treated silicon tetrachloride with sodium *t*-butoxide under various conditions was tri-*t*-butoxychlorosilane.

While other investigators have been able to effect the attachment of a fourth *t*-butoxy group to silicon only after considerable effort, they have been able to synthesize, with comparative ease, several tri-*t*-butoxyalkoxysilanes from the monochlorosilane and the sodium alkoxides of sterically less hindered alcohols. Thus, Backer and Klasens[7] have synthesized tetralkoxysilanes in which the fourth group is ethoxy or isopropoxy, and Breederveld and Waterman[1] have prepared similar compounds containing 1-ethylpropoxy and cyclohexyloxy groups.

The successful synthesis of tetra-*t*-butoxysilane reported herein depended upon the unique behavior exhibited by silicon tetrafluoride toward alcohols.[9] Contrary to the marked reactivity shown by other silicon halides, silicon tetrafluoride dissolves readily in all of the lower alcohols at room temperature with but slight evidence of reaction.[10,11] Unstable complexes of the type $SiF_4 \cdot 4ROH$[12] are evidently formed, which decompose when heated, liberating some silicon tetrafluoride.

The method of synthesis was similar to that used by Klippert[13] for the preparation of tetraethoxysilane, namely, the reaction of silicon tetrafluoride with a sodium alkoxide. In order to obtain a high yield of the fluorine-free product, it was found necessary to use a smaller excess of silicon tetrafluoride, and to reflux the reaction mixture for an extended period of time once the addition of the gaseous fluoride had been completed. Unless these conditions were employed, tri-*t*-butoxyfluorosilane became the major product of the reaction, although the total over-all yield of both products was lower. It is possible to account for the preponderance of the monofluorinated product under the less favorable conditions by assuming that the excess silicon tetrafluoride reacts with the tetra-*t*-butoxysilane present in the reaction mixture. A similar interaction is known to occur when tetraethoxysilane is treated with silicon tetrafluoride.[11]

The hydrolytic behavior of the monofluorinated material seemed interesting. The Si–F linkage was only partially hydrolyzed initially by 0.1 *N* sodium hydroxide, but when the alcoholic solution of the compound was allowed to stand overnight in the presence of excess dilute alkali, complete hydrolysis took place. It is likely that this effect can be accounted for, at least in part, by steric factors.

### Experimental

**Tetra-*t*-butoxysilane.**—Sodium *t*-butoxide was prepared from 57.5 g. (2.50 gram atoms) of sodium and 1.5 l. of *t*-butyl alcohol, freshly dried by distillation from sodium metal.[14] The mixture was stirred under reflux for 20 hours, then cooled slightly to just below reflux temperature. Silicon tetrafluoride (1.50 moles) was prepared by a modification of the procedure of Hyde and Domicone.[11] To a mixture of 178.0 g. (1.00 mole) of ammonium fluosilicate and 30.0 g. (0.50 mole) of powdered silica contained in a lead reactor was added 222.0 g. (2.14 moles, 120 ml.) of 95% sulfuric acid, dropwise over a period of 6 hours. The gas so generated was passed through a Dry Ice trap and then into the hot, stirred solution of sodium *t*-butoxide. After the addition had been completed, the reaction mixture was stirred under reflux for 112 hours, then tested with *p*H paper and found to be neutral. After filtering to remove solid inorganic fluorides, the mixture was distilled at atmospheric pressure to recover the excess *t*-butyl alcohol. The residue was fractionally distilled under reduced pressure. Five fractions were obtained, each of which was refractionated carefully to afford tetra-*t*-butoxysilane, b.p. 105–105.5° (15 mm.), m.p. 56.5–57° (uncor.), yield 103.2 g. (51.6%). The infrared spectrum showed a band at 9.37 $\mu$, characteristic of Si–O absorption. No Si–F absorption was noted.

*Anal.* Calcd. for $C_{16}H_{36}O_4Si$: C, 59.95; H, 11.32; Si, 8.75; mol. wt., 320.5. Found: C, 60.6; H, 11.7; Si, 8.76; mol. wt. (cryoscopic, in benzene), 330.4.

There also was obtained a small amount of impure tri-*t*-butoxyfluorosilane (see below), yield 9.0 g. (4.1%).

**Tri-*t*-butoxyfluorosilane.**—The same general procedure was used. Important variations involved the use of a larger excess of silicon tetrafluoride (0.75 mole for 1.00 mole of sodium *t*-butoxide) and the omission of the extended refluxing period following the addition of the silicon tetrafluoride. From the reaction mixture there was obtained tri-*t*-butoxyfluorosilane, b.p. 78.5–80.5° (15 mm.), $n^{25}_D$ 1.3831, $d^{25}_4$ 0.9054, yield 17.9 g. (20.2%). The infrared spectrum showed absorption bands at 9.25 and 11.35 $\mu$, characteristic of Si–O and Si–F absorption, respectively.

*Anal.* Calcd. for $C_{12}H_{27}FO_3Si$: C, 54.10; Si, 10.53; F, 7.13; mol. wt., 266.4; $MR_D$, 68.51.[15] Found: C, 53.0; Si, 10.62; F, 7.00; mol. wt. (cryoscopic, in benzene), 272.3; $MR_D$, 68.66.

A lesser amount of impure tetra-*t*-butoxysilane was isolated also, yield 10.7 g. (13.4%).

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[9] W. Knop, *J. prakt. Chem.*, [1] **74**, 41 (1858).

[10] G. Tarbutton, E. P. Egan, Jr., and S. G. Frary, THIS JOURNAL, **61**, 2555 (1939).

[11] J. F. Hyde and J. J. Domicone, unpublished data.

[12] A. V. Topchiev and N. F. Bogomolova, *Doklady Akad. Nauk S.S.S.R.*, **88**, 487 (1953).

[13] L. Klippert, *Ber.*, **8**, 713 (1875).

[14] W. S. Johnson and G. H. Daub, in "Organic Reactions," Vol. 6, John Wiley and Sons, Inc., New York, N. Y., 1951, p. 44.

[15] Calculated from bond refractivities listed in the following references: K. G. Denbigh, *Trans. Faraday Soc.*, **36**, 936 (1940), and A. I. Vogel, W. T. Cresswell and J. Leicester, *J. Phys. Chem.*, **58**, 174 (1954).

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## Regeneration of Sugars from Anilides and Sugar Acids from Phenylhydrazides[1]

BY G. W. HUFFMAN AND F. SMITH

RECEIVED JANUARY 6, 1955

The anilides of sugars and the phenylhydrazides of sugar acids have long been used for purposes of characterization and purification and not infrequently it becomes necessary to recover the parent sugar or sugar acid from these derivatives. Usually the recovery entails cleavage of the anilide or phenylhydrazide with dilute mineral acid followed by neutralization of the mineral acid, extraction of the base and finally isolation of the sugar or sugar acid.

It has been shown previously that acids acting in solution as catalysts for acetal formation can be replaced satisfactorily by insoluble acids in the form of cation exchange resins.[2-4]

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[1] Paper No. 3298, Scientific Journal Series, Minnesota Agricultural Experiment Station.

[2] J. E. Cadotte, F. Smith and D. Spriestersbach, THIS JOURNAL, **74**, 1501 (1952).

[3] F. Smith and D. Spriestersbach, *ibid.*, **76**, 4191 (1954).

[4] W. H. Wadman, *J. Chem. Soc.*, 3051 (1952).

We now have shown that these same insoluble cation exchange resins are effective in the liberation of sugars from sugars anilides and acids from their phenylhydrazides. The use of a cation exchange resin has certain advantages over mineral acid inasmuch as the reaction proceeds smoothly, it can be done on a micro-scale, the yield of product is essentially quantitative, and furthermore the base liberated in the reaction is absorbed completely by the resin thus facilitating the isolation of the desired sugar or sugar acid.

### Experimental

**Hydrolysis of Anilides.**—The general procedure was as follows: A suspension of the sugar anilide (0.05–0.1 g.) and the cation exchange resin (Amberlite IR 120)[5] (0.5 g.) in water (10 ml.) was refluxed until the anilide had gone into solution and the rotation became constant. This required from 20 minutes to one hour. The addition of 10 to 20% ethanol decreased the time required to solubilize the anilide. The resin was removed by filtration and the colorless solution concentrated *in vacuo* to a sirup which was crystallized if possible in the usual way. Some typical results are quoted in Table I.

TABLE I

| Anilide | Wt., mg. | Sugar regenerated Wt., mg. | Yield % | M.p., °C. | $[\alpha]_D^{H_2O}$ (equil.) | Ref. |
|---|---|---|---|---|---|---|
| 2,3,4,6-Tetra-*O*-methyl-D-glucose | 80 | 56.5 | 93 | 88 | + 83° | 6 |
| 2,3,4,6-Tetra-*O*-methyl-D-galactose | 100 | 41 | 54[a] | Liquid | +108 | 7, 8 |
| ,4-Di-*O*-methyl-D-galactose | 117 | 88.5 | 95 | 90–91 (hydrate) | + 82 | 9 |
| D-Galactose | 108 | 71.3 | 94 | 166 | + 77.5 | 10 |

[a] This was the yield of distilled product. Prior to distillation the yield was almost quantitative.

By the same procedure, the anilides of 2,3,4-tri-*O*-methyl-D-galactose, 2,4,6-tri-*O*-methyl-D-galactose, 2,3,4-tri-*O*-methyl-L-rhamnose and 2,4-di-*O*-methyl-D-arabinose have been converted into the parent methyl sugars.

**Hydrolysis of Sugar Acid Phenylhydrazides.**—The same reaction can be employed for the regeneration of sugar acids and their *O*-methyl derivatives from the corresponding phenylhydrazides. For example, 2,3,6-tri-*O*-methyl-D-mannonic acid was obtained readily from its phenylhydrazide and crystallized as the lactone,[11] m.p. 83–84°, $[\alpha]^{22}\text{D}$ +68° (water, *c* 1). The time for the hydrolysis of the phenylhydrazides is somewhat longer.

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(5) Product of Rohm and Haas Co., Philadelphia, Pa.

(6) T. Purdie and J. C. Irvine, *J. Chem. Soc.*, **85**, 1049 (1904).

(7) J. C. Irvine and A. Cameron, *ibid.*, **85**, 1071 (1904).

(8) W. N. Haworth and C. W. Long, *ibid.*, 544 (1927).

(9) F. Smith, *ibid.*, 1724 (1939).

(10) Polarimetry, Saccharimetry and the Sugars, p. 717, U. S. Govt. Print. Office, Circular C440, 1942.

(11) F. Smith, THIS JOURNAL, **70**, 3249 (1948).

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## Unsymmetrically N-Substituted Piperazines. VIII. Amide Derivatives[1]

BY WALTER S. IDE, EMIL LORZ AND RICHARD BALTZLY

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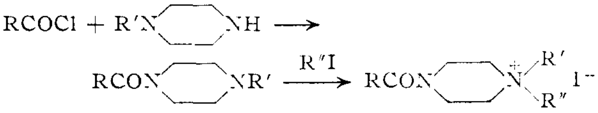
In a search for compounds having anti-acetylcholine activity, a number of quaternary salts derived from N-monoacylpiperazines were prepared. The general synthetic route was



Compound V was prepared by catalytic debenzylation of the benzyl tertiary amine IV. Compound XI was obtained from the base of V by refluxing with excess ethyl iodide in the presence of potassium carbonate.

In most cases the tertiary amines were isolated and characterized as the hydrochlorides. These salts showed little or no physiological activity and were not investigated intensively. The quaternary salts XV–XVIII showed appreciable atropine-like activity (20–200% of atropine when tested on isolated guinea pig ileum) and are being examined with a view to possible chemical trial.

### Experimental

Diphenylacetic acid and β,β-diphenylpropionic acid were obtained from commercial sources. 1-Phenylcyclohexanecarboxylic acid[2] (for compounds XII–XV), xanthene-9-carboxylic acid[3] and N-methylpiperazine[4] were prepared by literature methods. N-Ethylpiperazine was prepared by a modification of the Moore procedure.[5] Since this variation offers some practical conveniences it is given in detail.

**N-Ethylpiperazine.**—In a 3-l. flask was placed 159 g. (1 mole) of piperazine dihydrochloride (recovered from previous operations), 200 cc. of water and 84 g. (1 mole) of sodium bicarbonate. The solution was warmed until the carbon dioxide had been driven off and 1 l. of alcohol was added. To the stirred refluxing solution was added 156 g. (1 mole) of ethyl iodide[6] and 84 g. of solid sodium bicarbonate. The solution was allowed to reflux overnight. It then was cooled and 84 g. of sodium bicarbonate was stirred in while 100 cc. (113 g., 1.05 moles) of ethyl chlorocarbonate was added. After standing an hour the solution was acidified to congo paper with hydrochloric acid and the solvent was removed *in vacuo*. Water was added to dissolve the salts and dicarbethoxypiperazine (70.7 g., 31%) was removed by extraction with ether. To the aqueous layer was added cracked ice and 200 cc. of 40% potassium hydroxide solution. The bases were extracted with ether and dried over potassium carbonate. Fractional distillation afforded 10 g. (7%) of diethylpiperazine and 71 g. (38%) of N-ethyl-N′-carbethoxypiperazine[5] (b.p. 127–130° at 17 mm.).

The carbethoxyethyl piperazine was refluxed 30 hours with 120 cc. of water and 180 cc. of concd. hydrochloric acid and the solution was evaporated *in vacuo*. The residue was dissolved in methanol, neutralized with sodium methylate (from 9 g. of sodium) filtered from salt, and distilled at atmospheric pressure under a fractionating column. There was obtained 34 g. (30% from piperazine) of N-ethylpiperazine, boiling at 126–129°.

**N-(β,β-Diphenylpropionyl)-N′-benzylpiperazine** (IV).—Six grams of benzylpiperazine[7] was added to a solution of β,β-diphenylpropionyl chloride in 50 cc. of anhydrous ether. There was considerable evolution of heat and solid separated. The mixture was allowed to stand overnight and then filtered. The solid was washed with benzene and recrystallized from aqueous alcohol. It melted at 255° and at 236–240° when mixed with benzylpiperazine dihydrochloride.[7] The yield was 8.5 g. (63%).

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(1) The work here reported is part of a joint project with the Pharmacology Department of these laboratories.

(2) C. H. Tilford, M. G. Van Campen, Jr., and R. S. Shelton, THIS JOURNAL, **69**, 2902 (1947).

(3) W. S. Ide, E. Lorz and R. Baltzly, *ibid.*, **76**, 1122 (1954).

(4) L. P. Albro, R. Baltzly and A. P. Phillips, *J. Org. Chem.*, **14**, 771 (1949).

(5) T. S. Moore, M. Boyle and V. M. Thorn, *J. Chem. Soc.*, 39 (1929).

(6) Ethyl sulfate presumably could be substituted.

(7) R. Baltzly, J. S. Buck, E. Lorz and W. Schoen, THIS JOURNAL **66**, 263 (1944).