Hill.[7] The ozonide was reduced with zinc dust and acetic acid, and the acetaldehyde formed was collected in a solution[8] of 2,4-dinitrophenylhydrazine. The phenylhydrazone weighed 2.5 g. (22%) and gave m.p. 164–166°. Admixture with authentic acetaldehyde 2,4-dinitrophenylhydrazone of m.p. 165–166° showed no depression in melting point. The recorded[9] value for this derivative is 168°. The residual material resulting from the decomposition of the ozonide was purified in the previously described[7] manner and 3.4 g. (54%) of 2-ethylcyclohexanone, $n^{20}D$ 1.4555, was obtained, the 2,4-dinitrophenylhydrazone of which gave a melting point of 133–134°.

Anal. Calcd. for $C_{14}H_{18}O_4N_4$: C, 54.89; H, 5.92; N, 18.29. Found: C, 55.21; H, 5.68; N, 18.60.

Since the melting point of the 2,4-dinitrophenylhydrazone differed from that reported in the literature[10] (166°) this derivative was prepared from authentic 2-ethylcyclohexanone, derived from 2-chlorocyclohexanone, and this phenylhydrazone also gave a melting point of 133–134°. A mixed melting point with the derivative prepared from the ozonolysis product was unchanged. It would appear that 2-ethylcyclohexanone 2,4-dinitrophenylhydrazone exists in two forms.

The isolation of acetaldehyde and 2-ethylcyclohexanone, in fair yield, from the dehydration product of 1,2-diethylcyclohexanol of $n^{20}D$ 1.4665 indicates the structure of the olefin to be 1-ethyl-2-ethylidenecyclohexane rather than one of the expected cyclohexenes.

(7) A. L. Henne and P. Hill, THIS JOURNAL, **65**, 752 (1943).

(8) R. L. Shriner and R. C. Fuson, "Identification of Organic Compounds," Third Edition, John Wiley and Sons, Inc., New York, N. Y., 1948, p. 171.

(9) Reference 8, p. 229.

(10) F. E. King, J. A. Barltrop and R. J. Walley, *J. Chem. Soc.*, 277 (1945).

RESEARCH LABORATORIES
BLOCKSON CHEMICAL COMPANY
JOLIET, ILLINOIS

The Isolation of Reserpine from *Rauwolfia canescens* Linn

BY M. W. KLOHS, M. D. DRAPER, F. KELLER AND F. J. PETRACEK

RECEIVED DECEMBER 18, 1953

The isolation of reserpine[1] from *Rauwolfia serpentina* Benth and the subsequent report of its sedative and hypotensive activity[2] has created widespread interest in this compound. In a search for other possible plant sources[3] of this alkaloid we have recently isolated reserpine, by the method previously employed in our investigation of *Rauwolfia serpentina*,[4,5] from the "oleoresin fraction" of *Rauwolfia canescens* Linn.

An earlier investigation of the alkaloidal fraction of *Rauwolfia canescens* by A. Chatterjee yielded one crystalline alkaloid, rauwolscine,[6] to which the hypotensive activity of the crude drug has been ascribed.[7] It now appears that there are at least two hypotensively active alkaloids present in this species.

(1) J. M. Müller, E. Schlittler and H. J. Bein, *Experientia*, **8**, 338 (1952).

(2) H. J. Bein, *ibid.*, **9**, 107 (1953).

(3) The isolation of reserpine from *Rauwolfia heterophylla* Roem. and Schult. has been reported in a recent communication by Carl Djerassi, Marvin Gorman, A. L. Naussbaum and J. Reynoso, THIS JOURNAL, **75**, 5446 (1953).

(4) M. W. Klohs, M. D. Draper, F. Keller and F. J. Petracek, *ibid.*, **75**, 4867 (1953).

(5) M. W. Klohs, M. D. Draper, F. Keller, W. Malesh and F. J. Petracek, *ibid.*, **76**, 1332 (1954).

(6) A. Chatterjee (née Mookerjee), *J. Indian Chem. Soc.*, **18**, 33 (1941).

(7) J. N. Mukherjee, *Science and Culture*, **18**, 338 (1953).

Experimental

The Isolation of Reserpine from the "Oleoresin Fraction."—The "oleoresin fraction" from the ground dried roots of *Rauwolfia canescens*[8] was obtained in the same manner as previously described for fraction I in our investigation of *Rauwolfia serpentina*.[5] Ten grams of this fraction was dissolved as much as possible in 2% methanol–chloroform (50 ml.). The solution was filtered and the filtrate was applied to a chromatographic column (5.5 × 25 cm.) containing silicic acid–celite 3:1. The column was developed with the same solvent system until the most rapid moving band had reached the bottom of the column. The adsorbent was then extruded and examined under ultraviolet light and with the aid of spot tests using Fröhdes reagent. A colorless zone in the lower section of the column, which exhibited blue fluorescence and the characteristic Fröhdes color reaction (yellow → yellow-green → light blue) for reserpine, was removed by sectioning and washed thoroughly with methanol (150 ml.). The methanol was concentrated *in vacuo* to approximately 10 ml. On the addition of several drops of ammonium hydroxide reserpine separated as flat needles (150 mg.). The material was recrystallized several times from methanol by dissolving in an excess and concentrating on the steam-bath; m.p. 254° dec., $[\alpha]^{24}D$ −121.8° (*c* 1.03 in $CHCl_3$). A mixed melting point with an authentic sample gave no depression. The infrared and ultraviolet absorption spectra were identical. For analysis the sample was dried to constant weight at 110° (2 mm.).

Anal. Calcd. for $C_{33}H_{40}O_9N_2$[9]: C, 65.11; H, 6.62; mol. wt., 608.67. Found: C, 65.13; H, 6.70; mol. wt., 611,[12] 614.[13]

(8) The plant material in this investigation was kindly identified by Dr. H. W. Youngken, Mass. College of Pharmacy, Boston, Mass.

(9) The empirical formula $C_{33}H_{44}O_{10}N_2$ originally proposed by us for reserpine has now been revised to $C_{33}H_{40}O_9N_2$ which is in agreement with that suggested by other investigators.[3,10,11] Although the elementary analyses of reserpine and its derivatives reported by us fit both empirical formulas the results of more accurate equivalent weight determinations were incompatible with the original formula. The empirical formula for reserpinolic acid has likewise been changed to $C_{22}H_{28}O_4N_2$.

(10) A. Furlenmier, R. Lucas, H. B. MacPhillamy, J. M. Müller and E. Schlittler, *Experientia*, **9**, 331 (1953).

(11) N. Neuss, H. E. Boaz and J. W. Forbes, THIS JOURNAL, **75**, 4870 (1953).

(12) Potentiometric titration in glacial acetic acid with 0.01 *N* perchloric acid in dioxane.

(13) Potentiometric titration in 75% dimethylformamide-water with 0.01 *N* HCl.

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1,1,1-Trichloro-2-methylpropyl-2-phosphoric Acid from 1,1,1-Trichloro-2-methyl-2-propanol

BY DONALD G. KUNDIGER AND THEODORE J. COLLIER

RECEIVED NOVEMBER 6, 1953

We have found that 1,1,1-trichloro-2-methyl-2-propanol (I) is converted to the intermediate $Cl_3C–C(CH_3)_2–O–PBr_4$ (III) by the action of phosphorus pentabromide upon I under anhydrous conditions. III can be hydrolyzed to 1,1,1-trichloro-2-methylpropyl-2-phosphoric acid (IV),[1] which can be obtained in 26% yield from (I).

The structure of IV was established by ultimate analyses, by neutralization equivalent and by cleavage with aqueous potassium hydroxide to potassium phosphate and the known cleavage products, *viz.*, carbon monoxide and acetone,[2] of I.

(1) *Cf.* the report by C. Willgerodt and F. Durr, *Ber.*, **20**, 539 (1887), wherein only replacement of the hydroxyl in I to give 1,1,1-trichloro-2-methyl-2-bromopropane (II) was indicated as the product of the reaction of phosphorus pentabromide upon I; no other product was indicated. This is the only previous report of this reaction.

(2) Bressanin and Segre, *Gass. chim. ital.*, **41**, [I] 673 (1911).

The unusually high strength of the carbon-to-oxygen bond in trichloromethylpropanol is demonstrated by our isolation of 26% of $Cl_3C-C(CH_3)_2O-P(=O)(OH)_2$.[3,4] The unusual volatility of 1,1-1-trichloro-2-methyl-2-bromopropane prevented its isolation in more than 5% conversion from I.

Experimental Part

1,1,1-Trichloro-2-methylpropyl-2-phosphoric Acid (IV).—Preparation of IV is attended by extreme lachrymatory effects. All operations should be carried out in a hood, and with a gas mask and rubber gloves.

Freshly prepared phosphorus pentabromide (295 g., 0.685 mole) and 121.8 g. (0.685 mole) of purified anhydrous 1,1,1-trichloro-2-methyl-2-propanol (I) were mixed in a flask bearing a drying tube, and heated at 100° for 8 hours. The anhydrous reaction mixture and became dark amber in color and was cooled and allowed to stand at 25–30° for two weeks; then it was hydrolyzed slowly at 30–35° (2 to 4 hours) by taking it up with ether and with mechanical stirring, adding dropwise 100 ml. of distilled water. While the hydrolyzed mixture was allowed to stand at room temp., a crystalline mass formed which was collected after six days, and washed repeatedly with 10-ml. portions of carbon tetrachloride until the washes gave no residue on evaporation. The remaining crystals were dried under 20 mm. pressure, wt. 45.8 g. (26%) of IV, m.p. 159–163°, which analyzed for 11.3% phosphorus (calcd. 12.0%). The yield of pure IV, after recrystallization from water, was 30.4 g. (17%), m.p. 181–182.5°.

Three recrystallizations of IV from water gave analytically pure IV, m.p. 184.5–185.5°, the m.p. of which did not change upon a fourth recrystallization. IV is slightly soluble in cold water, moderately soluble in boiling water, and insoluble in carbon tetrachloride. It is acid to congo red and liberates carbon dioxide from bicarbonate solutions.

Anal. Calcd. for $C_4H_8Cl_3O_4P$: Cl, 41.3; P, 12.0; neut. equiv., 257.5. Found: Cl, 41.7, 41.1; P, 12.0, 12.1, 12.2, 12.1, 12.2; neut. equiv., 259.5, 256.1, 261.8.

When this substance is cleaved by 60% aqueous potassium hydroxide at 25–40°, carbon monoxide (molybdenum blue test), phosphate ion (ammonium phosphomolybdate test) and acetone are produced. The last was identified after distillation of the diluted reaction mixture as its 2,4-dinitrophenylhydrazone, m.p. 127.5–128°, undepressed by an authentic sample, and by a positive iodoform test (m.p. 118.5–119.5°).

The combined carbon tetrachloride washes were concentrated and the residue was sublimed to give II, m.p. 160–169°, which after recrystallizing from ether was found to be analytically pure, m.p. 169–170° (sealed tube).

(3) This finding agrees with the observation reported by W. Gerrard and P. L. Wyvill in *Research* **2**, 536 (1949), that phosphorus trichloride does not interact with I under mild conditions in which *t*-butyl alcohol readily affords the chloride, and that much more rigorous treatment affords the chlorophosphites $ROPCl_2$, $(RO)_2PCl$, but still no chloride; also, that an unusually vigorous treatment with phosphorus pentachloride is required to convert I into the corresponding chloride, RCl. Gerrard and Wyvill did convert I into the chloride in apparently about 90% yield only by refluxing I with phosphorus pentachloride for several hours. No product other than the chloride was mentioned.

(4) No method has yet been described, until the present, for converting the hydroxyl of I to a derivative of phosphoric acid.

DEPARTMENT OF CHEMISTRY
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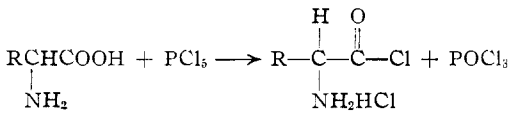
Synthesis of Glycyl and Alanyl Chlorides[1]

BY SUMNER LEVINE

RECEIVED OCTOBER 15, 1953

Fischer[2] has reported a fairly general method for the synthesis of amino acid chlorides. However, this method suffers from the disadvantage of requiring a preliminary recrystallization of the amino acids and in addition, the reaction is conducted in acetyl chloride as the solvent. Because of these disadvantages and the relatively low yield obtained by Fischer's procedure, a modified method was developed. The synthesis was conducted as a heterogeneous reaction in the more convenient solvent carbon tetrachloride, in which the phosphorus pentachloride is dissolved. Since carbon tetrachloride is hydrophobic and less volatile than acetyl chloride, the product is less sensitive to atmospheric moisture during the filtration operation. In addition, the yield obtained by the present method is considerably higher than that of the earlier procedure. The reaction proceeds smoothly according to the equation



Because of the salt formation at the amino nitrogen further condensation of the product to polypeptides does not occur under these conditions. In addition, since hydrochloric acid generated during the course of the reaction is bound, very little, if any, pressure build-up was noticed.

Experimental Part

Glycyl Chloride Hydrochloride.—The reaction was conducted in a glass-stoppered vessel. Five grams of glycine was suspended in 200 ml. of purified carbon tetrachloride.[3] Fifteen grams of phosphorus pentachloride was added and the tightly (wired) stoppered vessel shaken vigorously for ten hours at room temperature. The product was filtered on a long necked sintered glass filter. During the filtration, the top of the sintered glass filter was protected with a stopper containing a drierite filled tube. The product was washed three times with carbon tetrachloride and then three times with anhydrous petroleum ether. After a final washing with anhydrous ether, the product was dried on the filter; yield 90 to 95%. The product was recrystallized from redistilled acetyl chloride; yield 75 to 80%.

Anal. Calcd. for $C_2H_5ONCl_2$: C, 18.48; H, 3.88; N, 10.78; Cl, 54.56. Found: C, 18.50; H, 3.85; N, 10.75; Cl, 54.53.

Alanyl Chloride Hydrochloride.—This compound was prepared by the same method given above; yield 92%.

Anal. Calcd. for $C_3H_7NOCl_2$: C, 25.02; H, 4.90; N, 9.73; Cl, 49.24. Found: C, 25.05; H, 4.85, N, 9.75; Cl, 49.28.

(3) L. F. Fieser, "Experiments in Organic Chemistry," D. C. Heath and Co., Inc., New York, N. Y., 1941.

DEPARTMENT OF BIOCHEMISTRY
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Oxymercuration of *trans*-1,2-Diphenyl-1-propene

BY ALAN RODGMAN AND GEORGE F WRIGHT

RECEIVED NOVEMBER 25, 1953

Studies in progress in this Laboratory show that a previous report of a single product from oxymercuration of 1-phenyl-1-propene is erroneous.[1] Since oxymercurations of related compounds such as styrene and 1-phenyl-2-methyl-1-propene give

(1) This work was supported by an institutional grant from the Damon Runyon Memorial Fund for Cancer Research.

(2) E. Fischer, *Ber.*, **38**, 2914 (1905).

(1) G. F Wright, THIS JOURNAL, **57**, 1993 (1935).