966. 12-*Benzyl-* and 12-*Alkyl*-6-*aminochrysenes.*

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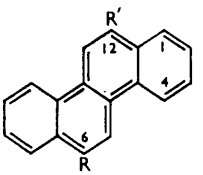
12-Benzyl-, 12-hexyl-, and 12-heptyl-6-aminochrysene have been synthesised for biological evaluation as antileukæmia agents. Several functional derivatives of these amines and other new substituted chrysenes were also prepared.

6-HEXYLCHRYSENE (I; $n = 4$) and 6-heptylchrysene (I; $n = 5$) were readily prepared by Wolff–Kishner reduction of 6-hexanoyl- and 6-heptanoyl-chrysene by the Huang-Minlon modification;[1] these two ketones were obtained in excellent yields, and free from isomers, by Friedel–Crafts acylation of chrysene in the presence of aluminium chloride in methylene chloride. 6-Heptanoylchrysene and its reduction-product had already



(I); R = H, R' = $CH_2 \cdot [CH_2]_n \cdot CH_3$
(II); R = NO_2, R' = $CH_2 \cdot [CH_2]_n \cdot CH_3$
(III); R = NH_2, R' = $CH_2 \cdot [CH_2]_n \cdot CH_3$
(IV); R = NO_2, R' = CH_2Ph
(V); R = NH_2, R' = CH_2Ph

been prepared by Carruthers and Cook[2] by Clemmensen's method, which gave less satisfactory results. Nitration of the hydrocarbons (I) with fuming nitric acid in acetic acid gave 12-hexyl-6-nitro- (II; $n = 4$) and 12-heptyl-6-nitro-chrysene (II; $n = 5$), reduced to the corresponding amines by use of hydrazine hydrate in the presence of Raney

[1] Huang-Minlon, *J. Amer. Chem. Soc.*, 1946, **68**, 2487.
[2] Carruthers and Cook, *J.*, 1954, 2047.

nickel, a procedure which, applied to 6-nitrochrysene, was more satisfactory than that described in the literature.[3]

Nitration of 6-benzylchrysene furnished, in addition to the expected 12-benzyl-6-nitrochrysene (IV), a substance of unknown structure. Reduction of the nitro-compound (IV) was also achieved with hydrazine hydrate and Raney nickel The *meso*-position of the amino-group was confirmed by oxidation of 6-acetamido-12-benzylchrysene with chromic acid to 12-benzylchrysene-5,6-quinone, also obtained by similar oxidation of 6-benzylchrysene, the main product in this case being 12-benzoylchrysene-5,6-quinone.[4]

Condensation with hexane-2,5-dione and phenacylacetone of the three 12-substituted 6-aminochrysenes readily gave the corresponding 1-6′-chrysenyl-2,5-dimethylpyrroles and -2-methyl-5-phenylpyrroles.

Preliminary biological investigations show that the aminochrysenes (III) possess antileukæmia activity in mice, whereas the pyrroles are inactive.

Experimental

6-*Hexanoylchrysene*.—To anhydrous methylene chloride (500 c.c.) were added, with stirring, finely powdered aluminium chloride (18 g.), hexanoyl chloride (17·5 g.), and a suspension of chrysene [5] (22 g.) in methylene chloride (300 c.c.). The dark greenish-brown solution was left for 2 hr. at room temperature and then refluxed for 7 hr. After cooling and decomposition with ice and hydrochloric acid, the organic layer was washed with dilute aqueous sodium hydroxide and then with water, and dried ($CaCl_2$). The residue, obtained by removal of solvent, was crystallised twice from ethanol (450 c.c.), giving shiny needles (26 g., 80%), m. p. 85°, whose solutions in sulphuric acid were orange-yellow (Found: C, 88·2; H, 6·6. $C_{24}H_{22}O$ requires C, 88·3; H, 6·8%).

6-Heptanoylchrysene was similarly prepared in 80% yield, and no isomers were isolated. The product crystallised as needles, m. p. 67°, from ethanol (lit.,[2] m. p. 66°).

6-*Hexylchrysene* (I; $n = 4$).—A mixture of 6-hexanoylchrysene (24·5 g.), hydrazine hydrate (95%; 24 g.), potassium hydroxide (20 g.), and diethylene glycol (750 c.c.) was refluxed for 5 hr. with removal of water. Cooling, dilution with water, and acidification with hydrochloric acid gave a precipitate, which was washed with water and recrystallised from ethanol. The product (23 g., 98·3%) had m. p. 87—88° (Found: C, 92·5; H, 7·5. $C_{24}H_{24}$ requires C, 92·3; H, 7·7%).

6-Heptylchrysene (I; $n = 5$), similarly prepared and in similar yield, crystallised as needles, m. p. 86°, from ethanol (lit.,[2] m. p. 83—84°).

12-*Hexyl*-6-*nitrochrysene* (II; $n = 4$).—To a suspension of 6-hexylchrysene (15·6 g.) in acetic acid (500 c.c.), a solution of fuming nitric acid (15 c.c., *d* 1·4) in acetic acid (100 c.c.) was added in one portion at 45° and with stirring. The precipitate that formed on cooling was collected, washed with acetic acid, water, and finally with ethanol, and recrystallised from ethanol–acetone (2 : 1 v/v). The golden-yellow leaflets (13 g., 73%), m. p. 111°, gave no halochromy in sulphuric acid (Found: C, 80·8; H, 6·6; N, 4·1. $C_{24}H_{23}NO_2$ requires C, 80·6; H, 6·5; N, 3·9%).

12-*Heptyl*-6-*nitrochrysene* (II; $n = 5$) was prepared from 6-heptylchrysene (13·1 g.) and fuming nitric acid (14 c.c., *d* 1·4) in acetic acid (500 c.c.); it crystallised as yellow needles (10 g.), m. p. 107°, from ethanol–acetone (Found: C, 80·9; H, 6·5; N, 3·8. $C_{25}H_{25}NO_2$ requires C, 80·8; H, 6·8; N, 3·8%).

6-*Amino*-12-*hexylchrysene* (III; $n = 4$).—To 12-hexyl-6-nitrochrysene (10·7 g.) in benzene–ethanol (1 : 1 v/v) hydrazine hydrate (98%; 10 g.) and Raney nickel (3 g.) were added (evolution of nitrogen). After 1 hour's refluxing the Raney nickel was filtered off and the filtrate concentrated (to 250 c.c.) and left overnight in the refrigerator. The cream-coloured needles (9·7 g., 98%) crystallised from ethanol–benzene with considerable loss but furnished almost colourless needles (6 g.), m. p. 135°. These gave no halochromy in sulphuric acid and darkened on exposure to light and heat (Found: C, 88·0; H, 7·7; N, 4·4. $C_{24}H_{25}N$ requires C, 88·0; H, 7·7; N, 4·3%). 6-*Acetamido*-12-*hexylchrysene*, prepared by refluxing for 3 min. a solution of

[3] Newman and Cathcart, *J. Org. Chem.*, 1940, **5**, 618.
[4] Funke and Ristic, *J. prakt. Chem.*, 1936, **146**, 151.
[5] Cf. Mabille and Buu-Hoï, *J. Org. Chem.*, 1960, **25**, 1937.

the foregoing amine (1·6 g.) and acetic anhydride (5 c.c.) in benzene (25 c.c.), crystallised as needles (1 g.), m. p. 215° (from toluene) (Found: C, 84·6; H, 7·2; N, 3·9. $C_{26}H_{27}NO$ requires C, 84·5; H, 7·4; N, 3·8%).

1-(12-*Hexyl*-6-*chrysyl*)-2,5-*dimethylpyrrole*.—A mixture of the corresponding amine (0·8 g.) and hexane-2,5-dione (0·8 g.) was heated at 130° for 30 min.; the brown oil obtained on cooling solidified on treatment with ethanol–acetone. Recrystallisation from ethanol furnished needles (0·3 g.), m. p. 133°, giving a yellowish-brown halochromy in sulphuric acid (Found: C, 88·9; H, 7·5; N, 3·7. $C_{30}H_{31}N$ requires C, 88·8; H, 7·7; N, 3·5%). 1-(12-*Hexyl*-6-*chrysyl*)-2-*methyl*-5-*phenylpyrrole*, similarly prepared from the amine (0·8 g.) and phenacylacetone (0·6 g.), crystallised as cream-coloured needles (0·3 g.), m. p. 138°, from ethanol, giving a yellow halochromy in sulphuric acid (Found: C, 89·7; H, 7·1; N, 3·1. $C_{33}H_{33}N$ requires C, 89·9; H, 7·1; N, 3·0%).

6-*Amino*-12-*heptylchrysene* (III; $n = 5$).—Prepared as for the lower homologue from 12-heptyl-6-nitrochrysene (9·27 g.), hydrazine hydrate (15 c.c.), and Raney nickel (3 g.), this *amine* crystallised from ethanol–benzene as needles (5·1 g.), m. p. 118°, darkening on exposure to light and heat (Found: C, 88·2; H, 7·8; N, 4·2. $C_{25}H_{27}N$ requires C, 87·9; H, 8·0; N, 4·1%).

6-*Acetamido*-12-*heptylchrysene* crystallised as prisms, m. p. 213° (acetone–benzene) (Found: C, 84·6; H, 7·6; N, 3·9. $C_{27}H_{29}NO$ requires C, 84·6; H, 7·6; N, 3·7%).

1-(12-*Heptyl*-6-*chrysyl*)-2,5-*dimethylpyrrole*.—Prepared from the amine (0·6 g.) and hexane-2,5-dione (0·7 g.), this *pyrrole* crystallised as shiny needles (0·4 g.), m. p. 128° (from ethanol) (Found: C, 88·4; H, 8·0; N, 3·5. $C_{31}H_{33}N$ requires C, 88·7; H, 7·9; N, 3·3%). 1-(12-*Heptyl*-6-*chrysyl*)-2-*methyl*-5-*phenylpyrrole*, obtained from the amine (0·6 g.) and phenacylacetone (0·8 g.), crystallised as prisms (0·1 g.), m. p. 130—131° (from acetone) (Found: C, 89·8; H, 7·0; N, 3·1. $C_{36}H_{35}N$ requires C, 89·8; H, 7·3; N, 2·9%).

Nitration of 6-*Benzylchrysene*.—To a suspension of 6-benzylchrysene (15·92 g.) in acetic acid (1 l.) at 40°, a solution of fuming nitric acid (15 c.c.) and sulphuric acid (1·5 c.c.) in acetic acid (200 c.c.) was added in one portion, with stirring. Stirring was continued for 30 min. at 40°, and after cooling, the precipitate was washed with acetic acid, then with water, giving a crude product (12 g.), m. p. 188—189°. Dilution of the filtrate with water and crystallisation from benzene yielded yellow needles (3 g.), m. p. 186—188°. The two crops were combined and crystallised, furnishing yellow prisms (12 g., 66%) of 12-*benzyl*-6-*nitrochrysene* (IV), m. p. 189°, which gave no halochromy in sulphuric acid (Found: C, 82·7; H, 4·6; N, 3·9. $C_{25}H_{17}NO_2$ requires C, 82·6; H, 4·7; N, 3·9%). Oxidation of 12-benzyl-6-nitrochrysene (3 g.) with sodium dichromate (15 g.) in acetic acid (220 c.c.) (14 hr. under reflux) afforded 12-nitrochrysene-5,6-quinone.[6]

6-*Amino*-12-*benzylchrysene* (V).—Reduction of 12-benzyl-6-nitrochrysene (5·44 g.) in ethanol (500 c.c.)–benzene (300 c.c.) by means of hydrazine hydrate (2·5 g.) and Raney nickel (3 g.) was complete after 5 hours' refluxing and gave a crude amine (4·5 g., 90%), m. p. 217°. Crystallisation from benzene gave prisms (3·3 g.), m. p. 218°. The ethanol or benzene solutions displayed a blue fluorescence, and the solutions in sulphuric acid were colourless (Found: C, 90·2; H, 5·9; N, 4·2. $C_{25}H_{19}N$ requires C, 90·1; H, 5·7; N, 4·2%). 6-*Acetamido*-12-*benzylchrysene* crystallised as short needles, m. p. 271° (from toluene) (Found: C, 86·5; H, 5·6; N, 3·6. $C_{27}H_{21}NO$ requires C, 86·4; H, 5·6; N, 3·7%).

1-(12-*Benzyl*-6-*chrysyl*)-2,5-*dimethylpyrrole*.—Prepared by refluxing for 30 min. a mixture of the corresponding amine (0·5 g.) and hexane-2,5-dione (1 g.), this *pyrrole* crystallised as cream-coloured needles (0·2 g.), m. p. 244—245°, from ethanol–benzene (Found: C, 90·2; H, 6·2; N, 3·5. $C_{31}H_{25}N$ requires C, 90·5; H, 6·1; N, 3·4%).

1-(12-*Benzyl*-6-*chrysyl*)-2-*methyl*-5-*phenylpyrrole*, obtained by heating for 20 min. at 180° a mixture of the amine (0·5 g.) and phenacylacetone, crystallised as cream-coloured needles (0·3 g.), m. p. 219—220°, from ethanol–benzene (Found: C, 91·3; H, 5·9; N, 3·0. $C_{36}H_{27}N$ requires C, 91·3; H, 5·7; N, 3·0%).

Oxidation of 6-*Acetamido*-12-*benzylchrysene*.—This compound (1 g.), sodium dichromate (3 g.), and acetic acid (85 c.c.) were refluxed for 150 min. then cooled and stored for 12 hr.; the precipitate was washed with acetic acid, and crystallised from toluene, giving 12-*benzylchrysene*-5,6-*quinone* (V) as needles (0·4 g.), m. p. 263—264° (decomp. >233—235° on prolonged heating), whose solutions in sulphuric acid were Indigo-blue (Found: C, 86·4; H, 4·7; O, 9·4. $C_{25}H_{16}O_2$

[6] Buu-Hoï, *J. Org. Chem.*, 1954, **19**, 1396.

requires C, 86·2; H, 4·6; O, 9·2%). The same compound (0·5 g.) was obtained by refluxing for 150 min. a mixture of 6-benzylchrysene (2 g.), sodium dichromate (6 g.), and acetic acid (80 c.c.). As a by-product, 12-benzoylchrysene-5,6-quinone was obtained, and characterised by its phenazine [yellowish prisms (from acetic acid), m. p. 222° (lit.,[7] m. p. 207°)], giving a violet halochromy in sulphuric acid. The *phenazine* corresponding to 12-benzylchrysene-5,6-quinone was prepared from the quinone (0·3 g.) and *o*-phenylenediamine (0·2 g.) in acetic acid; it crystallised as greenish-yellow needles (0·2 g.), m. p. 230° (from toluene), and gave, in sulphuric acid, an olive-green colour which rapidly turned blue (Found: C, 88·5; H, 4·8; N, 6·8. $C_{31}H_{20}N_2$ requires C, 88·5; H, 4·8; N, 6·7%).

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