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SOME DERIVATIVES OF ACENAPHTHENE OF PHARMACOLOGICAL INTEREST

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Very few reports have appeared describing the chemistry and pharmacology of acenaphtnene-containing compounds, particularly 1-acenaphthenyl derivatives. The substitution of the benzene nucleus of pressor bases by 5-acenaphthene has been stated to result in increased activity (1). Although the preparation of a series of 3- and 5-acenaphthenyl amino alcohols structurally related to ephedrine has been reported, no physiological data were included (2). In a series of cyclopentenylacetate esters possessing antispasmodic properties, β-diethylaminoethyl Δ^2-cyclopentenyl-1-acenaphthenylacetate was described as being weakly active (3). It has been shown that acenaphthene inhibits the growth of grafted tumors in mice (4).

The purpose of this investigation was to prepare for pharmacological study a variety of 1-acenaphthenyl drug types patterned after well-known chemotherapeutic agents in an effort to determine the relative pharmacological effect of acenaphthene as compared to other aromatic nuclei. The synthesis of representative histamine antagonists, antispasmodics, growth inhibitors, hypnotics, anti-convulsants, and sympathomimetics containing the 1-acenaphthene moiety was undertaken. These included the analogs of Benadryl, Pyribenzamine, Trasentin, Phenobarbital, and Benzedrine.

The preparation of these 1-acenaphthenyl derivatives depended upon the synthesis of the necessary intermediates, 1-acenaphthenol, 1-acenaphthenyl chloride, and 1-acenaphthenone. The alcohol was prepared by the excellent method of Cason (5) from acenaphthene by oxidation with red lead in glacial acetic acid. The chloride was obtained by the action of gaseous hydrogen chloride on the alcohol in cold dry ether. The bromide has been reported to result from the reaction of phosphorus tribromide with the alcohol in ether (6). These halides are unstable, easily losing hydrogen halide, and are best prepared only as needed. Oxidation of 1-acenaphthenol with chromic anhydride in acetic acid according to Fieser and Cason (7) gave 1-acenaphthenone in satisfactory yield.

Two compounds similar in structure to Benadryl, the benzhydryl ether of β-dimethylaminoethanol, were synthesized as possible histamine antagonists. These were the 1-acenaphthenyl ethers of β-dimethylaminoethanol and β-diethylaminoethanol, respectively. The procedure described for the preparation of Benadryl (8), involving the reaction between benzhydryl bromide and β-dimethylaminoethanol in refluxing xylene, was entirely unsatisfactory in the case of the corresponding 1-acenaphthenyl ethers due to the almost complete de-

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hydrohalogenation of 1-acenaphthenyl chloride. The desired ethers were conveniently obtained by the Williamson reaction between the sodium salt of 1-acenaphthenol and the appropriate dialkylaminoethyl halide in toluene. The high-boiling amino ethers formed stable hydrochlorides which were easily purified by recrystallization from anhydrous ethanol-ether for analysis and pharmacological appraisal.

Two other potential antihistaminics containing 1-acenaphthene were prepared. These were patterned after the well-known ethylenediamine derivatives, Pyribenzamine and Antergan. The 1-acenaphthenyl analogs of these drugs, N,N-dimethyl-N′-(1-acenaphthenyl)-N′-(α-pyridyl)ethylenediamine and N,-N-diethyl-N′-(1-acenaphthenyl)-N′-phenylethylenediamine, were obtained by reacting 1-acenaphthenyl chloride with the sodium salts of 2-(β-dimethylaminoethyl)aminopyridine and β-diethylaminoethylaniline, respectively. The final products as well as the indicated intermediates were prepared by the general procedures of Huttrer, *et al.* (9). The yields of the 1-acenaphthenyl ethylenediamines, distilling as high-boiling amber oils, were rather low (about 15%) due to the predominance of the dehydrohalogenation side reaction giving acenaphthylene polymer.

Trasentin, β-dimethylaminoethyl diphenylacetate, an active antispasmodic agent, served as the model for two presumptive spasmolytics containing 1-acenaphthene. The compounds prepared were the β-diethylaminoethyl esters of 1-acenaphthenylacetic acid and α-(1-acenaphthenyl)butyric acid, respectively, and were obtained by following the general scheme outlined by Blicke and Feldkamp (10) for a series of α-naphthylacetates,

$$\mathrm{RCl} + \mathrm{R'CH(CO_2Et)_2} \xrightarrow{\mathrm{NaOEt}} \mathrm{R{-}C(R')(CO_2Et)_2} \xrightarrow{\mathrm{H_2O}} \mathrm{R{-}C(R')(CO_2H)_2} \xrightarrow{-\mathrm{CO_2}} \mathrm{RCH(R')CO_2H\ (I)}$$

$$\mathrm{I} + \mathrm{ClCH_2CH_2NEt_2} \longrightarrow \mathrm{RCH(R')C(=O)OCH_2CH_2NEt_2 \cdot HCl}$$

R = 1-acenaphthenyl; R′ = H or C_2H_5

In the case where R′ was ethyl, hydrolysis of the malonic ester under the conditions described by the above authors was incomplete, and a mixture of the malonic acid and its half-ester was obtained, which upon decarboxylation gave the desired acetic acid and the corresponding ethyl ester. The latter compound was a satisfactory intermediate for other syntheses so no attempt was made to effect a complete saponification by the use of additional solvent and increased reaction time. The potential antispasmodic esters were prepared from the acetic acids by the method of Horenstein and Pahlicke (11). This same

procedure was used for the synthesis of the bis-β-diethylaminoethyl ester of ethyl-1-acenaphthenylmalonic acid.

The 1-acenaphthenyl analog of the hypnotic and antiepileptic, Phenobarbital (5-ethyl-5-phenylbarbituric acid), was synthesized by condensing urea with diethyl ethyl-1-acenaphthenylmalonate. Increased reaction time gave a higher yield than those reported for Phenobarbital (12, 13).

The reported activity of 2-phenylbutyrylurea as an anticonvulsant (14) led to the preparation of the corresponding 1-acenaphthenyl compound. The procedure of Stendal (15), involving the condensation of an ester with urea, gave the desired ureide from ethyl α-(1-acenaphthenyl)butyrate but in poorer yield than expected by this method.

Three potential sympathomimetic amines similar to Benzedrine were synthesized. These were α-methyl-β-(1-acenaphthenyl)ethylamine and its N-methyl and N-ethyl derivatives. The preparative method involved synthesis of 1-acenaphthenyl acetoacetic ester, alkaline cleavage of the ester to give 1-acenaphthenylacetone, and reductive amination of the ketone with the appropriate amine or ammonia. The ketonic cleavage of the acetoacetic ester was accomplished in excellent yield by the alkaline saponification procedure of Drake and Riemenschneider (16). Dilute sulfuric acid had practically no effect on the ester while the phosphoric acid hydrolysis method of Dehn and Jackson (17) caused almost complete polymerization of the slowly formed ketone. The reductive aminations were accomplished by catalytic hydrogenation according to published procedures (18, 19), and the products were isolated and purified as the hydrochloride salts for pharmacological testing.

The activity of acenaphthene as a tumor inhibitor (4) and the bacterial growth-inhibiting property of certain unsaturated ketones (20) and lactones (21) led to the preparation of cinnamylideneacenaphthenone. The procedure of Sircar and Rajagopalan (22) was followed. The reaction of crotonaldehyde with acenaphthenone gave a polymeric product by this method.

1-Acenaphthenylamine has been prepared in relatively low yield by the chemical reduction of acenaphthenone oxime (23). A considerable improvement in yield can be obtained by using the catalytic hydrogenation procedure of Hartung (24).

The authors are indebted to the Sterling-Winthrop Research Institute for the financial support of this investigation and for the preliminary pharmacological data. The 1-acenaphthenyl analogs of Benadryl were found to be lacking in antihistamine activity. The acenaphthene antispasmodics possess no appreciable activity against acetylcholine induced spasms.

EXPERIMENTAL

All melting and boiling points are uncorrected.

1-Acenaphthenyl chloride (25). A stirred suspension of 1-acenaphthenol (17 g., 0.1 mole) and a few grams of anhydrous calcium chloride granules in 150 ml. of dry ether was treated with a fast stream of hydrogen chloride gas while cooling in an ice-bath. The insoluble alcohol was converted to the ether-soluble chloride in about 30 minutes. The clear yellow solution was poured onto crushed ice; the ether layer was separated, washed with ice-

water, 5% sodium bicarbonate, and again with ice-water, and dried over magnesium sulfate. Removal of the solvent *in vacuo* gave 17–18 g. (90–95%) of pale yellow crystals; m.p. 36–38°. Recrystallization from ether raised the melting point to 41–43°. The chloride was unstable and was generally used in the form of its dried ether solution without isolation.

β-Diethylaminoethyl 1-acenaphthenyl ether. A solution of 12 g. (0.07 mole) of 1-acenaphthenol in 200 ml. of dry toluene was heated to 95° and treated with 1.1 g. (0.05 g.-atom) of sodium in small portions. The mixture was refluxed for five hours and was then treated with 6.8 g. (0.05 mole) of freshly distilled β-diethylaminoethyl chloride (26) at 50–70° and maintained at this temperature for 17 hours. The cooled solution was extracted with 200 ml. of 10% hydrochloric acid, and the acidic aqueous solution was made strongly alkaline with sodium hydroxide and extracted with ether. Distillation of the dried extracts gave 7.5 g. (55.5%) of a yellow oil, b.p. 160–168°/1.5 mm. Treatment of an ether solution of the material with propanolic hydrogen chloride gave 7.5 g. (50%) of white crystalline hydrochloride, m.p. 121–122° (d). Recrystallization from anhydrous ethanol-ether raised the melting point to 123–124° (d).

Anal. Calc'd for $C_{18}H_{23}NO \cdot HCl$: C, 70.69; H, 7.91; Cl, 11.59.
Found: C, 71.22; H, 7.75; Cl, 11.46.

The use of sodamide in the preparation of similar ethers of aryl substituted methanols has recently been reported (27, 28).

β-Dimethylaminoethyl 1-acenaphthenyl ether. This compound was synthesized by the above procedure except that the hydrobromide salt of β-dimethylaminoethyl bromide (11.6 g., 0.05 mole), was added to 0.1 mole of sodium 1-acenaphthenate prepared from 17 g. (0.1 mole) of 1-acenaphthenol and 2.2 g. (0.1 atom) of sodium. The product was obtained in a yield of 6.0 g. (50%), b.p. 136–138° (1 mm.). The hydrochloride was prepared and purified in the same manner as the previous amino ether salt; m.p. 160–161° (d).

Anal. Calc'd for $C_{16}H_{19}NO \cdot HCl$: C, 69.18; H, 7.25; N, 5.04; Cl, 12.76.
Found: C, 69.44; H, 7.00; N, 4.98; Cl, 12.66.

N,N-Dimethyl-N'-(1-acenaphthenyl)-N'-(α-pyridyl)ethylenediamine. A suspension of sodamide (29), prepared from 1.1 g. (0.048 g.-atom) of sodium in 100 ml. of anhydrous toluene was treated with 8.0 g. (0.048 mole) of 2-(β-dimethylaminoethyl)aminopyridine. The stirred mixture was refluxed for three hours and cooled. 1-Acenaphthenyl chloride [from 8.2 g., 0.048 mole) of the alcohol] was dissolved in 100 ml. of toluene and added to the reaction mixture in the course of two hours at room temperature. The mixture was kept at 40–70° for two hours and was then hydrolyzed by the dropwise addition of 75 ml. of water. The toluene layer was extracted with dilute hydrochloric acid and the acid solution containing the relatively insoluble gummy hydrochlorides was made strongly alkaline with 40% sodium hydroxide solution. The free amines were extracted with ether and the dried ethereal solution distilled. After a forerun of starting material the desired product was obtained as a viscous amber oil, b.p. 182–192° (1 mm.); yield 2.0 g. (13%). Treatment of the base in ether with methyl iodide gave 2.5 g. of crude salt which, on careful purification from anhydrous ethanol-ether, yielded 1.5 g. of the monomethiodide which crystallized from solution with a molecule of ethanol; m.p. 154–155° (d).

Anal. Calc'd for $C_{21}H_{23}N_3 \cdot CH_3I \cdot C_2H_5OH$: C, 57.03; H, 6.38; N, 8.32.
Found: C, 56.85; H, 6.00; N, 8.43.

N,N-Diethyl-N'-(1-acenaphthenyl)-N'-phenylethylenediamine. This compound was prepared by the method described above. From 9.6 g. (0.05 mole) of β-diethylaminoethylaniline, 1.2 g. (0.05 g.-atom) of sodium, and 8.5 g. (0.05 mole) of 1-acenaphthenol, there was obtained 3.0 g. (17.5%) of product distilling at 183–193° (0.5 mm.). The base was converted to the monoöxalate salt in dry ether and by treatment with an ethereal solution of anhydrous oxalic acid. The salt was recrystallized from anhydrous ethanol; m.p. 153–155° (d).

Anal. Calc'd for $C_{24}H_{28}N_2 \cdot H_2C_2O_4$: C, 71.86; H, 6.96; N, 6.45.
Found: C, 71.88; H, 7.07; N, 6.40.

Diethyl ethyl-1-acenaphthenylmalonate. This ester was prepared by a modification of the procedure described by Bachmann and Sheehan (6). A cold ether solution of 1-acenaph-

thenyl chloride [prepared from 17 g. (0.1 mole) of 1-acenaphthenol] was added to a cold solution of sodioethylmalonic ester obtained from 4.6 g. (0.2 g.-atom) of sodium and 37.5 g. (0.2 mole) of diethyl ethylmalonate in 250 ml. of anhydrous ethanol. After standing in a refrigerator for three days with occasional shaking, the solution was refluxed for three hours, and the solvent was then evaporated. The residue was treated with 200 ml. of water acidified with hydrochloric acid, and extracted with ether. Distillation of the dried ether extract yielded 31 g. (91%) of a viscous, pale-yellow oil, b.p. 183–186° (1.5 mm.), n_D^{20} 1.5571.

Diethyl 1-acenaphthenylmalonate. The procedure outlined for the preparation of the above ester was followed. From 20 g. (0.115 mole) of 1-acenaphthenol, 5.0 g. (0.22 g.-atom) of sodium, and 37 g. (0.23 mole) of diethyl malonate, there was obtained 24.0 g. (67%) of product, b.p. 165–168° (1 mm.), n_D^{20} 1.5633.

Ethyl-1-acenaphthenylmalonic acid, α-(1-acenaphthenyl)butyric acid, and ethyl α-(1-acenaphthenyl)butyrate. Diethyl ethyl-1-acenaphthenylmalonate (14 g., 0.041 mole) was hydrolyzed by refluxing with 9.6 g. of potassium hydroxide in 40 ml. of 80% ethanol for five hours. The solvents were removed by distillation *in vacuo* and the residue dissolved in water. After washing with ether to remove organic impurities, the cold aqueous solution was acidified with concentrated hydrochloric acid and extracted with ether. The oily residue remaining after removal of the ether was a mixture of the desired malonic acid and its monoethyl ester. When a sample of this oily mixture was stirred with hexane the ester dissolved and the malonic acid crystallized as a white solid; m.p. 166–168° after recrystallization from acetone-benzene.

Anal. Calc'd for $C_{17}H_{16}O_4$: Neut. equiv., 142.1. Found: Neut. equiv., 147.5.

The remainder of the oily mixture was decarboxylated by heating at 175–190° for one hour. The product was treated with 50 ml. of 10% sodium carbonate and extracted with ether to remove ethyl α-(1-acenaphthenyl)butyrate. The cooled alkaline solution was acidified with concentrated hydrochloric acid and the precipitated oil was taken up in ether and distilled. The α-(1-acenaphthenyl)butyric acid was obtained in a yield of 5.0 g. (50.5%) as a viscous yellow oil, b.p. 190–193° (2 mm.).

Anal. Calc'd for $C_{16}H_{16}O_2$: Neut. equiv., 240.3. Found: Neut. equiv., 248.5.

The ether solution of ethyl α-(1-acenaphthenyl)butyrate from above was also distilled. The product was a yellow oil; yield 4.5 g. (41%); b.p. 166–169° (2.5 mm.), n_D^{20} 1.5720, d_4^{20} 1.089, MR_D (calc'd) 78.02, MR_D (observed) 81.00.

Anal. Calc'd for $C_{18}H_{20}O_2$: C, 80.56; H, 7.51.
Found: C, 80.34; H, 7.47.

1-Acenaphthenylacetic acid. This acid was prepared by the above method from 10 g. (0.032 mole) of diethyl 1-acenaphthenylmalonate, 6.9 g. of potassium hydroxide, and 30 ml. of 80% ethanol. The crude intermediate malonic acid was decarboxylated by heating for several hours at 190°. The warm melt was dissolved in acetone, the solution charcoaled, filtered, and evaporated to remove solvent. The crude acetic acid, 6.5 g., was recrystallized from benzene-hexane (1:4); yield, 4.6 g. (67%); m.p. 114–116°. Bachmann and Sheehan report m.p. 115–116° (6).

Anal. Calc'd for $C_{14}H_{12}O_2$: Neut. equiv., 212.2. Found: Neut. equiv., 210.2.

β-Diethylaminoethyl β-(1-acenaphthenyl)butyrate. A mixture of 5 g. (0.021 mole) of β-(1-acenaphthenyl)butyric acid, 3.8 g. (0.028 mole) of β-diethylaminoethyl chloride, and 50 ml. of 99% propanol-2 were refluxed for 45 hours, cooled, and filtered to remove the excess β-diethylaminoethyl chloride as its insoluble hydrochloride. The filtrate was evaporated, the residual syrup dissolved in water, extracted with ether and then made alkaline with 40% sodium hydroxide to liberate the amino ester free base which was taken up in ether. Treatment of the dried ether solution with a saturated ether solution of anhydrous oxalic acid precipitated the monoöxalate salt as a white solid, yield 7.0 g. (78%); m.p. 76–78° (d). The product analyzed as an alcoholate after recrystallization from anhydrous ethanol-ether; m.p. 80–81° (d).

Anal. Calc'd for $C_{22}H_{29}NO_2 \cdot H_2C_2O_4 \cdot C_2H_5OH$: C, 65.66; H, 7.84; N, 2.94.
Found: C, 66.05; H, 7.81; N, 3.00.

β-Diethylaminoethyl 1-acenaphthenylacetate hydrochloride. 1-Acenaphthenylacetic acid (3.5 g., 0.016 mole), 2.9 g. (0.02 mole) of β-diethylaminoethyl chloride, and 54 ml. of 99% propanol-2 were refluxed for 45 hours, cooled and filtered to remove the insoluble quaternary salt of the excess aminoethyl halide. The ester hydrochloride, which separated from the filtrate upon dilution with 200 ml. of anhydrous ether and cooling, was filtered, washed with ether, and dried; yield 2.9 g. (51%); m.p. 140–141.5° (d).

Anal. Calc'd for $C_{20}H_{25}NO_2 \cdot HCl$: N, 4.03; Cl, 10.20.

Found: N, 4.25; Cl, 10.52.

Bis-(β-diethylaminoethyl) ethyl-1-acenaphthenylmalonate. A mixture of ethyl-1-acenaphthenylmalonic acid and its monoethyl ester (2.5 g., approx. 0.008 mole) was refluxed for 40 hours with 2.5 g. (0.018 mole) of β-diethylaminoethyl chloride and 70 ml. of anhydrous ethanol. The amino ester was obtained as a sesquioxalate salt upon treatment of the base in ether with a saturated ether solution of anhydrous oxalic acid; yield 1.5 g. (35%). Recrystallization from dry ethanol-ether gave a white crystalline product containing ethanol of crystallization, m.p. 72–73° (d).

Anal. Calc'd for $C_{29}H_{42}N_2O_4 \cdot 3/2\ H_2C_2O_4 \cdot C_2H_5OH$: C, 61.52; H, 7.74; N, 4.22.

Found: C, 61.73; H, 7.50; N, 3.97.

5-(1'-Acenaphthenyl)-5-ethylbarbituric acid. Dry powdered urea (6 g., 0.1 mole) was added to a warm solution of 4.6 g. (0.2 g.-atom) of sodium in 100 ml. of anhydrous ethanol. Diethyl ethyl-1-acenaphthenylmalonate (31 g., 0.09 mole), was then added and the resulting mixture refluxed for 17 hours. The residue remaining after evaporation of ethanol was dissolved in water, extracted with ether to remove unreacted ester and organic by-products, and slowly treated in the cold with concentrated hydrochloric acid until the solution was weakly acidic. The barbituric acid separated as a chalky white precipitate which was filtered, washed with 50% ethanol, and dried; yield 19 g. (68%); m.p. 226–229°. Recrystallization from methanol gave 15 g. (53.5%) of pure product melting at 235–235.5°.

Anal. Calc'd for $C_{18}H_{16}N_2O_3$: C, 70.11; H, 5.23; N, 9.09.

Found: C, 70.16; H, 5.44; N, 9.01.

2-(1'-Acenaphthenyl)butyrylurea. A mixture of 4.0 g. (0.015 mole) of ethyl α-(1-acenaphthenyl)butyrate, 1.5 g. (0.025 mole) of powdered urea, 60 ml. of 25% sodium ethoxide-ethanol solution, and 9 ml. of anhydrous pyridine was allowed to stand for 24 hours at room temperature. The reaction mixture was added to 100 ml. of cold 15% aqueous acetic acid and the solution filtered after standing overnight. The crude solid, after washing with aqueous ethanol and drying, weighed 1.5 g. Recrystallization from ethanol gave 0.6 g. of pure product, m.p. 220–222° (d).

Anal. Calc'd for $C_{17}H_{18}N_2O_2$: C, 72.32; H, 6.43; N, 9.92.

Found: C, 72.53; H, 6.54; N, 9.85.

Ethyl 1-acenaphthenylacetoacetate. Ethyl acetoacetate (26 g., 0.2 mole), was added to a solution of 4.6 g. (0.2 atom) of sodium in 150 ml. of anhydrous ethanol. After refluxing for 30 minutes the solution was cooled in an ice-bath and treated with a cold solution of 1-acenaphthenyl chloride in 100 ml. of ether, prepared from 17 g. (0.1 mole) of 1-acenaphthenol. The reaction mixture was allowed to stand in a refrigerator for three days, then refluxed for three hours. The solvents were removed by distillation and the residue treated with water and dilute hydrochloric acid. The acidic solution was extracted with ether and the dried ether extracts were distilled. The product was obtained as a pale yellow oil in a yield of 17.0 g. (60%), b.p. 180–185° (2 mm.), n_D^{20} 1.5813.

1-Acenaphthenylacetone. A solution of 48 g. (0.73 mole) of 85.4% potassium hydroxide in 260 ml. of water was heated to 105° with stirring and treated with 16 g. (0.056 mole) of ethyl 1-acenaphthenylacetoacetate during the course of 45 minutes. The solution was kept at 105° for five hours, cooled, and extracted with ether. The ether extracts, after drying over magnesium sulfate, were evaporated to remove the solvent. The residual crude product weighed 10 g. (84%), m.p. 41–43°. Recrystallization from low-boiling petroleum ether yielded 9.3 g. (78%) of white crystals melting at 45.5–46.5°. The compound could be distilled without decomposition, b.p. 130–135° (0.5 mm.), n_D^{20} 1.6085.

Anal. Calc'd for $C_{15}H_{14}O$: C, 85.68; H, 6.71.
Found: C, 85.91; H, 7.10.

1-Acenaphthenylacetone oxime melted at 111.5–112.5° after recrystallization from ethanol. The *phenylhydrazone* melted at 76.5–78° (d) after recrystallization from absolute methanol. The latter compound was unstable in air, gradually becoming dark red in color.

α-Methyl-β-(1-acenaphthenyl)ethylamine. 1-Acenaphthenylacetone (5.3 g., 0.025 mole), was dissolved in 100 ml. of 10% ammonia in anhydrous ethanol and hydrogenated using 3.0 g. of Raney nickel at 50° under 60 p.s.i. until the theoretical amount of hydrogen was absorbed. The oily amine was dissolved in 25 ml. of *n*-propanol and 150 ml. of anhydrous ether and treated with an excess of hydrogen chloride gas. The hydrochloride separated as a voluminous white precipitate which was collected, washed with ether, and dried; yield 4.0 g. (65%); m.p. 235–238° (d). The melting point was not raised by further recrystallization.

Anal. Calc'd for $C_{15}H_{17}N \cdot HCl$: C, 72.71; H, 7.32; N, 5.65; Cl, 14.31.
Found: C, 72.70; H, 7.33; N, 5.67; Cl, 14.22.

N-α-Dimethyl-β-(1-acenaphthenyl)ethylamine. 1-Acenaphthenylacetone (4.2 g., 0.02 mole) was dissolved in 150 ml. of anhydrous ethanol containing 2.5 g. (0.08 mole) of dry methylamine and hydrogenated over 0.1 g. of platinum oxide at room temperature and 60 p.s.i. The theoretical amount of hydrogen was absorbed in about one hour. The crude amine was dissolved in 150 ml. of anhydrous ether and treated with hydrogen chloride gas to precipitate the white hydrochloride which was collected, washed with ether, and dried; yield 5.0 g. (95%); m.p. 141–144° (d). Recrystallization from anhydrous ethanol-ether yielded 3.5 g. (67%) of pure product, m.p. 154–155° (d).

Anal. Calc'd for $C_{16}H_{19}N \cdot HCl$: C, 73.40; H, 7.70; N, 5.35; Cl, 13.54.
Found: C, 73.30; H, 7.82; N, 5.37; Cl, 13.53.

N-Ethyl-α-methyl-β-(1-acenaphthenyl)ethylamine was prepared as was the N-methyl derivative, using 3 g. (0.014 mole) of 1-acenaphthenylacetone and 1.3 g. (0.028 mole) of anhydrous ethylamine in 75 ml. of dry ethanol; the mixture was hydrogenated in the presence of 0.1 g. of platinum oxide catalyst. The hydrochloride separated as a gummy precipitate which slowly crystallized to a solid on rubbing with ether. The yield of this crude product was 2.0 g. (52%); m.p. 135–145° (d). Recrystallization from anhydrous ethanol-ether gave 1.0 g. (26%) of purified product, m.p. 163–165° (d).

Anal. Calc'd for $C_{17}H_{21}N \cdot HCl$: C, 74.02; H, 8.04; N, 5.08; Cl, 12.86.
Found: C, 73.55; H, 7.82; N, 4.87; Cl, 13.12.

Cinnamylideneacenaphthenone. Acenaphthenone (5 g., 0.03 mole) and 4.0 g. (0.03 mole) of cinnamaldehyde were dissolved in 125 ml. of 95% ethanol and treated with 3.0 ml. of 10% alcoholic potassium hydroxide. The temperature of the reaction mixture rose to 40° and a yellow solid began to separate. After standing for 24 hours in a refrigerator the product was collected, washed with ethanol, and dried; yield 6.0 g. (71%); m.p. 120–140° (d). Two recrystallizations from ethyl acetate gave 3.0 g. (35%) of very fine yellow needles, m.p. 168–168.5°.[2]

Anal. Calc'd for $C_{21}H_{14}O$: C, 89.34; H, 5.00.
Found: C, 89.25; H, 5.13.

1-Acenaphthenylamine hydrochloride. Acenaphthenone oxime (23) (5 g., 0.027 mole) was dissolved in a hot mixture of 25 ml. of dry toluene and 150 ml. of anhydrous ethanol containing 3.0 g. of hydrogen chloride. The warm solution was hydrogenated over 1.0 g. of 10% palladium-on-charcoal catalyst under a pressure of sixty pounds. The theoretical quantity of hydrogen was absorbed in about three hours. The crude product was purified by dissolving in warm anhydrous ethanol, adding an equal volume of ether, and cooling. The hydrochloride salt of 1-acenaphthenylamine separated as white crystals in a yield of 3.5 g. (63%),

[2] The product obtained in this work is not identical with the substance called cinnamylideneacenaphthenone by Sircar and Rajagopalan (22) which was a colorless microcrystalline powder melting at 214–215°. Cinnamylideneacenaphthenone should be a colored compound.

melting with partial decomposition around 270°. A sample of the hydrochloride was converted to the free base; m.p. 131–134°. Morgan and Stanley (23) report that the hydrochloride decomposes partially at 270° and that the sublimed base melts at 135°.

SUMMARY

In order to study the physiological effect of the acenaphthenyl group a number of 1-acenaphthenyl derivatives patterned after well-known synthetic medicinals have been prepared.

During the course of this work a number of new 1-acenaphthenyl intermediates were synthesized.

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