1089. *Tautomerism of 2-Iminoselenazolidin-4-ones.*

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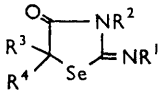
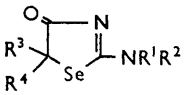
Spectroscopic comparison with *N*-alkyl derivatives unambiguously related to 2-iminoselenazolidin-4-one and 2-amino-2-selenazolin-4-one shows that the cyclized products from α-halogeno-carboxylic acids and selenourea have the 2-imino-structure in aqueous solution.

Condensation of α-halogeno-carboxylic acids and selenourea gives products which are potentially capable of exhibiting imino–amino-tautomerism (I $\rightleftharpoons$ II) and have been designated as either 2-iminoselenazolidin-4-ones [1] (I) or 2-amino-2-selenazolin-4-ones [2] (II). To establish which tautomeric form predominates, several compounds unequivocally related to the imino- (I) and the amino-form (II) were prepared for spectroscopic comparison. Amide–imide tautomerism was excluded, since all compounds with a hydrogen atom attached to the 3- or the 5-position were transparent in the 3400 cm.$^{-1}$ region.

[1] Hofmann, *Annalen*, 1889, **250**, 312.
[2] Zingaro, Bennett, and Hamar, *J. Org. Chem.*, 1953, **18**, 292.

Instead, strong absorption at about 1750 attributable to the ring-carbonyl,[3] and 1630 cm.$^{-1}$ (cf. ref. 4) was observed in every case, including 5,5-dimethyl-2-dimethylamino-2-selenazolin-4-one (II; all R's = Me) in which O–H stretching is not possible.


(I)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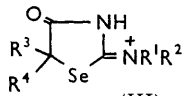
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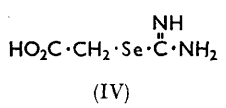
(IV)

Condensation of *NN*-dimethylselenourea with chloroacetic acid gave 2-dimethylamino-2-selenazolin-4-one [2] (II; R′ = R^2 = Me, R^3 = R^4 = H), which is undoubtedly related to structure (II). Similarly, compounds unambiguously related to structure (I) were obtained from *NN*′-diethylselenourea [2] and α-halogeno-carboxylic acids. Since the influence of alkyl groups on the wavelengths and intensity of ultraviolet absorptions is negligible,[5] these compounds were used for spectroscopic comparison with the condensation products from α-halogeno-carboxylic acids and selenourea. The 2-iminoselenazolidin-4-ones (I) showed a characteristic absorption maximum about 225 mμ, while the 2-amino-2-selenazolin-4-ones (II) absorbed about 243 mμ (see Table). The derivatives from selenourea absorbed about 225 mμ and must, therefore, exist in the imino-form (I) in aqueous solution. The corresponding oxygen analogues exist primarily in the amino-form,[6,7] but the sulphur analogues are probably better formulated as 2-imino-compounds.

Ultraviolet spectra of selenazolidin-4-ones (I) and 2-selenazolin-4-ones (II) in water.

R^1	R^2	R^3	R^4	$\lambda_{max.}$ (mμ)	ε	R^1	R^2	R^3	R^4	$\lambda_{max.}$ (mμ)	ε
			Selanazolidinones (I)						*Selenazolidinones* (I)		
H	H	H	H	227	17,600	Et	Et	Ph	H	224 *	20,300 *
H	H	H	Me	227	22,000	H	Me	Et	H	227	22,100
H	H	H	Et	228	18,600						
H	H	H	Ph	225	17,100				*Selenazolinones* (II)		
Et	Et	H	H	225	22,100	Me	Me	H	H	242	18,200
Et	Et	Et	H	225	12,000	Me	Me	Et	H	243	19,000
						Me	Me	Me	Me	243	18,600
						Ac	H	H	H	244	22,100

* In aqueous ethanol containing an equivalent amount of hydrochloric acid.

The wavelength of the peak absorption of the 2-iminoselenazolidin-4-ones at 225 mμ was not affected at low pH, but a hyperchromic effect was produced and a small shoulder or peak appeared about 265 mμ. A similar hyperchromic effect is observed with pyridine and picolines and has been ascribed to protonation of the lone pair of electrons of the nitrogen atom.[8] However, the peak shown by 2-dimethylamino-2-selenazolin-4-one at 242 mμ underwent a hypsochromic shift at low pH and the spectrum then resembled that of the 2-imino-compounds, probably owing to formation of the cation (III) (R^1 = R^2 = Me). This indicates protonation of the doubly bonded nitrogen in both series of compounds and is consistent with the behaviour of cyclic amidines.[9]

As with its sulphur analogue,[10] formation of 2-iminoselenazolidin-4-one (I) proceeds through an acyclic intermediate, in this case, the hydrochloride of isoselenohydantoic acid (IV) which cyclizes in boiling ethanol to 2-iminoselenazolidin-4-one and in water to selenazolidine-2,4-dione. Acetylation of 2-iminoselenazolidin-4-one gave a product with a

[3] Pianka and Poulton, *J.*, 1960, 983.
[4] Bellamy, " The Infra-red Spectra of Complex Molecules," Methuen, London, 1954, p. 227.
[5] Katritzsky and Lagowski, " Heterocyclic Chemistry," Methuen, London, 1960, p. 257.
[6] Howell, Quinones, and Hardy, *J. Org. Chem.*, 1962, **27**, 1686.
[7] Najer, Giudicelli, Menin, and Loiseau, *Bull. Soc. chim. France*, 1962, 1186.
[8] Jaffe and Orchin, " Theory and Application of Ultraviolet Spectroscopy," Wiley, London, 1962.
[9] Angyal and Angyal, *J.*, 1952, 1461.
[10] Ray and Fernandes, *J.*, 1914, 2159; Desai, Hunter, and Koppar, *Rec. Trav. chim.*, 1935, **54**, 118.

maximum at 224 mμ (Table), which was, therefore, 2-acetamido-2-selenazolin-4-one (II; R^1 = Ac, R^2 = R^3 = R^4 = H). Acetylation of the sulphur analogue takes the same course.[11] Alkylation of 2-iminoselenazolidin-4-one failed to give a pure product but its 5-ethyl derivative (I; R^3 = Et, R^1 = R^2 = R^4 = H) with methyl iodide gave 5-ethyl-2-imino-3-methylselenazolidin-4-one (I; R^1 = R^3 = H, R^2 = Me, R^4 = Et) as shown by its absorption maximum at 227 mμ (Table). Alkylation of the ring-nitrogen atom was confirmed by acid hydrolysis of this product to 5-ethyl-3-methylselenazolidine-2,4-dione. Rearrangement during hydrolysis[12] was excluded since the latter was obtained directly from 5-ethylselenazolidine-2,4-dione and methyl iodide.

Nucleophilic reactivity of the methylene-carbon atom is enhanced by an electron-withdrawing group in the 2-position.[13] Thus selenazolidine-2,4-dione and 2-acetamido-2-selenazolin-4-one readily gave benzylidene derivatives with benzaldehyde in presence of acetic anhydride and sodium acetate, but 2-iminoselenazolidin-4-one did not react. With 3-ethyl-2-ethyliminoselenazolidin-4-one (I; R^1 = R^2 = Et, R^3 = R^4 = H) decreased nucleophilic activity was overcome by using the stronger basic catalyst,[14] sodium hydroxide, to give the anion necessary for formation of the 5-benzylidene derivative.[15] Acid-hydrolysis of 2-iminoselenazolidin-4-ones gave the selenazolidine-2,4-diones, but the 2-ethylimino-compounds were unchanged after several days in boiling 50% sulphuric acid. Nucleophilic replacement of the ethylimino-group, giving the 2,4-dione, took place smoothly with 5-benzylidene-3-ethyl-2-ethylimino-4-selenazolidinone (I; R^1 = R^2 = Et, R^3R^4 = Ph·CH:).

Dissolution of selenazolidin-4-ones in cold sodium hydroxide gave 1,3-diethylurea. 3-Phenyl-2-phenyliminothiazolidin-4-one similarly gave 1,3-diphenylurea.[16]

Experimental

Selenium was determined spectrophotometrically.[17]

Isoselenohydantoic Acid Hydrochloride (cf. IV).—Selenourea (1·20 g.) and chloroacetic acid (2·3 g.) were suspended in acetone (50 ml.) and kept at room temperature for 48 hr. The crude solid (2·4 g.) was carefully separated by elutriation from grey selenium, washed with acetone, and dried in a vacuum, to give the *product*, m. p. 168—170° (decomp.) (Found: Cl, 16·1; N, 13·15; Se, 38·7. $C_3H_7ClN_2O_2Se$ requires Cl, 16·7; N, 12·9; Se, 36·3%) [*picrate*, needles m. p. 158° (from ethanol) (Found: N, 16·7; Se, 19·5%; *M*, 415.[18] $C_9H_9N_5O_9Se$ requires N, 17·1; Se, 19·2%; *M*, 410)].

2-*Iminoselenazolidin-4-one Hydrochloride* (cf. I).—(*a*) Selenourea (5·0 g.) and chloroacetic acid (3·84 g.) were refluxed together in ethanol (20 ml.) for 30 min. and the hot solution was filtered and cooled. The solid (4·1 g.) that separated crystallised from ethanol, giving the *hydrochloride* as needles, m. p. 220—224° (decomp.) (Found: Cl, 17·6; N, 14·3; Se, 39·4. $C_3H_5ClN_2OSe$ requires Cl, 17·8; N, 14·05; Se, 39·6%).

(*b*) Isoselenohydantoic acid hydrochloride, when refluxed in ethanol, gave 2-iminoselenazolidin-4-one hydrochloride m. p. 219—221° (decomp.) [*picrate*, m. p. 182—184° (from methanol) (Found: N, 17·6; Se, 20·2. $C_9H_7N_5O_8Se$ requires N, 17·85; Se, 20·1%)].

2-*Acetamido-2-selenazolin-4-one* (II; R^1 = Ac, R^2 = R^3 = R^4 = H).—2-Iminoselenazolidin-4-one hydrochloride (0·81 g.) was heated on a water-bath with acetic acid (5 ml.) and acetic anhydride (5 ml.) until dissolved. Concentration and cooling gave the *acetyl derivative* (0·73 g.), m. p. 236—240° (decomp.) (from aqueous ethanol) (Found: N, 13·7; Se, 38·3. $C_5H_6N_2O_2Se$ requires N, 13·7; Se, 38·5%) [*picrate*, m. p. 203—204° (decomp.) (from ethanol) (Found: N, 16·4; Se, 18·3. $C_{11}H_9N_5O_9Se$ requires N, 16·1; Se, 18·2%)].

2-*Acetamido-5-benzylidene-2-selenazolin-4-one* (II; R^1 = Ac, R^2 = H, R^3R^4 = Ph·CH:).—2-Acetamido-2-selenazolin-4-one (1·04 g.), benzaldehyde (1·06 g.), acetic acid (3 ml.), and acetic

[11] Jap.P. 7811/1958 (*Chem. Abs.*, 1960, **54**, 4620).
[12] Wheeler and Johnson, *Amer. Chem. J.*, 1902, **28**, 121.
[13] Knott, *J.*, 1954, 1482.
[14] Davis and Dains, *J. Amer. Chem. Soc.*, 1935, **57**, 2627.
[15] Brown, Jones, and Kent, *Canad. J. Chem.*, 1963, **41**, 817.
[16] Lange, *Ber.*, 1879, **12**, 595.
[17] Dingwall and Williams, *J. Pharm. Pharmacol.*, 1961, **13**, 12.
[18] Cunningham, Dawson, and Spring, *J.*, 1951, 2305.

anhydride (0·5 ml.) were refluxed together for 45 min. at 150—160°. Water was added dropwise to the cooled mixture, giving the *5-benzylidene derivative* (0·54 g.) as yellow needles m. p. 270—285° (decomp.) (from ethanol) (Found: N, 9·55; Se, 27·1. $C_{12}H_{10}N_2O_2Se$ requires N, 9·6; Se, 26·9%).

2-Imino-5-methylselenazolidin-4-one Hydrobromide.—Condensation of selenourea (1·3 g.) and α-bromopropionic acid (1·51 g.) as above gave the *hydrobromide* (1·45 g.) m. p. 178—180° (decomp.), as needles (from ethanol–ether) (Found: C, 19·3; H, 3·0; Br, 30·8; N, 11·0; Se, 30·8. $C_4H_7BrN_2OSe$ requires C, 18·6; H, 2·7; Br, 30·6; N, 10·9; Se, 30·6%) [*picrate*, m. p. 192—194° (from aqueous ethanol) (Found: N, 17·2; Se, 19·2. $C_{10}H_9N_5O_8Se$ requires N, 17·25; Se, 19·4%)].

5-Ethyl-2-iminoselenazolidin-4-one Hydrobromide.—Condensation of selenourea (1·23 g.) and α-bromobutyric acid (1·67 g.) gave the *hydrobromide* (2·3 g.) m. p. 220—224° (decomp.) (from ethanol) (Found: C, 22·3; H, 3·3; Br, 29·55; N, 10·2; Se, 29·0. $C_5H_9BrN_2OSe$ requires C, 22·1; H, 3·3; Br, 29·4; N, 10·3; Se, 29·0%). Neutralization of an aqueous solution of the hydrobromide with ammonia gave *5-ethyl-2-iminoselenazolidin-4-one* m. p. 178—180° (decomp.) (Found: N, 15·0; Se, 40·9. $C_5H_8N_2OSe$ requires N, 14·7; Se, 41·3%) [*picrate*, m. p. 186—188° (from methanol) (Found: N, 16·5; Se, 18·6. $C_{11}H_{11}N_5O_8Se$ requires N, 16·7; Se, 18·8%)].

2-Imino-5-phenylselenazolidin-4-one (I; $R^1 = R^2 = R^4 = H$, $R^3 = Ph$).—Condensation of selenourea (1·3 g.) and α-chloro-α-phenylacetic acid (1·73 g.) as above gave the *product* (1·46 g.), m. p. 200—204° (decomp.) (from aqueous ethanol) (Found: N, 11·6; Se, 32·6. $C_9H_8N_2OSe$ requires N, 11·7; Se, 33·0%).

3-Ethyl-2-ethyliminoselenazolidin-4-one Hydrochloride.—*NN'*-Diethylselenourea (1·8 g.) and chloroacetic acid (0·96 g.) were refluxed together in ethanol (20 ml.) for 1 hr., then cooled, filtered, and evaporated to dryness. The residue, recrystallized from ethanol–ether, gave the *hydrochloride* (1·7 g.), m. p. 179—180° (Found: C, 33·3; H, 5·1; N, 11·05. $C_7H_{13}ClN_2OSe$ requires C, 32·9; H, 5·1; N, 11·0%). The *base*, m. p. 50—51° (from water), was liberated from the hydrochloride by ammonia (Found: C, 38·9; H, 5·55; N, 12·6. $C_7H_{12}N_2OSe$ requires C, 38·35; H, 5·5; N, 12·8) [*picrate*, m. p. 102—104° (from methanol–ether) (Found: N, 15·7. $C_{13}H_{15}N_5O_8Se$ requires N, 15·6%)].

3,5-Diethyl-2-ethyliminoselenazolidin-4-one Hydrobromide.—*NN'*-Diethylselenourea (1·8 g.) and α-bromobutyric acid (1·7 g.) were refluxed in ethanol as above, to give the *hydrobromide* (2·4 g.), m. p. 154—156° (from ethanol–ether) (Found: C, 33·1; H, 5·4; N, 8·6. $C_9H_{17}BrN_2OSe$ requires C, 32·9; H, 5·2; N, 8·5%). The *base* was obtained as a colourless oil, n_D^{20} 1·5316, on neutralization of the hydrobromide with ammonia and extraction into ether (Found: C, 44·1; H, 7·0; N, 10·85. $C_9H_{16}N_2OSe$ requires C, 43·7; H, 6·5; N, 11·3%).

3-Ethyl-2-ethylimino-5-phenylselenazolidin-4-one (I; $R^1 = R^2 = Et$, $R^3 = Ph$, $R^4 = H$).—*NN'*-Diethylselenourea (1·8 g.) and α-chloro-α-phenylacetic acid (1·71 g.) were refluxed together in ethanol as above and the solvent removed under reduced pressure. The residue was basified with ammonia and extracted with ether (2 × 20 ml.). The extract was dried (Na_2SO_4) and the ether removed. The *product* (0·74 g.), m. p. 96—97°, was obtained as plates on crystallizing the residue from aqueous ethanol (Found: C, 53·7; H, 5·8; N, 9·25. $C_{13}H_{16}N_2OSe$ requires C, 52·9; H, 5·45; N, 9·5%) [*picrate*, m. p. 167—168° (from methanol) (Found: C, 44·3; H, 3·5; N, 13·5. $C_{19}H_{19}N_5O_8Se$ requires C, 43·5; H, 3·6; N, 13·4%)].

5-Benzylidene-3-ethyl-2-ethyliminoselenazolidin-4-one.—3-Ethyl-2-ethyliminoselenazolidin-4-one (0·219 g.) was dissolved in ethanol (10 ml.), and benzaldehyde (0·106 g.) was added. Two drops of 20% aqueous sodium hydroxide were added and the mixture was heated till only a faint smell of benzaldehyde remained (*ca.* 2 min.). The *product* (0·24 g.) was precipitated by addition of water (20 ml.) and recrystallized as plates, m. p. 63—64°, from aqueous ethanol (Found: C, 55·0; H, 5·1; N, 8·8. $C_{14}H_{16}N_2OSe$ requires C, 55·2; H, 5·3; N, 9·1%) [*picrate*, m. p. 195—196° (from methanol) (Found: C, 44·45; H, 3·5; N, 12·9. $C_{20}H_{19}N_5O_8Se$ requires C, 44·8; H, 3·6; N, 13·1%)].

5-Benzylidene-3-ethylselenazolidine-2,4-dione.—5-Benzylidene-3-ethyl-2-ethyliminoselenazolidin-4-one (0·25 g.) was heated for 16 hr. under reflux in concentrated hydrochloric acid (10 ml.) and allowed to cool. Ether (20 ml.) was poured through the condenser, and the acid solution was extracted with ether (2 × 20 ml.). The combined ether extracts were evaporated. The residue recrystallized from water, to give the *dione* (0·16 g.), m. p. 104—105° (Found: C, 51·8; H, 4·2; N, 4·9. $C_{12}H_{11}NO_2Se$ requires C, 51·4; H, 4·0; N, 5·0%).

5-Ethyl-2-imino-3-methylselenazolidin-4-one Hydriodide.—5-Ethyl-2-iminoselenazolidin-4-one

(0·41 g.) and methyl iodide (1 ml.) were refluxed together in ethanol (5 ml.) for 1 hr. Concentration and cooling gave the *hydriodide* (0·44 g.), m. p. 223° (decomp.) (from ethanol) (Found: I, 30·8; N, 8·4; Se, 23·3. $C_6H_{11}IN_2OSe$ requires I, 31·8; N, 8·4; Se, 23·7%) [*picrate*, m. p. 192—194° (from methanol) (Found: N, 16·2; Se, 18·4. $C_{12}H_{13}N_5O_8Se$ requires N, 16·1; Se, 18·2%)]. The hydriodide, when refluxed with dilute hydrochloric acid for 2 hr., gave 5-ethyl-3-methylselenazolidine-2,4-dione (infrared spectrum identical with authentic material below).

3-*Methylselenazolidine*-2,4-*dione*.—(*a*) Selenazolidine-2,4-dione (1·14 g.), potassium hydroxide (0·44 g.), and methyl iodide (5 ml.) were heated together in ethanol (15 ml.) for 2 hr. The mixture was concentrated, water (10 ml.) added, and the mixture was extracted with ether (3 × 20 ml.). Removal of the ether left an oil which was dried in a vacuum and distilled, giving the *dione* as an alliaceous yellow oil, b. p. 64°/0·8 mm., which very slowly solidified to a waxy solid, m. p. 33° (Found: N, 7·6; Se, 44·1. $C_4H_5NO_2Se$ requires N, 7·9; Se, 44·35%).

(*b*) Methylation of 2-iminoselenazolidin-4-one as above and hydrolysis without further purification of the product gave the dione, identical with the product obtained as in method (*a*).

5-*Ethyl*-3-*methylselenazolidine*-2,4-*dione*.—5-Ethylselenazolidine-2,4-dione similarly gave 5-*ethyl*-3-*methylselenazolidine*-2,4-*dione* in 76% yield as a yellow alliaceous oil, b. p. 82°/1 mm., n_D^{21} 1·5349 (Found: N, 6·9; Se, 38·05. $C_6H_9NO_2Se$ requires N, 6·8; Se, 38·2%).

5,5-*Dimethyl*-2-*dimethylamino*-2-*selenazolin*-4-*one* (II; all R's = Me) *Hydrobromide*.—α-Bromo-α-methylpropionic acid (2·31 g.) and *NN*-dimethylselenourea (2·1 g.) were refluxed together in ethanol for 1 hr. The *product* (1·95 g.) was precipitated by ether and recrystallized in yellow plates, m. p. 230—232° (decomp.) (from ethanol–ether) (Found: Br, 27·1; N, 9·35; Se, 25·8. $C_7H_{13}BrN_2OSe$ requires Br, 26·6; N, 9·3; Se, 26·3% [*picrate*, m. p. 156—157° (from water) (Found: N, 15·4; Se, 17·2). $C_{13}H_{15}N_5O_8Se$ requires N, 15·6; Se, 17·6%].

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