undergo thermal fragmentation. Di-*t*-butylamine[5] hydrochloride on melting gave isobutylene and *t*-butylamine hydrochloride. 1,1-Dimethylallylamine hydrochloride[6] heated at 260° decomposed to give isoprene and ammonium chloride.

Important degradation products are obtained by pyrolysis under reduced pressure of certain alkaloid hydrochlorides[7] and we wish to point out that this method might be useful for obtaining degradative compounds from other natural products. Preliminary findings indicate that pyrolysis of N-*t*-butyl-N-methyl tertiary amine hydrochlorides to N-methyl secondary amine salts can be synthetically useful.

Acknowledgment.—The physical data were supplied by H. E. Boaz, D. O. Woolf, Jr. (infrared), and R. R. Pfeiffer and Ann Van Camp (X-ray). W. Hargrove prepared di-*t*-butylamine hydrochloride.

(5) F. Klages and H. Setz, *Ber.*, **92**, 2606 (1959).
(6) Prepared according to the general method of G. F. Hennion and E. G. Teach, *J. Am. Chem. Soc.*, **75**, 4297 (1953).
(7) M. Gorman, N. Neuss, and K. Biemann, *ibid.*, **84**, 1058 (1962).

Communications TO THE EDITOR

Observations on the Acetylation of Carbohydrates in Aqueous Solution

Sir:

In an attempt to prepare disaccharides containing D-glucose linked through the C-2 hydroxyl group, we considered the use of 1,3,4,6-tetra-*O*-acetyl-α-D-glucose. The preparation of this acetate by acetylation of D-glucose in aqueous solution has been described recently.[1,2]

In our hands, several acetylations of glucose by this method all gave a crystalline product in 60–70% yield which had physical constants in good agreement with those reported by Prey and Aszalos[1] (m.p. 98°, $[\alpha]_D$ +63°) although the specific rotation of our product as well as that of the above authors was very different from the value of +145° previously reported.[3]

Acetyl determination[4] indicated that the product contained five acetyl groups per glucose unit, and no hydroxyl absorption could be detected in the infrared. Gas-liquid partition chromatography[5] showed that the product was a mixture of the α- and β-anomers of penta-*O*-acetyl-D-glucopyranose. No other compound was detected. The two anomers are difficult to separate by fractional crystallization but a synthetic mixture, prepared in the ratio indicated by the optical rotation, had the same melting point and infrared absorption spectrum.

We would also like to point out that the physical constants reported[1] for "sorbital pentaacetate" and "mannitol pentaacetate" are in excellent agreement with those of the corresponding hexaacetates; and when we applied the acetylation method to mannitol, the crystalline product contained no free hydroxyl group and did not depress the melting point of mannitol hexaacetate.

PIONEERING RESEARCH DIVISION
QUARTERMASTER RESEARCH & ENGINEERING CENTER
U.S. ARMY
NATICK, MASSACHUSETTS

D. H. BALL
F. PARRISH[6]

RECEIVED JULY 11, 1962

(1) V. Prey and A. Aszalos, *Monatsh. Chem.*, **91**, 729 (1960).
(2) A. Aszalos and V. Prey, *Die Stärke*, **14**, 50 (1962).
(3) R. U. Lemieux and G. Huber, *Can. J. Chem.*, **31**, 1040 (1953).
(4) S. Hestrin, *J. Biol. Chem.*, **180**, 249 (1949).
(5) We would like to thank Dr. M. B. Perry of Queen's University, Kingston, Ont., Can., for the gas chromatographic analysis.
(6) Present address: Corn Products Co., Technical Division, P. O. Box 345, Argo, Ill.

A New Synthesis of Diarylphosphinous Chlorides[1]

Sir:

In spite of the current interest in organophosphorus chemistry, the diarylphosphinous chlorides, Ar_2PCl, remain rather inaccessible and therefore little explored,[2] even though they serve as valuable precursors of other phosphorus compounds. We have devised for these chlorides a new synthesis which appears to have considerable versatility and the potential of making these compounds more readily available.

The reaction of aryldiazonium fluoroborates with arylphosphonous dichlorides is known to give a type of intermediate which may be hydrolyzed to diarylphosphinic acids.[3]

$$ArN_2BF_4 + Ar'PCl_2 \longrightarrow [ArAr'PCl_2{}^+BF_4{}^-] \xrightarrow{H_2O} ArAr'P(O)OH$$

(1) Supported by Research Grant CY-5507 from the National Cancer Institute, Public Health Service.
(2) G. M. Kosolapoff, "Organophosphorus Compounds," John Wiley & Sons, Inc., New York, N. Y., 1950, Chap. 3.
(3) L. D. Freedman and G. O. Doak, *J. Am. Chem. Soc.*, **74**, 2884 (1952).

The structure of the intermediate has not been established, but formulation as a type of phosphorane, shown above, appears reasonable.[4] We now have found that the intermediate, in keeping with chlorophosphorane character, may be reduced with aluminum, forming the diarylphosphinous chlorides in moderate yield. We have previously employed a similar reduction in a synthesis of arylphosphonous dichlorides, which involved reaction of magnesium with aryldiazonium fluoroborate–phosphorus trichloride reaction products.[5]

The synthesis of (*p*-cyanophenyl)phenylphosphinous chloride is illustrative. A slurry of 0.332 mole of *p*-cyanophenyldiazonium fluoroborate and 2.4 g. of cuprous bromide catalyst in 300 ml. of isopropyl acetate was treated with 0.332 mole of phenylphosphonous dichloride. A vigorous reaction occurred after about 20 min. When the reaction was complete, 0.296 mole of granular aluminum was added, and the mixture was stirred at 40° for 2 hr. The liquid was decanted from residual aluminum and treated with 51 g. of phosphorus oxychloride to break any complex aluminum salt. The mixture was distilled; a forerun was removed and (*p*-cyanophenyl)phenylphosphinous chloride (0.157 mole, 47% yield) was collected over the range 158° at 0.7 mm. to 195° at 3.1 mm. There remained a large solid residue; some decomposition occurred toward the end of the distillation, making pressure control difficult. On redistillation, b.p. 162° at 0.20 mm. was observed. *Anal.* Calcd. for $C_{13}H_9ClNP$: C, 63.56; H, 3.69; Cl, 14.43; P, 12.61. Found: C, 63.21; H, 3.51; Cl, 14.25; P, 12.77. (*p* - Carboxyphenyl)phenylphosphinic acid, m.p. 258–260°, was obtained by hydrolysis and alkaline potassium permanganate oxidation. *Anal.* Calcd. for $C_{13}H_{11}O_4P$: C, 59.55; H, 4.23; P, 11.81; neut. equiv. 131.1. Found: C, 59.75; H, 4.35; P, 11.86; neut. equiv. 132.1.

In a similar manner was obtained (*p*-chlorophenyl)phenylphosphinous chloride from *p*-chlorophenyldiazonium fluoroborate and phenylphosphonous dichloride; 34% yield, b.p. 134° at 0.80 mm. *Anal.* Calcd. for $C_{12}H_9Cl_2P$: C, 56.50; H, 3.56; P, 12.14. Found: C, 56.15; H, 3.84; P, 12.11. (*p*-Chlorophenyl)phenylphosphinic acid, m.p. 158.5–159.5°, was formed on hydrolysis and oxidation. *Anal.* Calcd. for $C_{12}H_{10}ClO_2P$: P, 12.26; neut. equiv., 252.6. Found: P, 12.19; neut. equiv., 252.2.

To avoid distillation of product from the large amount of nonvolatile material, a preliminary extraction was found to be effective. The residual viscous liquid remaining from solvent-stripping of the reduction mixture was continuously extracted with cyclohexane for several hours. The extract left little residue on distillation. This procedure was employed in the isolation of phenyl(*m*-trifluoromethylphenyl)phosphinous chloride (from *m*-trifluoromethylphenyldiazonium fluoroborate); 27% yield, b.p. 95° at 0.30 mm. (*Anal.* Calcd. for $C_{13}H_9ClF_3P$: C, 54.09; H, 3.14; P, 10.73. Found: C, 54.05; H, 3.51; P, 10.77) and of (*p*-bromophenyl)phenylphosphinous chloride[6] (from *p*-bromophenyldiazonium fluoroborate); 35.4% yield,[7] b.p. 127° at 0.19 mm. (*Anal.* Calcd. for $C_{12}H_9BrClP$: P, 10.34. Found: P, 10.40). Hydrolysis and oxidation gave, respectively, phenyl(*m*-trifluoromethylphenyl)phosphinic acid, isolated as the *p*-toluidine salt, m.p. 174° (*Anal.* Calcd. for $C_{20}H_{19}F_3NO_2P$: C, 61.07; H, 4.87; P, 7.87. Found: C, 61.13; H, 4.95; P, 8.05) and (*p*-bromophenyl)-phenylphosphinic acid, m.p. 173.5–174.5°.[6]

Further work is in progress to define the scope of the new synthesis.

DEPARTMENT OF CHEMISTRY
DUKE UNIVERSITY
DURHAM, NORTH CAROLINA

LOUIS D. QUIN
RONALD E. MONTGOMERY

RECEIVED AUGUST 6, 1962

(4) P. C. Crofts, *Quart. Rev.* (London), **12**, 341 (1958).

(5) L. D. Quin and J. S. Humphrey, Jr., *J. Am. Chem. Soc.*, **82**, 3795 (1960); **83**, 4124 (1961). In a somewhat related reaction, E. P. Komkov, K. U. Karavanov, and S. Z. Even, *Zh. Obshch. Khim.*, **28**, 2963 (1958), have reduced with metals compounds of the type $R_3PCl_2^+$-$AlCl_4^-$ to produce dialkylphosphinous chlorides.

(6) Previously prepared [by W. C. Davies and F. G. Mann, *J. Chem. Soc.*, 276 (1944)] from *p*-bromophenylphosphonous dichloride and diphenylmercury, b.p. 203–204° at 11 mm. The corresponding phosphinic acid had m.p. 174.5°.

(7) Based on phenylphosphonous dichloride consumed; a small amount of this compound was recovered in the distillation.

A New Skeletal Rearrangement of 14-Bromocodeine

Sir:

Conroy[1] reported that the reduction of 14-bromocodeinone (I) with sodium borohydride first afforded 14-bromocodeine (II), which could be further reduced to neopine (III) with the same reagent.

We wish to report a new rearrangement of the morphine skeleton during the reduction of II with sodium borohydride. As described by Conroy,[1] I was reduced with this reagent at 0° and then further treated at 40° without isolation of II. Three products, A (IV), B (V), and C (III), were isolated by chromatography on a silica gel column in 30, 10, and 50% yield, respectively. A was eluted first [m.p. 129–131°, $[\alpha]^{20}D$ +23.7° ($CHCl_3$); C, 72.51; H, 7.10; N, 4.77]; A·HCl, m.p. 249–254°; A·HBr, m.p. 262–266°. Secondly B was eluted [m.p. 155–157°, $[\alpha]^{20}D$ −7.5° ($CHCl_3$); C, 72.01; H, 7.00; N, 4.68]. The analyses of A and B corresponded to that of codeine (VI), but both differed from any known isomer of codeine. Lastly C was eluted; it gave a hydrobromide [m.p. 282–283°, $[\alpha]^{20}D$ +17.0° (H_2O)], which was

(1) H. Conroy, *J. Am. Chem. Soc.*, **77**, 5960 (1955).

identical[2] with the hydrobromide of neopine (III). These three products were also obtained by sodium borohydride reduction of II.

A was oxidized with silver carbonate[3] to the corresponding α,β-unsaturated ketone VII (m.p. 125–126°, $\nu^{C=O}_{CHCl_3}$ 1700; C, 72.61; H, 6.49; N, 4.71) and catalytically reduced to the dihydro compound VIII; VIII·HCl (m.p. 257–259°; C, 63.95; H, 7.18; N, 4.28). Oppenauer oxidation of VIII afforded the dihydro ketone IX, $\nu^{C=O}_{CHCl_3}$ 1738. The oxide ring of IX was opened by refluxing in ethanol with zinc dust and ammonium chloride.[4] The ketophenol X thus obtained [m.p. 196–198°, $\nu^{OH}_{CHCl_3}$ 3580 and $\nu^{C=O}_{CHCl_3}$ 1709, $[\alpha]^{20}D$ +18° (C_2H_5OH); C, 71.90; H, 7.87; N, 4.65] differed from *trans*-dihydrothebainone.[5] Hofmann degradation of the methiodide XI of A, m.p. 236–238°, gave a methine base. This was converted into a benzoate, m.p. 154–155°, which was shown to be identical[2] with the benzoate of β-codeimethine (XII)[6] prepared from neopine (III). These results suggest that the ethanamine chain is not attached to C-9 in A. The n.m.r. spectrum of VII shows two doublets (8H: τ = 3.17, $J_{7,8}$ = 10.1 c.p.s.; 7H: τ = 3.98, $J_{7,8}$ = 10.1 c.p.s.).[7] The spectrum of acetylated A (XIII),[8] $\nu^{C=O}_{CHCl_3}$ 1740, exhibited acetoxy CH_3 absorption at a rather high field, τ = 8.51. These data indicate that (1) there is no hydrogen at C-14 in VII and the ethanamine chain is linked to this position and (2) the conformation of ring C in XIII is half-chair and the orientation of 6-acetoxy group is α.[9] Consequently the structure of A was shown to be IV.[10]

B was catalytically reduced to a dihydro compound [m.p. 200°, $[\alpha]^{20}D$ −134.1° ($CHCl_3$)], which was identical[2] with dihydroisocodeine (XIV).[11] Thus B was proved to be the 6β-OH isomer V of neopine and was named isoneopine.

(2) In the identification of the hydrobromide of neopine (III), the benzoate of β-codeimethine (XII) and dihydroisocodeine (XIV), the infrared spectra were identical in each case with those of the authentic samples and mixed melting points were undepressed.

(3) H. Rapoport and H. N. Reist, *J. Am. Chem. Soc.*, **77**, 490 (1955).

(4) C. Schöpf and T. Pfeifer, *Ann.*, **483**, 157 (1930).

(5) L. Small and G. L. Browning, *J. Org. Chem.*, **3**, 618 (1939); M. Gates and G. Tschudi, *J. Am. Chem. Soc.*, **78**, 1380 (1956). Therefore A is not an isomer of codeine in which the B-C ring juncture is *trans*.

(6) C. F. Van Duin, R. Robinson, and J. C. Smith, *J. Chem. Soc.*, 903 (1926).

(7) The n.m.r. spectrum of codeinone showed two quartets (8H: τ = 3.31, 7H: τ = 3.94).

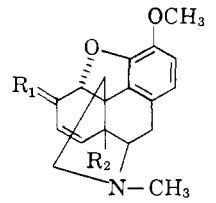
(8) Although this acetate was noncrystalline, the sample used for n.m.r. was shown to be sufficiently pure by p.p.c.

(9) Under these conditions, the methyl group of 6-acetoxy in XIII may be located above the center of ring A and more shielded.

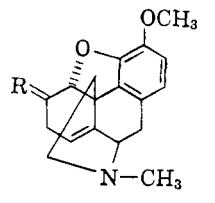
(10) We propose indolinocodeine as the name of A (IV) since this compound contains the hydroindoline skeleton.

(11) M. M. Baizer, A. Loter, K. S. Ellner, and D. R. Satriana, *J. Org. Chem.*, **16**, 543 (1951); D. Elad and D. Ginsburg, *J. Am. Chem. Soc.* **78**, 3691 (1956).

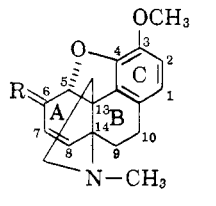
In the course of the reductive reaction, the cation XV is probably involved and the formation of IV occurs by C—N bond migration. Isoneopine (V) and some of neopine (III) might be formed by the reduction of neopinone (XVI).[12]



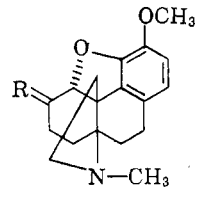
I. R_1 = O, R_2 = Br
II. R_1 = α-OH, R_2 = Br
VI. R_1 = α-OH, R_2 = H



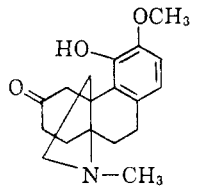
III. R = α-OH
V. R = β-OH
XVI. R = O



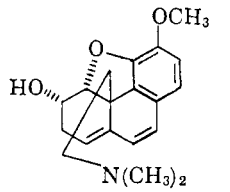
IV. R = α-OH
VII. R = O
XI. R = α-OH methiodide
XIII. R = α-acetoxy



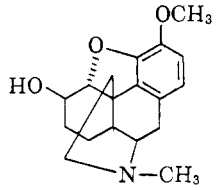
VIII. R = α-OH
IX. R = O



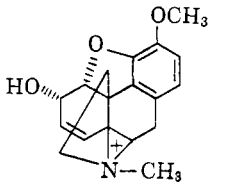
X



XII



XIV



XV

Acknowledgment.—The authors are indebted to Mr. Y. Kawazoe, Faculty of Pharmaceutical Science, The University of Tokyo, for the measurement of n.m.r. spectra and his kind discussion.

INSTITUTE OF APPLIED MICROBIOLOGY SHIGENOBU OKUDA
THE UNIVERSITY OF TOKYO KYOSUKE TSUDA
BUNKYO-KU, TOKYO, JAPAN

SANKYO CO. LTD. SADAO YAMAGUCHI
SHINAGA-KU, TOKYO

AUGUST 7, 1962

(12) Conroy reported[1] that neopinone (XVI) gave only neopine (III) by sodium borohydride reduction. However, we have found that this reduction gave both neopine (III) and isoneopine (V).