 (1959).
(2) L. H. Sommer and C. L. Frye, *ibid.*, **82**, 3796 (1960).
(3) L. H. Sommer and C. L. Frye, *ibid.*, **82**, 4118 (1960).
(4) See A. Fredga in "The Svedberg," Almqvist and Wikesells, Uppsala, 1944, p. 261, and J. Timmermans, *J. chim. phys.*, **49**, 162 (1952). Conclusions drawn on the basis of a *difference* in phase behavior without exception have proved accurate.
(5) K. Mislow and M. Heffler, *J. Am. Chem. Soc.*, **74**, 3668 (1952). For a recent application of "case 2" for determination of the configurational relationships between the pure enantiomers of 3-thioloctanedioic acid and 3-methyloctanedioic acid see K. Mislow and W. C. Meluch, *ibid.*, **78**, 5920 (1956). For other examples see J. Timmermans, ref. 4.