366. *Naphthimidazoles. Part III.*[1] *Some* 6,7,8,9-*Tetrahydronaphth*[1,2]*imidazoles.*

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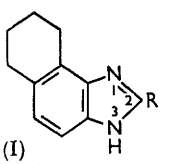
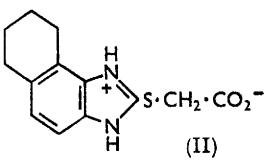
The first members of the angular 6,7,8,9-tetrahydronaphthimidazole series are reported. They include the unsubstituted parent compound, its 3-methyl and some 2-substituted derivatives. In ionization and ultraviolet spectra they all closely resemble the linear isomers described in Part II.[1]

Although the angular naphthimidazoles are fairly well known,[2] no members of the corresponding tetrahydro-series have been described. The parent compound (I; R = H) and a selection of 2-substituted derivatives have therefore been prepared for comparison with a similar series of linear tetrahydronaphthimidazoles recently reported.[1]

Angular tetrahydronaphthimidazole and its 2-methyl derivative were best prepared by the action of formic (or acetic) acid on 5,6,7,8-tetrahydronaphthalene-1,2-diamine in aqueous hydrochloric acid. 5,6,7,8-Tetrahydro-N^2-methylnaphthalene-1,2-diamine, made by methylation of the 2-amino-1-nitro-compound [3] followed by reduction, similarly condensed with formic acid to give the 3-methyl derivative of the imidazole (I). Methylation of the parent compound with dimethyl sulphate gave a mixture which was separated



(I)



(II)

by paper chromatography. One constituent was identical with the 3-methyl derivative above (paper chromatography in two solvents, and comparative ultraviolet spectrum in alcohol), but the other was unidentified. Fusion of 5,6,7,8-tetrahydronaphthalene-1,2-diamine with urea gave the 2-hydroxy-, and with thiourea, the 2-mercapto-derivative of the imidazole. Methylation of the latter produced tetrahydro-2-methylthionaphthimidazole (I; R = SMe), and sodium chloroacetate gave the 2-carboxymethylthio-analogue (II). Phosphoryl chloride converted the tetrahydrohydroxynaphthimidazole into the corresponding chloro-compound, which showed remarkable stability in withstanding boiling concentrated hydrochloric acid. The anilino- and the 2-dimethylamino-derivative were made from it with, respectively, aniline and aqueous dimethylamine, but with methylamine

[1] Part II, *J.*, 1959, 3332.
[2] Bibliography by Brown in "Current Trends in Heterocyclic Chemistry," Butterworths, London, 1958, p. 75.
[3] Schroeter, *Annalen*, 1922, **426**, 17.

no reaction occurred. As in the linear series, the 2-amino-compound was best prepared from the tetrahydronaphthalenediamine with cyanogen bromide.[4]

The pK_a values of the angular tetrahydronaphthimidazoles closely resemble those of their linear analogues.[1] As in that series, the parent compound is distinctly more basic (pK_a 6) than is the fully aromatic naphth[1,2]imidazole[5] (5·3), and approximates to dimethylbenzimidazole[1] (6·1). In the carboxymethylthio-derivative, the strongly acidic grouping must increase the basic strength of the nucleus,[6] so that the molecule is best represented as the zwitterion (II). This, moreover, should be stabilised by resonance with the form carrying a positive charge at position 3. The pK_a values are therefore recorded as loss of a first and a second proton from (II). No figure for gain of a proton could be obtained, because low solubility precluded potentiometry, and little spectral change occurred on lowering of the pH.

The ultraviolet spectra (see Table) of the parent compound (I; R = H) are similar to those of the linear analogue[1] but the peaks have been displaced some 5—10 mμ to shorter wavelengths, and the absorption is noticeably lower, except for the peak at <250 mμ, which is higher. These changes are almost exactly repeated in comparing all the angular and linear derivatives.

R in compound (I)	pK_a (20°) [a]	pH	$\lambda_{max.}$ (mμ) [c]	log ε
H		8·5	281, 273, 248	3·55, 3·55, 3·77
cation	5·99 ± 0·04	2·9	280, 272	3·64, 371
anion	*ca.* 12·8 [b]			
NMe_2		10·0	293, 250	3·99, 3·90
cation	7·58 ± 0·04	4·5	288	4·00
OH		8·8	285	3·72
anion	*ca.* 13 [b]			
Cl		6·7	283, 276, 247	3·76, 3·74, 3·83
cation	2·58 ± 0·02	−0·7	284, 277, 224	3·90, 3·93, 4·23
SMe		8·0	293, 285	4·13, 4·11
cation	*ca.* 4·7 [b]	1·0	294, 286	4·24, 4·20
$S{\cdot}CH_2{\cdot}CO_2H$				
first proton lost	5·13 ± 0·06	8·0	294, 286	4·10, 4·09
second proton lost	11·87 ± 0·07	14·1	298	4·10

[a] Spectrometrically determined. [b] The $\lambda_{max.}$ values of the species are too close for accurate pK_a determination. [c] In H_2O.

Experimental

5,6,7,8-*Tetrahydro*-N²-*methylnaphthalene*-1,2-*diamine*.—5,6,7,8-Tetrahydro-1-nitro-2-naphthylamine was prepared as described by Schroeter.[3] (N.B.: during vacuum-distillation of a 500 g. batch of crude mononitrotetralins a devastating explosion occurred.) The amine (2·46 g.) and dimethyl sulphate (1·78 g.) were heated on a steam-bath for 1 hr. The resulting oil was diluted with water and extracted with ether. After evaporation the residue was hydrogenated (3 atm.) over Raney nickel in ethanol. Distillation of the filtered solution gave the unstable oily *amine*, b. p. 140°/0·3 mm. (Found: C, 75·1; H, 9·2; N, 15·85. $C_{11}H_{16}N_2$ requires C, 74·95; H, 9·15; N, 15·9%).

6,7,8,9-*Tetrahydronaphth*[1,2]*imidazole*.—5,6,7,8-Tetrahydronaphthalene-1,2-diamine (1·0 g.) was refluxed with 90% formic acid (3 ml.) and 4N-hydrochloric acid (10 ml.). After 2 hr., the solvent was removed *in vacuo*, and the cooled solution poured on ice and adjusted to pH 8—9 with ammonia. Recrystallisation of the solid (1·2 g.) from 50% ethanol (30 parts) gave the *tetrahydronaphthimidazole*, m. p. 204—205° (Found: C, 76·75; H, 7·0; N, 16·3. $C_{11}H_{12}N_2$ requires C, 76·7; H, 7·0; N, 16·3%).

6,7,8,9-*Tetrahydro*-3-*methylnaphth*[1,2]*imidazole*.—5,6,7,8-Tetrahydro-*N*²-methylnaphthalene-1,2-diamine (1 g.) was treated with formic acid as above. The oil was removed with ether and distilled, giving the N-*methyl compound*, b. p. 114°/0·1 mm. (Found: C, 77·2; H, 7·9; N, 14·7. $C_{12}H_{14}N_2$ requires C, 77·4; H, 7·6; N, 15·0%). With anhydrous oxalic acid in ether, it gave an *oxalate* (from alcohol–ether), m. p. 172—173° (Found: C, 60·9; H, 5·85; N, 10·1. $C_{14}H_{16}N_2O_4$ requires C, 60·85; H, 5·85; N, 10·15%).

[4] Grippa and Maffei, *Gazzetta*, 1941, **71**, 418.
[5] Brown, *J.*, 1958, 1974.
[6] Albert, "Heterocyclic Chemistry," Athlone Press, London, 1959, p. 341.

6,7,8,9-*Tetrahydro*-2-*methylnaphth*[1,2]*imidazole*.—Prepared similarly to the parent compound, the *methyl* homologue (from 33% ethanol; 30 parts) had m. p. 188° (Found: C, 77·4; H, 7·7; N, 14·95. $C_{12}H_{14}N_2$ requires C, 77·4; H, 7·6; N, 15·0%).

6,7,8,9-*Tetrahydro*-2-*hydroxynaphth*[1,2]*imidazole*.—The diamine (1 g.) and urea (1 g.) were heated under nitrogen at 190°. After 5 min. the mass solidified and after a further 5 min. it was cooled and water (10 ml.) was added. The solid (1·2 g.) was recrystallised from 2-methoxyethanol (30 parts), to give the *hydroxy-derivative*, m. p. 307—308° (Found: C, 70·25; H, 6·3; N, 14·9. $C_{11}H_{12}N_2O$ requires C, 70·2; H, 6·4; N, 14·9%).

6,7,8,9-*Tetrahydro*-2-*mercaptonaphth*[1,2]*imidazole*.—Fusion of the diamine and thiourea as above, and recrystallisation from 2-methoxyethanol (70 parts) gave the *mercapto-derivative* (1 g.), m. p. 375° (Found: C, 64·5; H, 5·95; N, 13·5. $C_{11}H_{12}N_2S$ requires C, 64·7; H, 5·9; N, 13·7%).

6,7,8,9-*Tetrahydro*-2-*methylthionaphth*[1,2]*imidazole*.—The mercapto-derivative (0·5 g.), dissolved in hot N-sodium hydroxide (8 ml.), was diluted with water and cooled to 20°. Methyl iodide (0·38 g.) was added, and the mixture shaken for 1 hr., left overnight, and adjusted to pH 4. Recrystallisation from ethyl acetate gave the *methylthio-derivative* as prisms, m. p. 196—198° (Found: C, 65·9; H, 6·45; N, 12·85. $C_{12}H_{14}N_2S$ requires C, 66·0; H, 6·45; N, 12·85%).

2 - *Carboxymethylthio* - 6,7,8,9 - *tetrahydronaphth*[1,2]*imidazole*. — Tetrahydro - 2 - mercapto - naphthimidazole (0·75 g.), chloroacetic acid (0·35 g.), and N-sodium hydroxide (7·0 ml.) were heated at 100° for 2 hours. The cooled solution was diluted with water (3 ml.) and acidified to pH 3, and the solid dissolved in 5N-sodium carbonate and filtered from mercapto-compound. The product, liberated at pH 3, was recrystallised from 2-methoxyethanol (25 parts) to give the *carboxylic acid* (0·47 g.), m. p. 219° (Found: C, 59·3; H, 5·5; N, 10·55. $C_{13}H_{14}N_2O_2S$ requires C, 59·5; H, 5·4; N, 10·7%).

2 - *Chloro*-6,7,8,9 - *tetrahydronaphth*[1,2]*imidazole*. — Tetrahydro - 2 - hydroxynaphthimidazole (3·35 g.) was refluxed in phosphoryl chloride (50 ml.) for 6 hr. Volatile material was partially removed *in vacuo*, and the residue poured on ice (100 g.) and adjusted with dilute ammonia to pH 6. The precipitate was boiled for 5 min. with 10N-hydrochloric acid, and the residue re-extracted with fresh acid. The filtrates were adjusted to pH 6, and the solid (2·8 g.) was sublimed at 140°/0·1 mm., giving the *chloro-compound*, m. p. 175—178° (Found: C, 63·8; H, 5·4; N, 13·55; Cl, 17·25. $C_{11}H_{11}N_2Cl$ requires C, 63·9; H, 5·4; N, 13·55; Cl, 17·15%).

2-*Anilino*-6,7,8,9-*tetrahydronaphth*[1,2]*imidazole*.—The chloro-derivative (0·4 g.) and aniline (2 ml.) were refluxed under nitrogen for 2 hr. Steam-distillation removed residual aniline, and the solid (0·45 g.) was sublimed at 140°/0·1 mm. and recrystallised from 50% ethanol (25 parts). The *anilino-compound* had m. p. 198—199° (Found: C, 77·45; H, 6·45; N, 15·9. $C_{17}H_{17}N_3$ requires C, 77·5; H, 6·5; N, 15·95%).

2-*Dimethylamino*-6,7,8,9-*tetrahydronaphth*[1,2]*imidazole*.—The chloro-derivative (0·5 g.) and 30% aqueous dimethylamine (10 ml.) were heated at 175° for 5 hr. in the presence of copper powder. Volatile material was removed *in vacuo*, the residue dissolved in 2·5N-hydrochloric acid, and the filtrate adjusted to pH 8. Sublimation at 140°/0·1 mm. of the product (0·32 g.), and recrystallisation from 70% methanol (35 parts) gave the *dimethylamino-derivative*, m. p. 154—155° (Found: C, 72·5; H, 7·95; N, 19·5. $C_{13}H_{17}N_3$ requires C, 72·5; H, 7·95; N, 19·5%).

2-*Amino*-6,7,8,9-*tetrahydronaphth*[1,2]*imidazole*.—Cyanogen bromide [4] [from potassium cyanide (0·34 g.) in water (5 ml.) and bromine (0·73 g.)] in cold water (10 ml.) was added to a stirred suspension of the diamine (0·67 g.). Next day, the mixture was diluted with water and made alkaline with ammonia, and the solid was filtered off. Sublimation at 140°/0·1 mm. gave the amine as a very hygroscopic glass which sintered at 170° and decomposed at 178° (Found: C, 69·6; H, 7·2; N, 21·8. Calc. for $C_{11}H_{13}N_3$: C, 70·5; H, 7·0; N, 22·4%). The analysis quoted corresponds to a $\frac{1}{5}$ hydrate; other specimens were more hydrated, but all gave reasonable C : N ratios.

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