ganic layer with 20% alkali, and worked up by acidification, extraction with benzene, drying over sodium sulfate, and distillation. Neutral products were recovered following removal of the chlorobenzene by distillation. The results of the various experiments are summarized in Table I.

TABLE I

ACTION OF ALUMINUM BROMIDE ON α-PHENETHYL ARYL ETHERS

Aryl group	α^{25}D of the ether[a]	% yield of α-phenethylphenol	α^{25}D of the alkylphenol[a]
Phenyl	.....	22[b]	....
Phenyl	− 3.30	20[c]	0.30
2,6-Xylyl	.....	0[d]	....
p-Tolyl	−15.5[e]	41[f]	−6.10

[a] All rotations are for the homogeneous material, *l* = 1 dm. [b] The neutral material, b.p. 160–170° (2 mm.), from this run contained 73.2% C, 5.2% H and 17.0% Cl. The expected dichlorodiphenylethane was probably contaminated with monochlorodiphenylethane and some phenolic product which had been incompletely extracted. [c] Neutral product from this run was optically inactive. [d] 94% of the theoretical quantity of 2,6-xylenol was formed. Prepared from α-phenethyl chloride of rotation −51.5°. Using a value of 109° for optically pure α-phenethyl chloride (R. L. Burwell, A. D. Shields and H. Hart, THIS JOURNAL, **76**, 908 (1954)) and 17.1° for optically pure *o*-α-phenethyl-*p*-cresol,[3] one calculates 75.5% retention of optical purity over the two-step process (ether synthesis and rearrangement. [f] From a run with *dl*-material the product was identified *via* the corresponding aryloxyacetic acid, m.p. 165–166°, neut. equiv. 270. *Anal.* Calcd. for $C_{17}H_{18}O_3$: C, 75.6; H, 6.7. Found: C, 75.5; H, 6.9.

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2,4-Dichloro-1,3,5-triazine

BY I. HECHENBLEIKNER

RECEIVED DECEMBER 14, 1953

Since mixed "trimerization" of trichloroacetonitrile and acetonitriles in the presence of anhydrous hydrogen chloride resulted in good yields of 2,4-bistrichloromethyl-6-methyl-1,3,5-triazine,[1] the reaction was attempted with hydrogen cyanide and cyanogen chloride.

From a series of experiments carried out upon the reaction of hydrogen cyanide and cyanogen chloride, the following optimum conditions were found for the preparation of dichlorotriazine (see Experimental). The concurrent formation of monochlorotriazine was not established and in the light of Grundmann's experiments was not to be expected. However, cyanuric chloride was formed in small quantities. Dichlorotriazine is extremely reactive toward water and from preliminary observations it is believed that total rupture of the triazine ring occurs upon reacting with this solvent.

Experimental

Dichlorotriazine.—Three grams (0.082 mole) of dry hydrogen chloride was added to a mixture of 360 g. (6.0 moles) of cyanogen chloride and 81 g. (3.0 moles) hydrogen cyanide in a quart pop bottle. The bottle was capped and immersed in a 65° bath for 40 hours. The material in the bottle consisted of a clear liquid and an amorphous, brown solid. Distillation of the mixture from a 60° bath led to the recovery of 222 g. (3.6 moles) of cyanogen chloride and 64 g. (2.37 moles) of hydrogen cyanide. The residue from this distillation was leached with 250 ml. of benzene and filtered from a dark-brown residue of 45 g. of amorphous solid. Distillation of the filtrate gave 35 g. (0.233 mole), 37% yield, of (7.8% conversion based upon HCN) dichlorotriazine boiling at 80–90° (40 mm.); 20 g. (0.108 mole) of cyanuric chloride distilling at 70–80° (1 mm.), and nonvolatile residue of 5 g.

Anal. Calcd. for $C_3HN_3Cl_2$: C, 24.00; H, 0.67; N, 28.00; Cl, 47.34. Found: C, 24.82; H, 1.07; N, 25.6; Cl, 46.34.

Reaction of dichlorotriazine with excess aniline gave 2,4-bisphenylamino-1,3,5-triazine in 95% yield; m.p. 292–295°; mixture melting point with an authentic sample 292–294°. (2,4-Bisphenylamino-1,3,5-triazine was prepared from 1,5-diphenylbiguanide and methyl formate in the usual manner.[2])

Anal. Calcd. for $C_{15}H_{13}N_5$: C, 68.4; H, 4.92; N, 26.6. Found: C, 68.4; H, 5.06; N, 26.8.

Spectroscopic data upon dichlorotriazine will appear in a future issue of the *J. Chem. Phys.*

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[1] Grundmann, *et al.*, *Ann.*, **577**, 77 (1953).

[2] Rackman, *ibid.*, **367**, 163 (1910).

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STAMFORD, CONN.

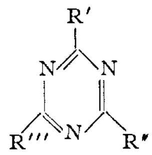
Basic Substituted Triazines

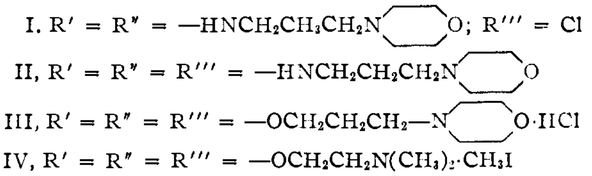
BY BRUCE W. HORROM

RECEIVED FEBRUARY 11, 1954

Many amino and alkoxy triazines have been made by the reaction of cyanuric chloride with amines and alcohols. Only two instances where trisubstituted products have been obtained from diamines appear to have been reported.[1,2]

The present paper reports the preparation of four new basic derivatives (I, II, III and IV) of cyanuric acid, three of which resulted from displacement of all three chlorine atoms of cyanuric chloride. In the fourth compound (I), one chlorine remained unreacted.





I. R′ = R″ = $—HNCH_2CH_3CH_2N\langle\ \rangle O$; R‴ = Cl

II, R′ = R″ = R‴ = $—HNCH_2CH_2CH_2N\langle\ \rangle O$

III, R′ = R″ = R‴ = $—OCH_2CH_2CH_2—N\langle\ \rangle O\cdot HCl$

IV, R′ = R″ = R‴ = $—OCH_2CH_2N(CH_3)_2\cdot CH_3I$

Experimental

2,4-Di-(γ-morpholinopropylamino)-6-chloro-*s*-triazine (I) and **2,4,6-Tri-(γ-morpholinopropylamino)-*s*-triazine** (II).—Cyanuric chloride (14.5 g., 0.079 mole) in 200 cc. of dry benzene was added dropwise with stirring to γ-morpholinopropylamine (43.2 g., 0.3 mole) and triethylamine (30.3 g., 0.3 mole) in 250 cc. of dry benzene. The temperature of the mixture was not allowed to rise above 35°. After the mixture was stirred at room temperature overnight it was refluxed for six hours and filtered warm. The benzene was removed by distillation, the semi-solid residue was triturated with ether and removed by filtration. The solid weighed 15 g. (47.5%), m.p. 148–151°. Three recrystallizations from methanol gave m.p. 154–155°.

Anal. Calcd. for $C_{17}H_{30}N_7ClO_2$ (I): C, 51.05; H, 7.56; N, 24.61; Cl, 8.86. Found: C, 51.16; H, 7.75; N, 24.95; Cl, 8.96.

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[1] H. S. Mosher and F. C. Whitmore, THIS JOURNAL, **67**, 662 (1945).

[2] W. O. Foye and A. E. Buckpitt, *J. Am. Pharm. Assoc.*, **41**, 385 (1952).

The ethereal filtrate from the trituration was concentrated and 18.5 g. (46%) of a thick yellow water-soluble oil was obtained. A sample was taken up in ether, decolorized with charcoal and taken to dryness under high vacuum.

Anal. Calcd. for $C_{24}H_{45}N_9O_3$ (II): C, 56.77; H, 8.93; N, 24.81. Found: C, 56.67; H, 8.96; N, 24.83.

2,4,6-Tri-(γ-morpholinopropyl) Cyanurate Trihydrochloride (III).—The procedure of Spielman, Close and Wilk[3] for non-basic cyanurates was modified for this preparation. Sodium hydride (2.52 g., 0.105 mole) was added to γ-morpholinopropanol (21.75 g., 0.15 mole) in 25 cc. of dry benzene and the mixture was refluxed overnight. To this stirred mixture, after cooling in ice, was added dropwise cyanuric chloride (6.072 g., 0.033 mole) dissolved in a minimum amount of dry benzene. The mixture was then refluxed for one hour, filtered and concentrated. The residual oil was submitted to distillation and the low-boiling material was removed at 64° (0.4 mm.). The distillation was stopped and the undistilled oil was dissolved in ether and filtered. The trihydrochloride was made by treatment with excess ethereal HCl. It was recrystallized by dissolving in dry methanol and adding an equal volume of dry isopropyl alcohol and cooling. There was obtained 15 g. (73%) of a white powder, m.p. 272–275° dec.

Anal. Calcd. for $C_{24}H_{42}N_6O_6 \cdot 3HCl$ (III): C, 46.48; H, 7.31; N, 13.55. Found: C, 45.98; H, 7.58; N, 13.01.

Tri-(β-dimethylaminoethyl) Cyanurate Trimethiodide (IV).—This compound was prepared in a manner similar to that employed in the preparation of III. In this case 4.8 g. (0.20 mole) of sodium hydride, 18.7 g. (0.21 mole) of β-dimethylaminoethanol and 12.14 g. (0.066 mole) of cyanuric chloride was used. The mixture was refluxed 1.5 hours instead of overnight. After removal of the solvent the dark brown semi-solid residue was stirred well with ether. After filtering, the ether solution was concentrated. The resulting thick oil was taken up in absolute alcohol and excess methyl iodide was added. Precipitation of the quaternary salt began almost immediately. After standing overnight and filtering, a crude yellow solid was obtained. After repeated recrystallization by suspending the solid in boiling ethanol or methanol and adding water dropwise until solution occurred, a 10% yield (based on cyanuric chloride) of colorless leaflets, m.p. 214–215° dec., was obtained.

Anal. Calcd. for $C_{16}H_{30}N_6O_3 \cdot 3CH_3I$ (IV): C, 28.16; H, 5.11; N, 10.93. Found: C, 27.92; H, 5.20; N, 10.73.

Acknowledgment.—The analyses were carried out by E. F. Shelberg, Chief Microanalyst, and his staff.

(3) M. A. Spielman, W. J. Close and I. J. Wilk, THIS JOURNAL, **73**, 1775 (1951).

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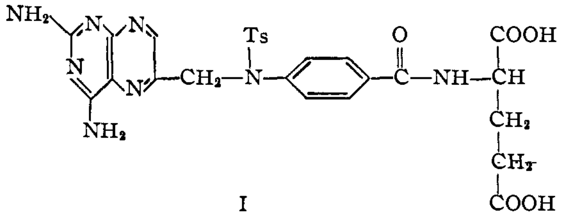
N-{*p*-[(2,4-Diamino-6-pteridylmethyl)-tosylamino]-benzoyl}-L-glutamic Acid, a Pteroylglutamic Acid Analog

BY BARNEY J. MAGERLEIN AND DAVID I. WEISBLAT

RECEIVED FEBRUARY 6, 1954

The condensation of 2,4,5,6-tetraminopyrimidine hydrochloride[1] with diethyl N-[N′-tosyl-N′-(3,3-diethoxy-2-ketopropyl)-*p*-aminobenzoyl]-L-glutamate[2] followed by saponification gave the pteridine, N-{*p*-[(2,4-diamino-6-pteridylmethyl)-tosylamino]-benzoyl}-L-glutamic acid (I).

This compound possessed neither folic acid activity nor antifolic acid activity when assayed with the test organism *S. faecalis R.*



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Acknowledgment.—The authors are indebted to Mr. L. Stubberfield and Mr. E. Stapert for the microbiological assays, to Dr. G. Pish and Mr. L. Scholten for the ultraviolet absorption data, and to Mr. W. A. Struck and associates for the microanalyses.

Experimental

N-{*p*-[(2,4-Diamino-6-pteridylmethyl)-tosylamino]-benzoyl}-L-glutamic Acid (I).—A solution of 4.77 g. of diethyl N-[N′-tosyl-N′-(3,3-diethoxy-2-ketopropyl)-*p*-aminobenzoyl]-L-glutamate,[2] 2.49 g. of 2,4,5,6-tetraminopyrimidine hydrochloride,[1] 1.5 ml. of concentrated hydrochloric acid and 5.0 ml. of 95% ethanol was heated under reflux for 2 hours. The ethanol was distilled under vacuum, the residue diluted with 25 ml. of water, and extracted with ethyl acetate. The *p*H of the aqueous solution was adjusted to 5.0, and, after cooling, the precipitate collected by centrifugation. It weighed 2.1 g. (45.7% yield).

A slurry of 0.50 g. of the crude pteridine and 0.15 g. of calcium hydroxide in 8 ml. of 0.5 *N* sodium hydroxide and 100 ml. of water was stirred at 25° for one hour and filtered. The filtrate was heated to 95° and again filtered. The *p*H of the hot filtrate was adjusted to 4.0. After 18 hours at 4° the yellow precipitate was separated by centrifugation. Following lyophilization this material was dried at 100° for 6 hours at 0.1 mm. pressure. It weighed 0.23 g.; $\lambda_{\max.}^{0.1\ N\ NaOH}$ 229 mμ, $E_{1\ cm.}^{1\%}$ 470; 259 mμ, $E_{1\ cm.}^{1\%}$ 580; 270 mμ, $E_{1\ cm.}^{1\%}$ 130.

Anal. Calcd. for $C_{26}H_{26}N_8O_7S$: C, 52.52; H, 4.4; N, 18.85; S, 5.4. Found: C, 51.71; H, 4.47; N, 19.24; S, 5.15; ash, 1.23. Found (corrected for ash): C, 52.4; H, 4.5; N, 19.5; S, 5.2.

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KALAMAZOO, MICHIGAN

[1] W. Traube, *Ber.*, **37**, 4544 (1904); M. F. Malette, E. C. Taylor, Jr., and C. K. Cain, THIS JOURNAL, **69**, 1814 (1947).

[2] D. I. Weisblat, B. J. Magerlein, D. R. Myers, A. R. Hanze, E. I. Fairburn and S. T. Rolfson, *ibid.*, **75**, 5983 (1953).

Crystalline Δ^4-Androsten-17β-ol-3,16-dione[1]

BY ANDRE S. MEYER AND MARJORIE C. LINDBERG

RECEIVED DECEMBER 31, 1953

Δ^4-Androsten-17β-ol-3,16-dione (III) (16-ketotestosterone) was required for purposes of comparison. This substance was obtained as an oil in 1942 by Stodola and Kendall[2] through the nitrosation of the Δ^4-androstene-3,17-dione 3-enol ethyl ether (I) to the 16-isonitroso derivative (II) and subsequent zinc–acetic acid reduction. Compound III yielded the crystalline monoacetate (IV) with a m.p. 194–195° from petroleum ether–acetone. An $[\alpha]^{25}_{4561}$ −56° in 95% ethanol was determined for IV synthesized by a second route.[3] Through their investigations on various 16,17-ketol steroids prepared by the nitrosation method[2] Huffman and Lott[4] were able to ascertain the steric arrangement of the hydroxyl group at position 17 as being β-oriented. Recently, in this Laboratory with the use of paper chromatography the resolution of compound III from the reduction mixture was accomplished. It

[1] This investigation was supported by a grant from G. D. Searle and Company, Chicago, Illinois.

[2] F. H. Stodola and E. C. Kendall, *J. Org. Chem.*, **7**, 336 (1942).

[3] F. H. Stodola and E. C. Kendall, *ibid.*, **6**, 837 (1941).

[4] M. N. Huffman and M. H. Lott, THIS JOURNAL, **71**, 719 (1949).