717. *Some Polycyclic Derivatives of Selenophen.*

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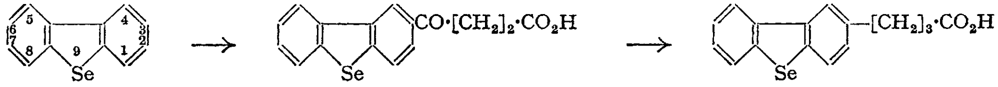
Syntheses are described of two isomeric 9-selenanaphthofluorenes, of two dibenzoselenaphenocarbazoles, and of two 9-selenafluorenocarbazoles, and various other selenafluorene derivatives, prepared for biological examination as potential carcinogens. The reactivity of 9-selenafluorene is compared with that of dibenzo-furan and -thiophen.

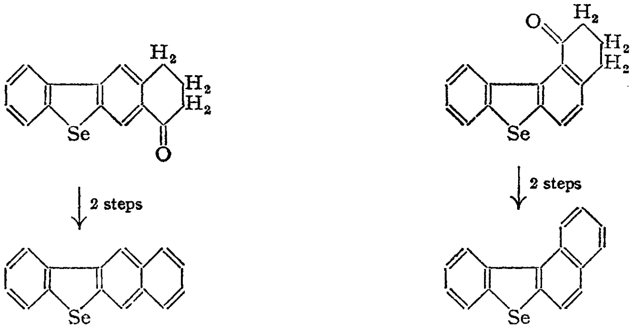
Although several heterocyclic compounds containing oxygen (Barry, Cook, Haslewood, Hewett, Hieger, and Kennaway, *Proc. Roy. Soc.*, 1935, *B*, **117**, 346; Buu-Hoï, *J.*, 1952, 489) and sulphur in a ring (Fieser and Sandin, *J. Amer. Chem. Soc.*, 1940, **62**, 3098; Tilak, 23rd Rep. Brit. Emp. Cancer Campaign, 1946, p. 109; Buu-Hoï and Hoán, *Rec. Trav. chim.*, 1948, **76**, 309; Buu-Hoï, Hoán, Khôi, and Xuong, *J. Org. Chem.*, 1949, **14**, 802; 1950, **15**, 957) have been tested for carcinogenic properties, very little is yet known about similar selenium compounds (Fieser and Hershberg, *J. Amer. Chem. Soc.*, 1941, **63**, 2561). Apart from their formal resemblance to carcinogenic hydrocarbons, such molecules would be of biological interest in view of the outstanding toxicity of cyclic selenium compounds already tested (cf. Buu-Hoï, *J.*, 1949, 2882). The present work deals with the preparation, from 9-selenafluorene (I), of several such compounds.

9-Selenafluorene (dibenzoselenophen), discovered by Courtot and Motamedi (*Compt. rend.*, 1934, **199**, 531), is more readily prepared by McCullough, Campbell, and Gould's procedure (*J. Amer. Chem. Soc.*, 1950, **72**, 5753) starting from 2-aminodiphenyl. The



(I) (II) (III)

Friedel–Crafts reaction of (I) with succinic anhydride, similarly to that of dibenzothiophen (Gilman and Jacoby, *J. Org. Chem.*, 1938, **3**, 108) gave the keto-acid (II) in excellent yield as sole product, whence Wolff–Kishner reduction readily gave γ-(9-selena-3-fluorenyl)-*n*-butyric acid (III). Cyclisation of the derived acid chloride resulted in a gummy ketonic product, although the equivalent sulphur-compound is known to have a high melting point. The consequent suspicion that a mixture of (IV) and (V) was present was confirmed

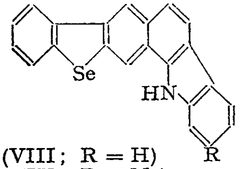


(IV) (V) (VI) (VII)

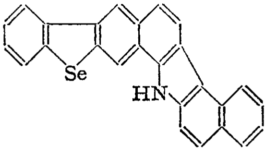
by Wolff–Kishner reduction and subsequent dehydrogenation with selenium to two crystalline 9-selenabenzofluorenes. By analogy, the higher-melting isomer should be 9-selena-2 : 3-benzofluorene (VI), an analogue of brasan (von Kostanekci and Lampe, *Ber.*, 1908, **41**, (2373) and of 2 : 3-benzothiophenanthrene (Mayer, *Annalen*, 1931, **488**, 259; Buu-Hoï and Cagniant, *Ber.*, 1943, **76**, 1269), and the lower-melting one should be the 3 : 4-benzo-compound (VII); similar observations had already been made with dibenzofuran and dibenzothiophen (Gilman and Jacoby, *loc. cit.*). Our inference was rigidly proved by conversion of the higher-melting isomer into 2-phenylnaphthalene by zinc and

Raney alloy powder. The two substances (VI) and (VII) are of interest for cancer research because of their structural relation to 1 : 2-benzanthracene, which is known to produce cirrhosis and hepatomas in rats when administered in the diet (White and Eschenbrenner, *Cancer Res.*, 1945, **5**, 594).

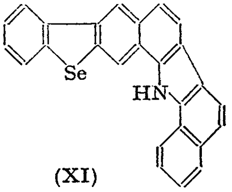
Within the framework of a general investigation into potential carcinogenic carbazoles, we have prepared some polycyclic selenium-containing carbazoles by the usual procedure (cf. Buu-Hoï, Hoân, and Khôi, *J. Org. Chem.*, 1949, **14**, 492), *viz.*, indolisation of the appropriate arylhydrazones of the ketone (IV) and dehydrogenation of the resultant dihydro-compounds by chloranil. Thus were prepared the two hexacyclic compounds (VIII) and (IX), and the two heptacyclic compounds (X) and (XI). In these syntheses, although the oily ketone mixture was used, only one carbazole was obtained in each instance, and the good yields showed that these carbazoles were derivatives of the major constituent (IV) of the ketone mixture.



(VIII; R = H)
(IX; R = Me)



(X)



(XI)

EXPERIMENTAL

γ-Keto-γ-(9-selena-3-fluorenyl)butyric Acid (II).—To an ice-cooled solution of 9-selenafluorene (54 g.) and succinic anhydride (26 g.) in redistilled nitrobenzene (400 c.c.), finely powdered aluminium chloride (64 g.) was added in small portions with stirring. The mixture was kept overnight at room temperature, then treated with dilute hydrochloric acid, and the nitrobenzene removed by steam-distillation. The greyish sticky residue was almost completely soluble in aqueous sodium carbonate; acidification with dilute hydrochloric acid yielded 72 g. of a solid *acid*, which crystallised as fine colourless needles, m. p. 153°, from benzene, giving an orange colour with sulphuric acid (Found : C, 57·8; H, 3·7. $C_{16}H_{12}O_3Se$ requires C, 58·0; H, 3·6%).

γ-(9-Selena-3-fluorenyl)butyric Acid (III).—A mixture of the foregoing acid (65 g.), 90% hydrazine hydrate (60 g.), potassium hydroxide (70 g.), and diethylene glycol (250 c.c.) was heated with removal of water up to 190—195°, and refluxed for 2 hours. After cooling, the mixture was diluted with water, and acidified with dilute hydrochloric acid. The semi-solid precipitate was taken up in benzene, the solution washed with water, dried (Na_2SO_4), freed from solvent, and the residue fractionated *in vacuo*, yielding the *acid* (52 g.), b. p. 235—240°/0·5 mm., which crystallised as fine, colourless needles, m. p. 119°, from benzene–ligroin (Found: C, 60·4; H, 4·6. $C_{16}H_{14}O_2Se$ requires C, 60·6; H, 4·4%). The corresponding acid chloride [from the acid (45 g.) and thionyl chloride (19 g.)] gave with β-naphthylamine in pyridine the corresponding β-naphthylamide, crystallising in shiny grey-tinged needles, m. p. 217° (decomp.), from chlorobenzene; the 4-diphenylylamide crystallised as fine, grey-tinged needles, m. p. 238° (decomp.), from chlorobenzene.

Cyclisation of the Acid (III).—An ice-cooled solution of the foregoing crude acid chloride (47 g.) in carbon disulphide (250 c.c.) was treated with aluminium chloride (22 g.), and the mixture kept overnight and worked up in the usual way. The pale yellow, viscous oily product (38 g.) failed to crystallise (Found : C, 64·1; H, 4·1. Calc. for $C_{16}H_{12}OSe$: C, 64·2; H, 4·0%). A well crystalline *semicarbazone* formed colourless microscopic needles, m. p. 285° (decomp.), from toluene (Found: N, 11·5. $C_{17}H_{15}ON_3Se$ requires N, 11·8%). The corresponding compound in the dibenzothiophen series had m. p. 280—282° (Mayer, *loc. cit.*). Crystallised chalkone-type compounds were also obtained by condensation with various aromatic aldehydes in the presence of potassium hydroxide; the *p*-chlorobenzylidene derivative formed pale yellow needles, m. p. 220°, from ethanol, giving a brown-red colour with sulphuric acid; the 2 : 4- and 3 : 4-dichlorobenzylidene derivatives showed similar properties; with the piperonylidene compound, the colour with sulphuric acid was deep violet.

The 9-Selenabenzofluorenes (VI) *and* (VII).—The ketonic mixture (10 g.), 90% hydrazine hydrate (25 g.), and potassium hydroxide (25 g.) in diethylene glycol (100 c.c.) were heated with removal of water to 195—200°, and refluxed for 2 hours. After the solution had cooled, water was added, and the mixture of (IV) and (V) thus obtained was taken up in benzene and yielded, by vacuum-distillation, a viscous, pale yellow oil (95%), b. p. 202—203°/0·6 mm., which partly solidified (Found: C, 67·1; H, 5·1. Calc. for $C_{16}H_{14}Se$: C, 67·4; H, 4·9%). Total separation of the two isomers was not attempted, and this material (6 g.) was heated with selenium powder (3 g.) at 350° for 3 hours. After cooling, the solid mass obtained was taken up in ether, and purified by vacuum-distillation (b. p. 228—230°/0·6 mm.). Fractional crystallisation from ethanol gave the less soluble 9-*selena*-2 : 3-*benzofluorene* (VI) as large, shiny, colourless, sublimable leaflets (3 g.), m. p. 191° (the corresponding sulphur-compound had m. p. 163°) (Found: C, 68·0; H, 3·5. $C_{16}H_{10}Se$ requires C, 68·3; H, 3·6%), and 9-*selena*-3 : 4-*benzofluorene* (VII) (0·8 g.) as large, shiny, colourless leaflets, m. p. 95° (Found: C, 68·4; H, 3·6%); the corresponding picrates formed needles, m. p. 159° (from ethanol) and m. p. 137° respectively. Distillation of (VI) (1 part) with a mixture of zinc and Raney alloy powder (5 parts) yielded 2-phenylnaphthalene, m. p. 101° alone or mixed with a sample prepared otherwise.

Carbazole Syntheses.—In this and the following carbazole syntheses, no attempt was made to isolate the small amounts of the theoretically expected isomeric carbazole. The carbazoles were obtained by heating the crude arylhydrazones with a saturated solution of hydrogen chloride in acetic acid and working up the product in the usual way. 9′-*Selenafluoreno*(2′ : 3′-1 : 2)*carbazole* (VIII) formed fine sublimable, colourless needles, m. p. 336°, from benzene, giving with sulphuric acid a brown colour which rapidly became green (Found: C, 71·6; H, 3·5. $C_{22}H_{13}NSe$ requires C, 71·3; H, 3·5%). Its 6-*methyl* derivative (IX), obtained by *p*-tolylhydrazine, etc., formed fine, sublimable, colourless needles, m. p. >340°, from benzene (Found: C, 72·2; H, 4·0. $C_{23}H_{15}NSe$ requires C, 71·8; H, 3·9%).

9-*Selena*-5′ : 6′-*benzocarbazolo*(1′ : 2′-2 : 3)*fluorene* (X), prepared from β-naphthylhydrazine, formed yellowish, sublimable needles, m. p. >340°, from benzene, giving a violet-brown colour with sulphuric acid (Found: C, 74·5; H, 3·6. $C_{26}H_{15}NSe$ requires C, 74·3; H, 3·5%). Its 7′ : 8′-*benzo*-analogue (XI) formed fine, grey-tinged needles, decomp. >300°, from benzene (Found: C, 74·6; H, 3·5%).

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