traction with benzene and removal of the solvent from the washed extract gave a residue which solidified on trituration with ether. The solid (0.55 g.) was recrystallized from ethyl acetate giving 0.50 g. of 1,1,4,4-tetraphenyl-1,3-butadiene, m.p. 192–193°; reported m.p. 192–193°[26] and 205–206°.[27]

(26) J. Salkind and V. Teterin, *Ber.*, **62**, 1748 (1929).
(27) P. Lipp, *ibid.*, **56**, 567 (1923).

Anal. Calcd. for $C_{28}H_{22}$: C, 93.8; H, 6.2. Found: C, 93.7; H, 6.1.

Evaporation of the ethereal filtrate from the above crystalline material gave a brown oil from which no pure compound could be isolated after distillation and chromatography on alumina.

ANN ARBOR, MICHIGAN

[CONTRIBUTION FROM THE WARNER–CHILCOTT RESEARCH LABORATORIES]

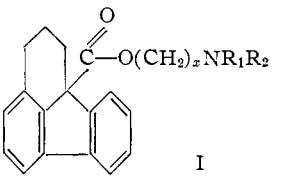
Aminoalkyl Esters of 1,2,3,10b-Tetrahydrofluoranthene-10b-carboxylic Acid

BY ELIOT STEINBERG, GEORGE A. CONRAD AND A. WAYNE RUDDY

RECEIVED MARCH 22, 1954

Several basic esters were prepared from tertiary aminoalkyl chlorides and 1,2,3,10b-tetrahydrofluoranthene-10b-carboxylic acid. The starting point for the preparations of the required acid was the parent hydrocarbon, fluoranthene. Fluoranthene was partially reduced with sodium amalgam to 1,2,3,10b-tetrahydrofluoranthene and the latter was then metalated in the 10b-position with sodamide. The intermediate sodio derivative was carboxylated to the acid. Most of the esters described were prepared by the Horenstein–Pahlicke condensation of the acid with a chloralkamine. These esters as hydrochlorides and methobromides were found to have significant antispasmodic activity. A brief description of the preliminary pharmacological data will be presented.

The present paper describes the synthesis of several alkamine esters of 1,2,3,10b-tetrahydrofluoranthene-10b-carboxylic acid (I).



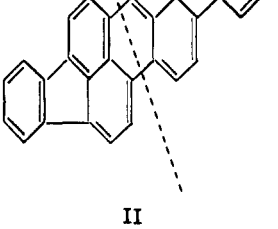
I

These esters in the form of their hydrochlorides and their quaternary salts were prepared in an effort to obtain more useful antispasmodics of the atropine type. The esters and their derivatives prepared in this present series are listed in Table I.

The acid moiety of the esters was prepared starting from the commercially available present hydrocarbon, fluoranthene.[1] This was reduced in almost quantitative yields with 10% sodium amalgam.[2] Other methods of reduction which have been reported are hydriodic acid and phosphorus at 180°,[3] powdered sodium in boiling decalin followed by alcohol to decompose the tetrasodio compound,[4] and catalytic reduction with Raney nickel[5] or palladized charcoal.[2]

The preparation of the desired acid from 1,2,3,-10b-tetrahydrofluoranthene has been described by Kruber.[6] He used two methods of synthesis: (1) by fusion of 1,2,3,10b-tetrahydrofluoranthene with sodium followed by the addition of carbon dioxide to the resulting melt (10% yield), and (2) by treating 1,2,3,10b-tetrahydrofluoranthene with a solution of ethylmagnesium bromide and then treating the intermediate Grignard compound with carbon dioxide (10% yield). In our laboratories 1,2,3,10b-tetrahydrofluoranthene-10b-carboxylic acid was prepared by treating 1,2,3,10b-tetrahydrofluoranthene with sodamide using dry toluene as a solvent. The resulting sodio derivative was treated with carbon dioxide followed by acidification to yield the desired acid (69% yield). The carboxylation was also carried out *via* a transmetalation using butyllithium to form the intermediate lithium compound which then reacted readily with carbon dioxide to yield the acid (72% yield). The former method was more convenient to use, especially for larger runs.

When the reaction of 1,2,3,10b-tetrahydrofluoranthene and sodamide was carried out in toluene a small amount of red material was obtained which appeared to go through the subsequent treatment with carbon dioxide without change. These deep red crystals did not melt up to 360° and were insoluble in the usual organic solvents. It is probably a compound similar to periflanthene[7] (II). It can be seen that periflanthene is a result of fusion of two molecules of fluoranthene through the bonds indicated by the dissecting dotted line. It is formed in 0.5% yield on heating fluoranthene with sodamide in boiling xylene. The compound isolated in the sodamide–tetrahydrofluoranthene reaction had the solubility, melting point and color characteristics of periflanthene.

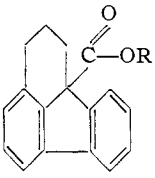


II

Esters of aminoalcohols are generally prepared

(1) Reilly Tar and Chemical Co.
(2) J. von Braun and G. Manz, *Ber.*, **63**, 2608 (1930).
(3) G. Goldschmidt, *Monatsh.*, **1**, 221 (1880).
(4) E. A. Coulson, *Chemistry & Industry*, **60**, 699 (1944); O. Kruber, *Ber.*, **64**, 84 (1931).
(5) J. M. Beaton and S. H. Tucker, *J. Chem. Soc.*, 3870 (1952). This was reported after the work described in this paper was completed. It would seem to be the method of choice for this reduction (80% yield).
(6) O. Kruber, *Ber.*, **67**, 1000 (1934).
(7) J. von Braun and G. Manz, *ibid.*, **70**, 1603 (1937).

TABLE I



No.	R	Salt	Formula	M.p.,[b] °C.	Analyses, %[a] Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Halogen Calcd.	Halogen Found	Soly., g./100 ml.	Activity
1	$(CH_3)_2NCH_2CH_2$	HCl	$C_{21}H_{24}ClNO_2$	227–227.5	70.47	70.07	6.76	6.70	9.92	9.83	3	0.025
2	$(CH_3)_2NCH_2CH_2$	CH_3Br	$C_{22}H_{26}BrNO_2$	217.5–218	63.46	63.37	6.29	6.46	19.17	18.99	> 20	0.25
3	$(C_2H_5)_2NCH_2CH_2$	HCl	$C_{23}H_{28}ClNO_2$	214 –215	71.60	70.76	7.31	7.35	9.19	9.79	0.25	0.05
4	$(C_2H_5)_2NCH_2CH_2$	CH_3Br	$C_{24}H_{30}BrNO_2$	157 –159	64.82	64.54	6.81	7.06	17.99	18.07	> 20	1.0
5	$(i\text{-}C_3H_7)_2NCH_2CH_2$	HCl	$C_{25}H_{32}ClNO_2$	187 –189	72.53	72.47	7.79	7.83	8.57	8.69	1	0.1
6	$(i\text{-}C_3H_7)_2NCH_2CH_2$	CH_3Br	$C_{26}H_{34}BrNO_2$	178 –180	66.09	66.11	7.25	7.38	16.92	17.18	0.5	0.81
7	$C_4H_8NCH_2CH_2$[c]	HCl	$C_{23}H_{26}ClNO_2$	196– 198	71.93	71.38	6.82	6.72	9.24	9.22	> 20	0.05
8	$C_4H_8NCH_2CH_2$[c]	CH_3Br	$C_{24}H_{28}BrNO_2$	201 –202	65.16	65.07	6.38	6.33	18.08	18.19	> 20	0.2
9	$C_5H_{10}NCH_2CH_2$[d]	HCl	$C_{24}H_{28}ClNO_2$	217 –218	72.44	71.86	7.09	7.03	8.92	8.95	0.75	0.05
10	$C_5H_{10}NCH_2CH_2$[d]	CH_3Br	$C_{25}H_{30}BrNO_2$	227.5–228.5	65.80	66.20	6.62	7.11	17.52	17.53	2	0.05
11	$(C_2H_5)_2NCH_2CH_2CH_2$	HCl	$C_{24}H_{30}ClNO_2$	209 –211	72.07	71.78	7.56	7.68	8.87	9.14	0.5	0.4
12	$(C_2H_5)_2NCH_2CH_2CH_2$	CH_3Br	$C_{25}H_{32}BrNO_2$	182 –184	65.49	64.51	7.04	6.91	17.43	17.57	> 20	0.6
	Atropine sulfate											1.0
	Methantheline bromide											1.0

[a] Halogen analyses carried out by G. Feri from this laboratory. Carbon and hydrogen analyses carried out by C. Tiedcke, Teaneck, N. J. [b] Uncorrected. [c] NC_4H_8 = pyrrolidyl. [d] NC_5H_{10} = piperidyl.

from either the interaction of an acid chloride and the alcohol, the interaction of an acid with the corresponding chloralkamine[8] or ester interchange of an alkyl ester with an aminoalcohol. For the esters obtained in Table I it was necessary to use one of the latter two methods as the corresponding acid chloride of 1,2,3,10b-tetrahydrofluoranthene-10b-carboxylic acid is unstable. All attempts to isolate the acid chloride from the reaction of 1,2,3,10b-tetrahydrofluoranthene-10b-carboxylic acid with active halogen donors led to decarboxylation and recovery of 1,2,3,10b-tetrahydrofluoranthene.

The Horenstein–Pählicke condensation of 1,2,3,-10b - tetrahydrofluoranthene - 10b - carboxylic acid and the chloroalkamines proceeded very smoothly in dry isopropyl alcohol to give the ester hydrochlorides directly in good yields. The only exception to this was the preparation of compound no. 7 which was made in 7% yield *via* the Horenstein–Pählicke condensation and in 25% yield *via* an ester change of γ-diethylaminopropyl alcohol with ethyl 1,2,3,10b-tetrahydrofluoranthene-10b-carboxylate. The chloroalkamines were synthesized according to published procedures. The quaternary methobromides were obtained by the conversion of the ester hydrochloride to the free base followed by the addition of methyl bromide under anhydrous conditions.

Pharmacological Activity.—The relative spasmolytic activities of the various esters as shown in Table I were determined in the intact cat by measuring the relaxation produced by the drug against spontaneous spasms.[9] The compounds were administered by the intravenous route. In most cases the methobromides were more potent than the corresponding hydrochloride.

Compound no. 4 has shown enough significant activity to warrant further pharmacological and clinical investigation.

(8) *H. Horenstein and H. Pahlicke, Ber.*, **71**, 1644 (1938).

(9) The pharmacological studies were carried out by Dr. C. C. Scott and his associates in the Department of Clinical Pharmacology of Warner-Chilcott Laboratories.

Experimental

1,2,3,10b-Tetrahydrofluoranthene.—A solution of 200 g. (1 mole) of fluoranthene in 4000 ml. of absolute alcohol was heated to 60° in a 12-liter flask fitted with a Hershberg stirrer. To this solution 1362 g. of 10% sodium amalgam (equivalent to 136.2 g., 5.93 moles of sodium) was added in about 200-g. portions. The temperature was maintained between 55–60°. After the addition was completed the reaction mixture was stirred for four hours at the same temperature. At the end of this time the reaction mixture was diluted with 1 liter of water and the solution adjusted to *p*H 4 with concentrated hydrochloric acid. The warm solution was then filtered to remove mercury and precipitated sodium chloride, and placed in the refrigerator overnight. The crystallized 1,2,3,10b-tetrahydrofluoranthene was filtered from the mother liquor and dried. This precipitate weighed 139.0 g., m.p. 72–73°.[10] The mother liquor was concentrated *in vacuo* to 1 liter. This solution on cooling yielded an additional 53.9 g. of product, m.p. 72–73°. The combined crops (94.6% yield) were used without further purification in the next step.

1,2,3,10b-Tetrahydrofluoranthene-10b-carboxylic Acid.—A mixture of 146 g. (3.7 moles) of sodamide (Farchan Laboratories) and 200 ml. of anhydrous toluene was placed in a 5-liter flask. A Hershberg stirrer was found to be the most satisfactory type for this reaction. The stirred contents was heated to 75° and an azeotropically dried solution of 700 g. (3.4 moles) of 1,2,3,10b-tetrahydrofluoranthene in 2000 ml. of toluene was added dropwise. There was an immediate evolution of ammonia and the reaction mixture became deep red. Nitrogen was bubbled through the reaction mixture during the course of the addition to aid in the removal of ammonia. The temperature was maintained at 75-90° and the addition was complete in 30 minutes. The reaction mixture was then refluxed for 3.5 hours at which time the evolution of ammonia had practically ceased. Dry carbon dioxide was then bubbled through the reaction mixture for two hours. Any other method of addition of carbon dioxide gave very poor yields. As the addition of carbon dioxide proceeded the reaction mixture lightened considerably in color. There was also a deposition of ammonium carbonate in the reflux condenser during the addition which occasionally had to be cleared. The heavy precipitate of the sodium salt of the acid was then removed by filtration and washed with 1 liter of ether. This sodium salt was air dried and subsequently slurried in 6 liters of water. The well stirred slurry was then acidified to *p*H 2 with 400 ml. of concentrated hydrochloric acid. The precipitated 1,2,3,10b-tetrahydrofluoranthene-10b-carboxylic acid was removed by suction filtration, and recrystallized from absolute methyl alcohol and decolorized with Norite A,

(10) Reported m.p. 74–75°, ref. 2.

yield 582 g. (69%), m.p. 189–191°. The toluene–ether filtrate was dried over calcium sulfate and then concentrated to dryness *in vacuo*. The residue was taken up in a minimum amount of ether. An ether-insoluble red crystalline material was filtered off. It did not melt at 360°. This is postulated to be a compound of the periflanthene type. The ether solution was evaporated to dryness and the residue recrystallized from ethyl alcohol. This unreacted, starting material weighed 62 g., m.p. 73–75°. There was no melting point depression with 1,2,3,10b-tetrahydrofluoranthene. The recovered material was reused in subsequent preparations.

Via **Lithium.**—Lithium ribbon (Metalloy Corp.), 3.0 g. (0.45 mole), was degreased and weighed under ether, cut into one cm. lengths and added in a stream of nitrogen to 150 ml. of absolute ether (dried over sodium) in a 500-ml. flask. The contents of the bath were chilled to −10° and a solution of 15.3 g. (0.17 mole) of butyl chloride in 50 ml. of ether was added dropwise. The butyl chloride was added over a 30-minute period at −10°. After the addition was complete 29.2 g. (0.14 mole) of 1,2,3,10b-tetrahydrofluoranthene was added in small portions. The reaction was mildly exothermic and there was an immediate evolution of butane. After refluxing for one hour, the reaction mixture was poured over powdered Dry Ice. The solution was then diluted with 200 ml. of water and extracted twice with ether to remove unreacted starting materials. The aqueous layer was acidified with 30% hydrochloric acid to precipitate the acid. The acid was filtered off and recrystallized with ethyl alcohol, 25.5 g. (72% yield).

β-Diethylaminoethyl 1,2,3,10b-Tetrahydrofluoranthene-10b-carboxylate.—A solution of 12 g. (0.05 mole) of 1,2,3,-10b-tetrahydrofluoranthene-10b-carboxylic acid in 90 ml. of anhydrous isopropyl alcohol was set to reflux. To this was added cautiously 6.5 g. (0.05 mole) of β-diethylaminoethyl chloride and the reaction mixture was refluxed for three hours. The ester hydrochloride which crystallized out on cooling the reaction mixture was filtered off and washed with isopropyl alcohol. It was obtained in 81% yield, m.p. 209.5–211°. A sample recrystallized from ethyl alcohol melted at 227–227.5°.

The other ester hydrochlorides excepting compound no. 11 were prepared in a like manner.

γ-Diethylaminopropyl 1,2,3,10b-Tetrahydrofluoranthene-10b-carboxylate.—A mixture of 26.3 g. (0.2 mole) of γ-diethylaminopropanol and 0.13 g. (0.005 mole) of sodium was heated in a dry flask for one hour. To the resulting solution 27.8 g. (0.1 mole) of ethyl 1,2,4,10b-tetrahydrofluoranthene-10b-carboxylate was added and the solution then refluxed for two hours at 160–170°. During this time the ethyl alcohol which was formed was collected through a short fractionating column. The residual solution was then distilled under 1 mm. pressure to remove excess γ-diethylaminopropanol. The residue was taken up in dry ether and acidified with 20% alcoholic hydrochloric acid using congo red as an indicator. The ester hydrochloride precipitated immediately. It was recrystallized from absolute ethanol; yield 6.6 g., m.p. 209–211°.

Methobromide of β-Diethylaminoethyl 1,2,3,10b-Tetrahydrofluoranthene-10b-carboxylate.—The ester hydrochloride was used without recrystallization. A mixture of 7.0 g. of the ester hydrochloride and 100 ml. of 5% sodium hydroxide was extracted with several portions of ether. The ether extract was dried over sodium sulfate and then the ether was removed *in vacuo*. The residual oil was taken up in 100 ml. of absolute ethyl alcohol and set to reflux under a Dry Ice condenser. Methyl bromide was led into the refluxing solution for 1.5 hours. The reaction mixture was then concentrated *in vacuo* and dry ether added. The precipitated, hygroscopic methobromide was removed by filtration, recrystallized from an alcohol–ether mixture and dried in an Abderhalden pistol at 100°. The dried material weighed 4 g. (50% yield), m.p. 157–159°.

The other methobromides were synthesized in a similar manner.

MORRIS PLAINS, NEW JERSEY

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT, FACULTY OF SCIENCE, CAIRO UNIVERSITY]

Action of Grignard Reagents. VI. (a) Cleavage by Organomagnesium and Lithium Compounds and by Lithium Aluminum Hydride; (b) Action of Phenyllithum on Phenanthraquinone and Benzil Monoximes

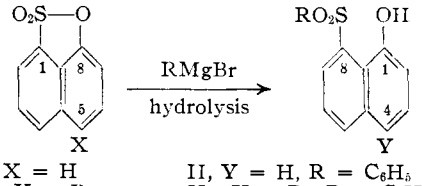
BY AHMED MUSTAFA, WAFIA ASKER, ORKEDE H. HISHMAT, AHMED F. A. SHALABY AND MOHAMED KAMEL

RECEIVED APRIL 5, 1954

Treatment with Grignard reagents, followed by hydrolysis, caused opening of the hetero ring in substituted 1,8-naphthosultones to give the corresponding derivatives of 8-arylsulfonyl-1-naphthol. Phenylmagnesium bromide also brought about cleavage of the N–S bond in N-arylsulfonyl derivatives, *e.g.*, N-diphenylsulfonylaniline, and cleavage of the N–C bond in N-aroyl derivatives, *e.g.*, N-dibenzoylaniline to give benzanilide and triphenylcarbinol. Similar results were obtained with phenyllithium. Hydrogenolysis with lithium aluminum hydride caused opening of the hetero ring of 1,8-naphthosultone and its substituted derivatives and of N-phenylsulfonylnaphthosultam to give the corresponding disulfides.

Organomagnesium Compounds.—Mustafa[1] has shown that Grignard reagents act upon 1,8-naphthosultone (I) and its substitution products to open the sultone ring, *i.e.*, to break the S–O linkage, with the formation of the corresponding 8-arylsulfonyl-1-naphthols (II); further investigation of this reaction has led to the synthesis of a number of new compounds as (I and II).

The constitution of the products was deduced from the fact that they are colorless, dissolve in aqueous alkali, contain active hydrogen and give a color reaction with ferric chloride; IIb and b′ form the corresponding methyl ethers with ethereal diazomethane.[2]



I, X = H
Ia, X = Br
Ib, X = $-CH_2Br$
Ic, X = $-CH_2Cl$
Id, X = CH_3

II, Y = H, R = C_6H_5
IIa, Y = Br, R = C_6H_5
IIa′, Y = Br, R = α-$C_{10}H_7$
IIb, Y = $CH_2C_6H_5$, R = C_6H_5
IIb′, Y = $CH_2C_{10}H_7$-α, R = α-$C_{10}H_7$

We have likewise found cleavage of the N–S linkage in N-diarylsulfonyl derivatives (IIIa-b) by Grignard reagents. N-Diphenylsulfonylaniline (IIIa) and N-di-(*p*-toluenesulfonyl)-α-naphthalamine (IIIb), treated with excess phenylmagnesium bromide, yield benzenesulfonanilide and diphenyl sulfone in the case of IIIa, and *p*-toluenesulfon-α-

(1) (a) A. Mustafa, *J. Chem. Soc.*, 2151 (1949); (b) A. Mustafa and M. K. Hilmy, *ibid.*, 1339 (1952); (c) A. Mustafa, *Chem. Revs.*, **54**, 195 (1954).

(2) A. Schönberg and A. Mustafa, *J. Chem. Soc.*, 605 (1948).